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**КОНКУРС
МОЛОДЫХ УЧЕНЫХ**



I МЕСТО

ПЛАЗМОЦИТОИДНЫЕ ДЕНДРИТНЫЕ КЛЕТКИ И ИХ РОЛЬ В ПАТОГЕНЕЗЕ И ИНТЕРФЕРОНОТЕРАПИИ ПРИ ХГС У ВЗРОСЛЫХ И ДЕТЕЙ

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Вирусные гепатиты являются одной из важнейших медико-социальных проблем во всем мире. Одно из первых мест среди них занимает вирусный гепатит С (ВГС), распространённость которого довольно высока как во всём мире, так и в Российской Федерации.

В настоящее время количество инфицированных ВГС, по разным данным, составляет 500-700 млн. человек. Число больных хроническим гепатитом С (ХГС) неуклонно растёт [1]. Хроническое течение ВГС является одной из основных причин формирования цирроза печени и гепатоцеллюлярной карциномы, унося ежегодно (по данным ВОЗ) около 1млн. человеческих жизней. В последние годы в течении и исходах ХГС всё большее значение придаётся характеру иммунного ответа организма.

Самые последние достижения в иммунологии проливают свет на некоторые уникальные особенности соотношения вируса ГС с врождёнными и приобретёнными иммунными реакциями, что позволяет глубже понять механизмы его патогенеза, формирования неблагоприятных исходов и ответа на противовирусную терапию (ПВТ).

С описанием в 1999 году плазмацитоидных дендритных клеток [2,3] (ПДК) и регулирующих их дифференцировку гена E2-2 [4,5] открыта новая страница в учении об иммунитете. Выяснилось, что эти уникальные клетки играют ключевую роль в иммунном ответе, обеспечивая взаимодействие врождённого (мощная выработка интерферона) и приобретённого (представление антигена) иммунитета [6]. В зрелом виде ПДК циркулируют в периферической крови, а также в очень малых количествах, присутствуют в костном мозге (до 1%), селезенке, тимусе, лимфоузлах (0,05-0,5%), практически отсутствуют в периферических тканях. Исключение составляют ткани печени [3], где их количество достигает 10%. Отличительными особенностями ПДК является немедленная (через 2-4 часа) выработка полного спектра интерферона (ИФН) I и III типа (λ), а также наличие специфических TLR-рецепторов (TLR7 и TLR9). В ПДК с помощью регулятора экспрессии ИФН I типа (IRF7) стремительно активируется распознавание TLR рецепторами вирусных нуклеиновых кислот [7], после чего начинается немедленная продукция ИФН I типа. Этому способствует то, что транскрипционные уровни IRF7 в ПДК выше, чем в обычных клетках [8].

Важнейшим событием явилось открытие в 2010 году в этих клетках при ХГС нового биологического механизма ИФН-образования. Его продемонстрировали в своём исследовании Takahashi et al. [9]: в инфицированном гепатоците, в котором

активно реплицируется вирус, ИФН-образование подавляется вирусными белками NS3 и NS4, при этом гепатоцит взаимодействует с ПДК, вызывая в ней массивную выработку ИФН, но не заражает саму клетку. Всё это вызывает огромный интерес к изучению ПДК как новой популяции иммунных клеток, особенно при ХГС, однако изучение это делает в мире первые шаги [10-15] и касается только взрослых пациентов. Сообщения об исследовании ПДК у детей, больных ХГС, в мировой литературе в настоящее время отсутствуют.

Цель

Целью нашего исследования было установление роли ПДК в патогенезе ХГС, а также влияние ИФН-терапии на количество и функциональное состояние ПДК у взрослых и детей.

Пациенты и методы

Исследование проводилось на базе ЦНИИ эпидемиологии Роспотребнадзора в период с октября 2010 по октябрь 2012 года.

Нами обследован 161 человек: 133 пациента в различные фазы ХГС (58 детей и 75 взрослых) вне зависимости от пола, возраста, уровня вирусной нагрузки, показателей трансаминаз, стадии фиброза (цирроза), 28 человек - здоровые лица (16 детей и 12 взрослых). При постановке диагноза ХГС учитывались: обнаружение маркёров HCV-инфекции в течение 6 месяцев и более, показатели трансаминаз, наличие или отсутствие вирусной нагрузки, стадия фиброза (цирроза) печени (результаты пункционной биопсии печени или фиброэластографии).

Помимо рутинного клинико-лабораторного обследования (анамнез, физикальные данные, клинический анализ крови и мочи, биохимическое исследование, УЗИ брюшной полости и эластография печени на аппарате «Фиброскан» т.д.).

Методами, использованными в данном исследовании, являются:

1. Определение относительного (% содержание клеток в выборке из 100.000 лимфоцитов) и абсолютного (число клеток в 1мкл крови) количества ПДК в крови методом проточной цитофлуориметрии на приборе EPICS XL компании Beckman Coulter, с помощью моноклональных антител к специфическим маркёрам ПДК (CD303 и CD123).

2. Определение ИФН-продуцирующей функции ПДК: выработ-

ка ИФН в пг/мл в супернатанте клеток методом ИФА ELISA, которому предшествует клеточная инкубация (24 часа в CO2 инкубаторе) со специфическим стимулятором клеточного роста-синтетическим олигонуклеотидом, который содержит неметилированный CpG динуклеотид в определённой последовательности и стимулирует сугубо TLR9 рецепторы в ПДК (ODN2216) и ИЛ-3, который является стимулятором дифференцировки мультипотентных гемопоэтических стволовых клеток.

Статистическую обработку материала проводили с помощью компьютерной программы GraphPad Prism 5. Определяли следующие статистические показатели: среднее значение, ошибка среднего, достоверность различий (p), использовался t-критерий Стьюдента, критерий Манна-Уитни, F-критерий Фишера, а также дискриминантный многофакторный анализ полученных данных.

Результаты исследования и их обсуждение.

Для установления нормальных показателей ПДК соответствующие исследования были проведены у здоровых детей (N=16) и взрослых (N=12). Оказалось, что как абсолютное, так и процентное содержание ПДК достоверно ниже у взрослых (10,2±1,7 клеток в 1 мкл периферической крови, 0,27±0,04% клеток при выборке из 100000 лимфоцитов) и у детей (17,3±1,4 и 0,38±0,03 соответственно, p<0,05).

Функциональное состояние ПДК мы оценивали по интенсивности выработки ими ИФН в ответ на специфическую стимуляцию. По нашим данным, в здоровом организме как взрослого, так и ребёнка степень выработки ИФН в ПДК в 100% случаев ниже уровня детекции используемого нами метода (<3пг/мл). Учитывая эти результаты, мы предположили наличие в крови здоровых людей неких ингибиторов, блокирующих выработку ИФН в ПДК. Для подтверждения данного предположения мы провели дополнительное исследование, суть которого заключалась в том, чтобы ПДК отмыть от плазмы, в которой эти ингибиторы предположительно могли содержаться. Для этого мононуклеарные лейкоциты периферической крови (МЛПК) выделяли из стабилизированной гепарином (25 ед/мл) периферической крови у 4 здоровых доноров (2 детей и 2 взрослых). Кровь, разведенную в 2 раза средой RPMI 1640, центрифугировали при 400g в течение 30 мин в градиенте плотности фиколл-ПАК. Мононуклеарные лейкоциты, образовавшие интерфазное кольцо, собирали и трехкратно отмывали в среде RPMI 1640. После каждой отмывки в 10-кратном объёме среды клетки осаждали центрифугированием при 200g. Затем «отмытые» клетки инкубировали при тех же условиях, что и не «отмытые», возбуждая выработку ИФН в ПДК специфичными для них стимуляторами (смотри раздел методы).

Данные, полученные при дополнительном исследовании (у взрослых выработка ИФН в ПДК резко возросла до 3337±1760пг/мл, у детей - 5227±2422пг/мл), подтверждают наше предположение о наличии в периферической крови здоровых лиц пока неизвестных нам ингибиторов. Предположительный биологический смысл обнаруженного нами феномена возможно заключается в том, что он защищает эти важнейшие иммунные клетки от «случайных», недостаточно биологически мотивированных воздействий.

Сравнение количественных показателей ПДК у больных ХГС и здоровых взрослых выявило достоверное снижение этих показателей в группе больных пациентов (абсолютное количество ПДК - 8,3±0,8 против 10,2±1,7 клеток в 1 мкл периферической крови, относительное - 0,18±0,01 против 0,27±0,04% кл., p<0,05). У детей, больных ХГС, абсолютное и относительное количество ПДК также достоверно ниже, чем в группе здоровых (абсолютное количество ПДК - 13,9±1,0 клеток в 1 мкл крови, относительное - 0,26±0,01 % кл., p<0,05), против 17,3±1,8 и 0,38±0,03 соответственно у здоровых детей. При одинаковой направленности этих изменений (снижение уровня ПДК у больных ХГС как детей, так и взрослых), исследуемые показатели достоверно сильнее снижаются у взрослых, чем у детей. Снижение числа ПДК, скорее всего является результатом повышения миграции клеток из периферической крови в лимфоидные органы или ткани, как это было описано для плазмацитоидных дендритных клеток при ВИЧ-инфекции [16, 17, 18], что приводит к недостаточности иммунного ответа при ХГС.

Функциональное состояние ПДК (выработка ИФН) у здоровых взрослых и детей, как указывалось, ниже уровня детекции используемого нами метода (3пг/мл). У больных ХГС этот показатель достоверно выше, как у взрослых пациентов (321±141,2пг/мл), так и у детей (113,3±21,7пг/мл), оставаясь более высоким у взрослых. У детей более низкие показатели выработки ИФН, обладающего антипролиферативным (антиростовым) действием вероятно обусловлены потребностями периода роста и развития.

Очень важным фактом представляется выявленная нами достоверная связь между выработкой ИФН в ПДК и уровнем вирусной нагрузки у взрослых и детей, больных ХГС. У взрослых пациентов при низком уровне вирусной нагрузки (до 10⁴ коп/мл) выработка ИФН в ПДК составляет 490,6±261,9 пг/мл, что в 3 раза выше, чем в группе с высокой вирусной нагрузкой (10⁵ коп/мл и более) - 147,1±59,8 пг/мл (p<0,05). У детей соотношение показателей выработки ИФН в ПДК и уровня вирусной нагрузки (153,5±38,1пг/мл и 75,8±20,7пг/мл соответственно) имеет тот же характер, что и у взрослых.

Таким образом, нами показано, что функциональное состояние ПДК может обуславливать степень виремии при ХГС: чем ниже способность ПДК вырабатывать ИФН, тем выше виремия. Полученные нами результаты говорят о тесной связи функционального состояния ПДК и уровня вирусной нагрузки.

Анализируя связь между функциональным состоянием ПДК и степенью цитолиза, удалось показать, что у взрослых больных ХГС при нормальном уровне трансаминаз выработка ИФН в ПДК достоверно ниже (132,8±42,7пг/мл), нежели у больных с повышенными показателями трансаминаз (314,9±137,7пг/мл). У детей достоверных различий между сходными группами нами получено не было. Возможно, причина в том, что связь с цитолизом опосредована виремией, степень которой у детей чаще чем у взрослых не соответствует уровню трансаминаз.

В работе продемонстрирована глубокая взаимосвязь показателей ПДК и степени фиброза. Так, при продвинутом фиброзе

(4 балла по шкале METAVIR) количественные показатели ПДК (абсолютное и процентное число клеток) максимально снижены в отличие от пациентов с минимальным уровнем фиброза ($3,9 \pm 0,9$ кл/мкл против $8,5 \pm 0,9$ кл/мкл и $0,12 \pm 0,04$ к $0,22 \pm 0,02\%$ клеток соответственно $p < 0,05$). Зависимость показателей ПДК от степени фиброза у детей показать не удалось, в связи с отсутствием группы детей с продвинутым фиброзом.

Таким образом, все представленные нами данные о закономерной связи параметров ПДК с основными показателями, характеризующими течение и исходы ХГС, говорят о важной роли, которую играют ПДК в патогенезе этой инфекции.

Переходя к рассмотрению связи интерферонотерапии (ИФН-терапия) с показателями ПДК, зафиксированы снижение количественных параметров ПДК и резкая стимуляция выработки ими ИФН. Количественные показатели ПДК у больных, находящихся на противовирусной терапии (ПВТ), снижены ($3,7 \pm 0,5$ кл/мкл, $0,14 \pm 0,02\%$ клеток против $9,2 \pm 0,9$ кл/мкл, $0,22 \pm 0,02\%$ соответственно, $p < 0,05$). У детей нами получены сходные данные ($7,1 \pm 1,1$, $0,19 \pm 0,03$ против $15,4 \pm 1,2$ кл/мкл, $0,3 \pm 0,02\%$ клеток, $p < 0,05$).

Продемонстрировано влияние ИФН-терапии на выработку ИФН в ПДК. Так, у взрослых больных, получавших ПВТ и обследованных на 12ой неделе её проведения, отмечается резкий подъём выработки ИФН в ПДК ($1887 \pm 330,9$ пг/мл) по сравнению с пациентами, никогда её не получавшими ($453,6 \pm 254,2$ пг/мл, $p < 0,05$). У детей уровень выработки ИФН в ПДК так же резко повышается, однако не достигает столь высоких цифр, как у взрослых ($492,6 \pm 228,8$ пг/мл против $134,4 \pm 27,17$ пг/мл соответственно), а абсолютное и процентное содержание клеток выше, чем у взрослых пациентов ($p < 0,05$).

Для анализа возможной связи показателей ПДК в ходе лечения с ответом на ПВТ были отобраны 2 группы пациентов:

1 группа - пациенты, которые находились на комплексной ПВТ и ответили на неё стойким прекращением репликации вируса как на терапии, так и после её окончания ($N=26$), 2 группа - пациенты, которые также получали ПВТ, но не ответили стойким прекращением репликации вируса ни на фоне проводимого лечения, ни после его окончания ($N=11$).

Выработка ИФН в 1гр. составила $1558 \pm 277,5$ пг/мл. во 2гр. - $69,11 \pm 54,33$ пг/мл. Данные, полученные в группах сравнения, высоко достоверны ($p < 0,001$). Таким образом, было показано, что положительный ответ на ПВТ тесно связан с уровнем ИФН-образования в ПДК в ходе лечения: чем выше уровень выработки ИФН, тем вероятнее благоприятный ответ на ПВТ. Наши результаты указывают на взаимозависимость стимуляции ИФН-образования в ПДК и ответа на ПВТ.

В связи с этим можно утверждать, что уровень подъёма ИФН-генеза в ПДК на 12ой неделе лечения может служить надёжным прогностическим тестом эффективности проводимой терапии. Степень повышения уровня ИФН в ПДК на 12ой неделе терапии в $2,6 \times 10^2$ раз у взрослых и $1,2 \times 10^2$ у детей позволяет предска-

зать стойкий вирусологический ответ с высокой достоверностью (вероятность прогноза - 96%). На основании полученных данных подана заявка на патент (рег. № 2012157606).

Всесторонний анализ состояния ИФН-генеза в ПДК в связи с ИФН-терапией выявил интересный факт, что у не получающих лечение взрослых пациентов с нерепликативным ХГС состояние авиремии достигается максимальным напряжением ИФН-генеза в ПДК (1620 ± 1386 пг/мл). Напротив, после ИФН-терапии, при благоприятном ответе (достигнута авиремия) происходит полная нормализация показателей ПДК как в отношении ИФН-генеза ($56,4 \pm 32,2$ пг/мл.- уровень, не отличимый от значения у здоровых), так и восстановление нормального абсолютного количества клеток ($7,3 \pm 1,5$ кл/мкл к $10,2 \pm 1,7$ кл/мкл у здоровых, $p < 0,005$).

Все представленные в этом исследовании данные получены впервые.

Выводы

1. Обнаруженная закономерная взаимосвязь количества и функции ПДК с вирусной нагрузкой, степенью цитолиза и фиброза при ХГС у взрослых и детей указывает на важное участие ПДК в патогенезе этой инфекции, её течении и исходах.

2. ИФН-терапия существенно влияет на показатели ПДК, резко стимулируя ИФН-генез в ПДК в процессе терапии.

3. Ответ на ИФН-терапию тесно связан с изменениями количества и функции ПДК. Степень повышения уровня ИФН в ПДК на 12ой неделе терапии может служить надёжным прогностическим тестом ответа на неё (заявка на патент, рег. № 2012157606).

4. ИФН-терапия при ХГС является не заместительной, а патогенетически обоснованной, нормализующей при благоприятном ответе количественные и функциональные параметры таких ключевых популяций иммуноцитов, как ПДК.

5. Состояние ПДК у детей, как здоровых, так и больных ХГС, по многим показателям существенно отличается от таковых у взрослых. Главной особенностью является значительно более высокое содержание этих клеток (как абсолютное, так и процентное по отношению к общему числу лимфоцитов) в норме, при ХГС без лечения и в ответ на ИФН-терапию, что возможно лежит в основе более благоприятного течения и результатов ПВТ у детей.

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II МЕСТО

КЛИНИКО-ЛАБОРАТОРНАЯ ОЦЕНКА ТЕЧЕНИЯ
И ПРОГНОЗИРОВАНИЕ ИСХОДОВ ТОКСИЧЕСКИХ ГЕПАТИТОВ

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Цель

провести клинико-лабораторную оценку течения и прогнозирование исходов токсических гепатитов, вызванных употреблением суррогатов алкоголя.

Материалы и методы

Материалом исследования послужил ретроспективный анализ клинико-лабораторных данных 54 пациентов (мужчин - 35, женщин - 19, средний возраст 43 (29-49) лет), поступивших в терапевтическое отделение МБУЗ ГКБ № 9 г. Челябинска за период 2006-2007гг. с однотипной клинической картиной токсического холестатического гепатита после употребления суррогатов алкоголя (спирт для наружного применения «Можжевельный»). В 2012 г. проведена оценка отдаленных результатов. Статистическая обработка проведена с помощью пакетов программ Statistica-6, Medcalc Version 11.5.0.0.

Результаты исследования.

По клиническим данным, на момент обращения в 100% случаев отмечались интенсивная желтуха, диспепсия, астенический синдром, в 60% случаев – кожный зуд, в 33% - боли в правом подреберье, гепатомегалия, в 12% - лихорадка, артериальная гипотензия, брадикардия. По биохимическим данным - в 100% случаев наблюдалась гипербилирубинемия (2 - 24 нормы) за счет пря-

мой фракции, повышение уровня ГГТП (4,5 -80 норм), щелочной фосфатазы(1,5 -5 норм), в 80 % случаев - гиперхолестеринемия до 2-3 норм, повышение уровня АСТ(3-32 нормы), АЛТ (4-25 норм). Желтуха сохранялась от 6 до 12 месяцев с достоверным снижением уровня общего и прямого билирубина, без значимой динамики ГГТП, щелочной фосфатазы и холестерина. В течение первого месяца умерло 10 пациентов(18%) вследствие печеночной недостаточности, за последующий анализируемый период - 7 больных(13%). По результатам логистической регрессии ($\chi^2=43,9$, $p<0,001$), факторами, ассоциированными с летальным исходом, явились уровень лейкоцитов в общем анализе крови (ОШ=4,8, 95% ДИ 1,12-20,55, $p=0,03$) и уровень креатинина в сыворотке крови (ОШ=1,1, 95% ДИ 0,99-1,22, $p=0,09$). Прогностическая ценность модели - 93,3%. Значимыми в отношении летального исхода по данным ROC-анализа стали: уровень лейкоцитов в общем анализе крови выше $9,7 \times 10^9/\text{л}$ (специфичность 100%, чувствительность – 71,3%, площадь под ROC-кривой – 0,93, $p<0,001$) и уровень прямого билирубина выше 109 мкмоль/л (чувствительность - 100%, специфичность – 60,3%, площадь под ROC-кривой – 0,72, $p=0,001$).

Выводы.

Токсические гепатиты, вызванные суррогатами алкоголя, имеют тяжелое течение, прогноз исходов требует применения собственной прогностической модели.

III МЕСТО

РИСК РАЗВИТИЯ И ПРЕДИКТОРЫ ДЕКОМПЕНСАЦИИ,
ГЦК И ПЕЧЕНОЧНО-СВЯЗАННОЙ СМЕРТНОСТИ У БОЛЬНЫХ ХРОНИЧЕСКОЙ HDV-ИНФЕКЦИЕЙ:
ДАННЫЕ 10-ЛЕТНЕГО НАБЛЮДЕНИЯ
В СПЕЦИАЛИЗИРОВАННОМ ГЕПАТОЛОГИЧЕСКОМ ОТДЕЛЕНИИ

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Хронический гепатит D (ХГД) – одно из наиболее тяжелых и быстро прогрессирующих заболеваний печени с высоким риском развития цирроза печени (ЦП) и гепатоцеллюлярной карциномы (ГЦК). HDV-инфекция, вызывая поражение печени с наиболее тяжелым прогнозом, одновременно является заболеванием с наименее изученным естественным течением и возможностями эффективной терапии.

Цель исследования

Цель исследования оценить риск развития и определить достоверные предикторы декомпенсации печеночного процесса, ГЦК и печеночно-связанной смертности у больных хронической HDV-инфекцией.

Материалы и методы

В исследование были включены больные, наблюдавшиеся в клинике нефрологии, терапии и профессиональных болезней им. Е.М.Тареева Первого МГМУ им. И.М.Сеченова в период с 2002 г. по 2011 г. Критерием включения в исследование было наличие в сыворотке крови маркеров гепатита дельта (anti-D и РНК HDV) у HBsAg (+) больных. Проведено изучение анамнеза, физическое обследование, клинические анализы крови и мочи, биохимические (АСТ, АЛТ, ГГТ, ЩФ, общий белок с электрофорезом белков, билирубин, холинэстераза, креатинин, азот мочевины), коагулограмма и иммунологическое исследование сыворотки крови (иммуноглобулины, альфа-фетопротеин, антинуклеарные антигены, криоглобулины). Маркеры HBV, HCV и HDV в сыворотке крови определялись методом иммуноферментного анализа (ИФА), ДНК HBV, РНК HCV и РНК HDV – методом полимеразной цепной реакции. У всех больных выполнены ультразвуковое исследование брюшной полости (при необходимости – мультиспиральная КТ или МРТ с контрастным усилением), эзофагогастродуоденоскопия по показаниям. 31 (30,4%) больным проведена оценка степени фиброза печени методом биопсии и эластометрией (Fibroscan, Echosens, Paris, France). Диагноз цирроза печени ставился на основании биопсии печени/эластометрии и/или клинико-лабораторных методов исследования.

Статистические расчеты проводились с помощью пакета SPSS v.17 (IBM Corporation, New York, USA). Достоверность различий оценивалась с помощью U-теста Манна-Уитни для независимых

выборок в случае ненормального распределения последних. Для количественных признаков в случае нормального распределения достоверность различий оценивалась с помощью t – критерия. Статистическая значимость различий качественных признаков в сравниваемых группах оценивалась при помощи критерия χ^2 , учитывались значения $p \leq 0,05$. При значениях p в пределах от 0,05 до 0,15, результат рассматривался как тенденция к различию. Для оценки значимости отдельных факторов на прогноз заболевания и выживаемость применялся многофакторный логистический регрессионный анализ. При оценке уравнений регрессии использовался метод обратного пошагового включения предикторов, который ранжирует признаки в соответствии с их вкладом в модель. Оценка выживаемости, риска развития декомпенсации и ГЦК проводилась с помощью теста по Каплану-Мейеру.

Результаты

Из 495 HBsAg (+) больных, наблюдавшихся в клинике в указанный период, 102 (20,6%) пациента (средний возраст 39 лет, мужчин 58%) имели маркеры HDV-инфекции.

У 65 (63,7%) пациентов на момент диагностики HDV-инфекции имели место гистологические и/или клинические признаки цирроза печени. При этом, 39 (38%) больных имели компенсированный ЦП, 26 (25,5%) были на стадии декомпенсации. У 2 пациентов HDV-инфекция была диагностирована на стадии ГЦК.

Декомпенсация ЦП

У 42 больных (средний возраст 44,3 лет, мужчин 47,6%) с компенсированным ЦП в течение наблюдения было отмечено развитие декомпенсации печеночного процесса. Средний промежуток времени между диагностированием ЦП и развитием первого эпизода декомпенсации составлял $45 \pm 33,1$ месяцев. Первым признаком декомпенсации наиболее часто являлся асцит (32 пациента, 76,2%), менее часто - желтуха (4 пациента, 9,5%), ЖКК (3 пациента, 7,1%) и ПЭ (3 пациента, 7,1%).

По результатам множественного логистического регрессионного анализа достоверными предикторами развития декомпенсации являлись (в порядке убывания значимости): гипоальбуминемия, гипер- γ -глобулинемия и гипербилирубинемия (таблица 1).

Таблица 1. Предикторы декомпенсации

ПРЕДИКТОРЫ	B	SIG.	EXP(B)	95% ДИ ДЛЯ EXP (B)	
				НИЖНЯЯ	ВЕРХНЯЯ
АЛБУМИН	-0,451	,011*	0,637	0,450	0,902
Г-ГЛОБУЛИНЫ	0,139	,069*	1,150	0,989	1,336
ОБЩИЙ БИЛИРУБИН	0,071	,106**	1,074	0,985	1,171

*- статистически значимое различие, ** - тенденция к различию

Годичный, 2-летний и 5-летний риск развития декомпенсации у больных с нормальным/низким уровнем альбумина равнялся 0%/15%, 5%/20% и 22%/50% соответственно (рисунок 1).

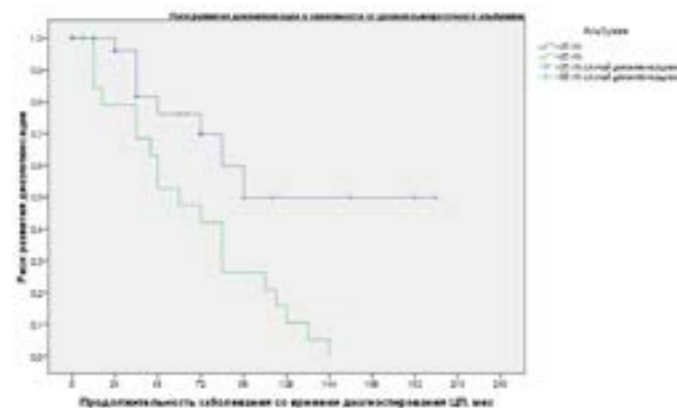


Рисунок 1. Риск развития декомпенсации в зависимости от уровня альбумина

ГЦК

В течение наблюдения у 8 (7.8%) больных (средний возраст 50.8 лет, мужчин 50%) было отмечено развитие ГЦК. Средняя длительность заболевания на момент диагностирования ГЦК равнялась 337±113.7 месяцам. Достоверными предикторами развития ГЦК являлись (в порядке убывания значимости): пожилой возраст, повышение уровней щелочной фосфатазы и АФП (таблица 2).

Таблица 2. Предикторы развития ГЦК

ПРЕДИКТОРЫ	B	SIG.	EXP(B)	95% ДИ ДЛЯ EXP (B)	
				НИЖНЯЯ	ВЕРХНЯЯ
ПОЖИЛОЙ ВОЗРАСТ	0,082	,058**	1,085	0,997	1,181
ЩФ	0,006	,070**	1,006	0,999	1,013
АФП	0,017	,180**	1,017	0,992	1,042

*- статистически значимое различие, ** - тенденция к различию

Выживаемость

В течение наблюдения скончались 18 (17.6%) больных (средний возраст 44.1 лет, мужчин 72.2%). Причины смерти: печеночная недостаточность с развитием комы (9 пациентов, 50%), развитие ГЦК (6 пациента, 33.3%), 1 пациентка скончалась от ЖКК, 1 пациентка - после ОТП и 1 больной скончался с диагнозом пневмонии.

Предикторами печеночно-связанной смертности были (в порядке убывания значимости): гипербилирубинемия и низкий протромбиновый индекс (таблица 3, рисунок 2).

Таблица 3. Предикторы печеночно-связанной смертности

ПРЕДИКТОРЫ	B	SIG.	EXP(B)	95% ДИ ДЛЯ EXP (B)	
				НИЖНЯЯ	ВЕРХНЯЯ
ОБЩИЙ БИЛИРУБИН	0,062	,007*	1,064	1,018	1,114
ПРОТРОМБИНОВЫЙ ИНДЕКС	-0,138	,075**	0,871	0,749	1,014

*- статистически значимое различие, ** - тенденция к различию

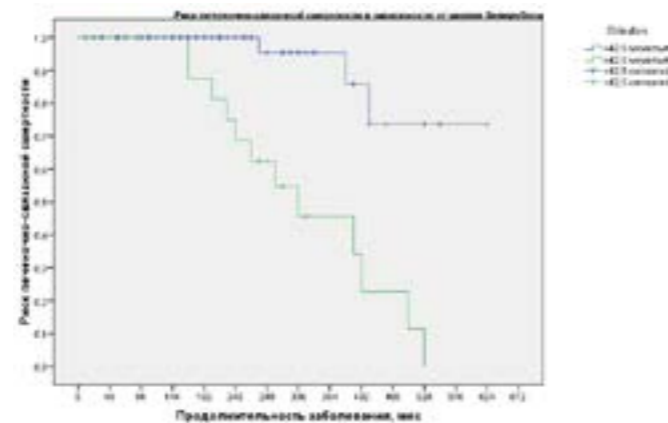


Рисунок 2. Риск печеночно-связанной смертности в зависимости от уровня билирубина

Заключение

Маркеры HDV выявлены у 20.6% пациентов, инфицированных HBV. HDV-инфекция характеризуется высокой активностью, стадия цирроза печени выявляется почти в 2/3 случаев при первом диагностировании больных. Достоверными предикторами декомпенсации печеночного процесса являются гипоальбуминемия, гипер-γ-глобулинемия и гипербилирубинемия. Наиболее частым признаком декомпенсации у больных ХГД был асцит. 5-летний риск декомпенсации у больных ХГД с гипоальбуминемией составляет 50%. У 7.8% больных отмечено развитие ГЦК, независимыми предикторами которой являлись пожилой возраст, повышение уровней щелочной фосфатазы и АФП. В период наблюдения скончались 17.8% больных, наиболее частыми причинами печеночно-связанной смерти были развитие печеночной недостаточности и ГЦК. Предикторами печеночно-связанной смертности являются гипербилирубинемия и низкий протромбиновый индекс.

**АЛКОГОЛЬНАЯ
БОЛЕЗНЬ ПЕЧЕНИ**

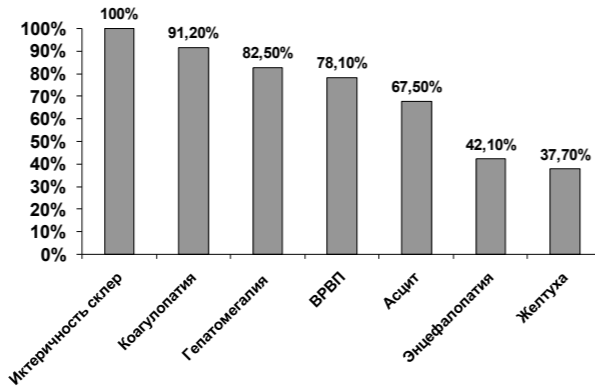


ВОЗМОЖНОСТИ КЛИНИЧЕСКОЙ ДИАГНОСТИКИ
АЛКОГОЛЬНОГО ЦИРРОЗА ПЕЧЕНИПавлов А.И.¹, Буверов А.О.², Белякин С.А.¹¹ФБУ «3 ЦВКГ им. А.А. Вишневского Минобороны России»,
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В процессе исследования наблюдались 163 больных циррозом печени, проходивших стационарное лечение в 3 ЦВКГ им. А.А. Вишневского с 2007 г. по 2012 г. – 32 (19,6%) женщины и 131 (80,4%) мужчина. Средний возраст пациентов составил 52,7±0,7 (24-78) лет. Диагноз цирроза печени был подтвержден согласно современным стандартам. По степени нарушения функции гепатоцитов по классификации Чайльда-Пью преобладали пациенты класса В.

Во время сбора анамнеза с целью подтверждения алкогольной этиологии заболевания более 27% больных при первом общении с врачом подтвердили своё злоупотребление алкоголем. Проводились также опрос родственников и изучение медицинской документации на предыдущих этапах оказания медицинской помощи. В процессе последующего общения почти все пациенты признали факт чрезмерного и систематического употребления алкоголя. Кроме того, практически у всех обнаруживались общеклинические признаки алкогольной интоксикации – контрактура Дюпюитрена, гинекомастия у мужчин, выраженная гепатомегалия, телеангиэктазии, поражение других органов-мишеней.

ЧАСТОТА ВЫЯВЛЕНИЯ ПРИЗНАКОВ ЦИРРОЗА



У всех пациентов имелась иктеричность склер, у 61 (37,7%) больных определялась желтушность кожных покровов. Асцит выявлялся у 110 (67,5%) человек, варикозно расширенные вены пищевода и желудка (БРВП) – у 128 (78,1%) больных. Печёночная энцефалопатия диагностирована у 69 (42,1%) исследуемых. Гепатомегалия определялась у 134 (82,5%) человек. Признаки коагулопатии были выявлены у 149 (91,2%) пациентов.

Вывод. Рутинные клинические методы исследования позволяют с высокой степенью достоверности определить алкогольную этиологию цирроза печени. Лабораторные и инструментальные методики подтверждают цирротическую стадию заболевания, уточняют его тяжесть и наличие осложнений.

ИСХОДЫ ТОКСИЧЕСКИХ ГЕПАТИТОВ,
ВЫЗВАННЫХ СУРРОГАТАМИ АЛКОГОЛЯПирогова И.Ю., Пономарева И.Ю., Силицын С.П., Самохина Е.П.,
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ГБОУ ВПО ЧелГМА Минздрава России, Челябинск, Россия

В Челябинской области в 2006-2007гг. зарегистрировано 3000 больных токсическими гепатитами после употребления суррогатов алкоголя. В течение 6 месяцев от начала заболевания вследствие печеночной недостаточности умерло 244 человека(8%). Цель исследования. Оценить отдаленные результаты токсических гепатитов после употребления суррогата алкоголя (спирт для наружного применения «Можжевельный») с определением предикторов летального исхода. Материалы и методы. Проведен ретроспективный анализ клинико-лабораторных данных и выживаемости 73 пациентов (мужчин 49, женщин 24, средний возраст 44 (32-49) лет), поступивших на стационарное лечение в 2006-2007гг. Статистическая обработка материала проведена с помощью пакета программ Statistica-6, Medcalc с применением логистической регрессии для прогнозирования течения заболевания, построением ROC-кривых для выявления диагностически значимых тестов. Для оценки прогноза заболевания определены индекс MELD и Hu's law, а также R (соотношения гепатоцеллюлярного и/или холестатического поражения). Результаты исследования. У всех пациентов наблюдалась клиника тяжелого токсического гепатита с выраженным синдромом холестаза, резистентного к терапии. В течение первого месяца заболевания по причине печеночной недостаточности умерло 16 пациентов(20%), за последующий период-13 больных(19%). Расчет индекса MELD и Hu's law показал их неинформативность у данной группы больных, индекс R в 78% случаев указывал на смешанное поражение и не влиял на прогноз. Разработана собственная прогностическая модель выживаемости пациентов: уровень лейкоцитов в общем анализе крови (ОШ=4,8, 95% ДИ 1,12-20,55, p=0,03) и уровень креатинина (ОШ=1,1, 95% ДИ 0,99=1,22, p=0,09) - прогностическая ценность модели - 93,3%. Значимыми для прогноза оказались уровень прямого билирубина (AUROC 0,79, ДИ 0,58-0,83, p=0,001) и лейкоцитов (AUROC 0,93, ДИ 0,83-0,98, p<0,001). Выводы. Согласно полученным данным, наиболее значимыми предикторами летального исхода явились выраженность воспалительного ответа, гипербилирубинемия и гепаторенальный синдром.

ПСИХОЛОГИЧЕСКИЕ ОСОБЕННОСТИ У ПАЦИЕНТОВ
С ЖИРОВОЙ БОЛЕЗНЬЮ ПЕЧЕНИ РАЗЛИЧНОЙ ЭТИОЛОГИИ

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Цель работы. Комплексное изучение психологических особенностей у пациентов с жировой болезнью печени алкогольной и неалкогольной этиологии.

Материалы и методы. Обследовано 59 пациентов с жировой болезнью печени алкогольной этиологии (АЖБП), 60 пациентов с жировой болезнью печени неалкогольной этиологии (НАЖБП), контрольную группу составили 32 здоровых волонтера аналогичного пола и возраста. Диагноз стеатогепатита был подтвержден клинически и морфологически. Психологический статус оценивался с помощью Сокращенного Многофакторного Опросника Личности и теста Айзенка. Каждый больной подписал «Информированное согласие» на участие в исследованиях. Различия между параметрами сравнения считались статистически различными при p<0,05.

Результаты и обсуждение. Психологический статус пациентов с жировой болезнью печени алкогольной и неалкогольной этиологии не отличался статистически значимо между исследуемыми группами, но отличался от контроля (p<0,05). В контрольной группе результаты исследования были ниже, чем в группах со стеатогепатитом по шкалам: первой «невротический сверхконтроль или ипохондрия», четвертой «импульсивность или психопатия», седьмой «реактивная тревожность или психастения», восьмой «индивидуалистичность» и девятой «оптимистичность». Результаты по тесту Айзенка были следующими – уровень нейротизма был самый высокий у пациентов с НАЖБП (p<0,05 в сравнение с контролем и АЖБП), при этом уровень экстраверсии был самым высоким у пациентов с АЖБП (p<0,05 в сравнение с контролем и НАЖБП).

Выводы: Нами был определен психологический портрет пациентов обследуемых групп – эмоционально лабильный, склонный к ипохондрии, самоуверенный, с высоким уровнем тревожности и нейротизма тип личности. Более акцентированы данные психологические особенности у пациентов с АЖБП.

ИММУНОЛОГИЧЕСКИЙ СТАТУС У БОЛЬНЫХ ХРОНИЧЕСКИМИ
АЛКОГОЛЬНЫМИ И АЛКОГОЛЬНО-ВИРУСНЫМИ ГЕПАТИТАМИ
НА СЕВЕРЕ

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Цель: Оценить иммунологический статус больных хроническими алкогольными и алкогольно-вирусными гепатитами на Севере.

Материалы и методы: Анализ иммунологических показателей проводили в группах больных алкогольным хроническим гепатитом (АХГ) – 56, алкогольно-вирусным хроническим гепатитом (АВХГ) 72 и 30 пациентов контрольной группе доноров.

Результаты: При АХГ выявлены более глубокие изменения со стороны показателей как клеточного, так и гуморального звеньев иммунитета. В группе АХГ наблюдалась тенденция к уменьшению абсолютного количества лимфоцитов (P<0,001). Количество всех субпопуляций Т-лимфоцитов при АХГ достоверно изменялось по отношению к контрольной группе (P<0,001) за исключением относительного содержания Т-супрессоров, число которых достоверно уменьшается лишь по сравнению с группой доноров (P<0,05). Показатели гуморального иммунитета характеризовались повышением концентрации IgA у больных АХГ (P<0,05) по сравнению с контрольной группой и группой АВХГ. Содержание IgG в сыворотке крови в группе больных АВХГ увеличивалось незначительно (P>0,05) по отношению к контролю. Концентрация ЦИК в сыворотке крови больных АХГ увеличивалась значительно по сравнению с контрольной группой (P<0,001) и была достоверно выше, чем аналогичные показатели в группе больных АВХГ. У больных АВХГ выявлена тенденция к снижению общего числа лимфоцитов как с наличием, так и с отсутствием активности (P<0,05). Уменьшение количества Т-лимфоцитов и их субпопуляций связано с токсическим действием алкоголя на уже поврежденные HBV клетки печени.

Дефицит Т-хелперов, возможно, связан с поражением костного мозга и других кровяных органов HBV, а также действием алкоголя и его метаболитов на эти органы

Выводы: При АХГ и АВХГ степень выраженности иммунологических нарушений зависит от активности заболевания.

АУТОИММУННЫЕ ЗАБОЛЕВАНИЯ ПЕЧЕНИ



ДИАГНОСТИЧЕСКОЕ ЗНАЧЕНИЕ СИСТЕМНЫХ ПРОЯВЛЕНИЙ ПЕРВИЧНОГО СКЛЕРОЗИРУЮЩЕГО ХОЛАНГИТА**АЛЕКСАНДРОВА Е.А., БУРНЕВИЧ Э.З., АРИОН Е.А.***Клиника нефрологии, внутренних и профессиональных болезней им. Е.М.Тареева, ГБОУ ВПО Первый МГМУ им. И.М.Сеченова, г. Москва, Российская Федерация*

Введение. Первичный склерозирующий холангит (ПСХ) – хроническое медленно прогрессирующее заболевание печени, характеризующееся негнойным деструктивным воспалением и фиброзом желчных протоков, что приводит к развитию вторичного билиарного цирроза печени.

Цель исследования. Изучение распространенности аутоиммунных заболеваний у больных ПСХ.

Материал и методы. 93 больных ПСХ, наблюдавшихся в Клинике нефрологии, внутренних и профессиональных болезней им. Е.М.Тареева. В группе было 47 мужчин и 46 женщин, средний возраст 32,6±11,1 лет, средняя продолжительность заболевания 1,9±2,8 лет. Материалами исследования являлись архивные данные из историй болезни и амбулаторных карт, а также медицинская документация проспективно прослеженных больных.

Результаты. Аутоиммунные заболевания как системные проявления были выявлены у 79,6% больных. У больных ПСХ отмечен широкий спектр системных проявлений: язвенный колит, болезнь Крона, геморрагический васкулит, аутоиммунный тиреоидит, синдром Шегрена, витилиго, рецидивирующая крапивница, склерит, кератит, конъюнктивит, саркоидоз, узловатая эритема, хронический гломерулонефрит, фиброзирующий альвеолит, псориаз, сахарный диабет 1 типа, аутоиммунная гемолитическая анемия. Чаще всего встречались язвенный колит (49,5%) и болезнь Крона (17,2%). У 20,3% больных ПСХ зарегистрировано более одного аутоиммунного заболевания: у 14% больных - 2 аутоиммунных заболевания, у 4,3% - 3, у 1,1% - 4, у 1,1% - 5 аутоиммунных заболеваний.

Выводы: 1) Более чем в 79% случаев ПСХ сопровождается внепеченочными проявлениями. 2) У каждого пятого больного ПСХ есть 2 и более аутоиммунных заболевания (помимо самого ПСХ). 3) Наиболее частыми внепеченочными проявлениями ПСХ в российской популяции больных являются поражение кишечника, кожи и щитовидной железы.

ФАКТОР НЕКРОЗА ОПУХОЛИ АЛЬФА У ПАЦИЕНТОВ С АУТОИММУННЫМИ ЗАБОЛЕВАНИЯМИ ПЕЧЕНИ И ХРОНИЧЕСКИМ ГЕПАТИТОМ С**Марченко Н.В.¹, Райхельсон К.Л.¹, Карев В.Е.², Смирнов Д.Р.³, Борисов А.А.³***1Северо-Западный государственный медицинский университет имени И.И.Мечникова, Санкт-Петербург, Россия
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Введение: Фактор некроза опухоли альфа (ФНОα) является одним из провоспалительных цитокинов и иммуномодуляторов. Роль ФНОα в развитии и поддержании хронического воспаления при аутоиммунных заболеваниях печени (АИЗП) и хроническом гепатите С (ХГС) активно изучается. Целью исследования явилось определение уровня экспрессии ФНОα в сыворотке крови и ткани печени у пациентов с АИЗП и ХГС.

Материалы и методы: 33 пациента, включающие 11 случаев ПБЦ, 10 случаев АИГ и 10 случаев ХГС, были обследованы. Уровень экспрессии ФНОα в сыворотке крови изучался методом иммуноферментного анализа (ИФА) Уровень экспрессии ФНОα и CD68+ клеток в ткани печени определялся иммуногистохимическим методом. Число CD68+ макрофагов и ФНОα определялись в 15 полях зрения (x400). Экспрессия ФНОα оценивалась как процент позитивных ФНОα клеток относительно CD68+ в целом. Уровень активности во всех группах был одинаковым (METAVIR A2-A3).

Результаты: У всех пациентов уровень ФНОα в сыворотке крови был в пределах референтных значений. Среднее значение экспрессии TNFα CD68+ клетками составило 0,23±0,21 (%) - при ПБЦ, 0,52±0,41 (%) - при АИГ, 1,42±1,05 (%) - при гепатите С. Экспрессия TNFα достоверно чаще определялась у пациентов с ХГС в сравнении с АИЗП (23 АИЗП vs 10 ХГС, p<0,02, 12 АИГ vs 10 ХГС, p<0,03, 11 ПБЦ vs 10 ХГС, p<0,006). С другой стороны, достоверного различия в экспрессии TNFα внутри группы АИЗП при сравнении АИГ и ПБЦ выявлено не было (11 ПБЦ vs 12 АИГ, p<0,06).

Заключение: Данное исследование не показало повышения уровня ФНОα в сыворотке крови у пациентов с АИЗП и ХГС. Выявлено различие в экспрессии ФНОα в ткани печени у пациентов с гепатитами различной этиологии (АИЗП и ХГС).

МИНЕРАЛЬНАЯ ПЛОТНОСТЬ КОСТНОЙ ТКАНИ ПРИ АУТОИММУННОМ ГЕПАТИТЕ, ПЕРВИЧНОМ БИЛИАРНОМ ЦИРРОЗЕ И ПЕРЕКРЕСТНОМ СИНДРОМЕ**М.К. Прашнова, Н.В. Марченко, К.Л. Райхельсон, Н.В. Семенов, Л.К. Пальгова***СЗГМУ им. И. И.Мечникова, Санкт-Петербург, Россия*

Остеопения является одним из осложнений аутоиммунных заболеваний печени, сопровождающихся синдромом внутрипеченочного холестаза. В ее генезе основную роль вероятно играет мальабсорбция витамина Д и кальция, возникающая вследствие дефицита желчи в кишечнике. Формированию остеопороза способствует часто назначаемая этим пациентам терапия глюкокортикостероидами. Целью данного исследования явилось определение минеральной плотности костной ткани (МПКТ) у пациентов с АИЗП: первичным билиарным циррозом (ПБЦ), аутоиммунным гепатитом (АИГ) и перекрестным синдромом (АИГ/ПБЦ).

Материалы и методы: Рентгеновская денситометрия поясничного отдела позвоночника L1-L4 проводилась у 13 женщин (5 – с АИГ, 4 – с ПБЦ и 4 – АИГ/ПБЦ). Средний возраст их составил 56,5 ± 7,9 лет, средняя продолжительность болезни 4,7±2,8 лет. В соответствии с рекомендациями ВОЗ оценивался критерий Т, основанный на сравнении полученных значений МПКТ с референтными данными. Все пациенты получали базисную терапию (глюкокортикостероидную при АИГ, УДХК при ПБЦ) и препараты кальция ДЗ.

Результаты: Среднее значение Т-score при АИГ составило (-1,62)±0,16, ПБЦ – (-3,18)±1,36, АИГ/ПБЦ – (-1,08)±1,28. Значение Т<-2,5 достоверно чаще диагностировалось при ПБЦ (75% больных, p<0,05), в сравнении с 20% при АИГ и 0% при АИГ/ПБЦ (p<0,05, p<0,04 соответственно). Между группами АИГ и АИГ/ПБЦ различий показателя не выявлено.

Заключение: Даже при небольшой длительности заболевания при ПБЦ развивается остеопороз, обусловленный, вероятно, более выраженным холестазом. Глюкокортикостероидная терапия АИГ в данном наблюдении в меньшей степени способствовала развитию остеопороза.

ГЕПАТОПРОТЕКТИВНОЕ ДЕЙСТВИЕ ИНГИБИТОРА ПОЛИ(АДФ-РИБОЗО) ПОЛИМЕРАЗЫ (ПАРП) 4-ГИДРОКСИКВИНАЗОЛИНА (4-ГК) ПРИ ЭКСПЕРИМЕНТАЛЬНОМ КОНКАВАЛИН А - ИНДУЦИРОВАННОМ ГЕПАТИТЕ**Павлович С.И., Мартынова Т.В., Грушка Н.Г., Брызгина Т.М., Сухина В.С., Макогон Н.В., Янчий Р.И.***Институт физиологии им. Богомольца НАН Украины, Киев, Украина*

ПАРП - семейство ферментов, синтезирующих поли (АДФ-рибозу) - ПАР. ПАРП-1, самая распространенная изоформа, активируется при разрывах ДНК и осуществляет посттрансляционную модификацию белков, прикрепляя ПАР к гистонам, белкам репарации ДНК, транскрипционным факторам. При чрезмерной активации ПАРП-1 вовлекается в процессы воспаления и повреждения тканей и рассматривается как перспективная терапевтическая мишень при ряде заболеваний. Роль ПАРП-1 и возможности применения ингибиторов фермента при аутоиммунных заболеваниях печени мало изучены. В данной работе исследовали влияние ингибитора ПАРП 4-ГК на морфофункциональное состояние печени мышей при ее повреждении, вызванном введением поликлонального активатора Т-лимфоцитов конканавалина А (КонА), что является распространенной моделью аутоиммунных заболеваний печени Т-клеточного генеза. Введение КонА (25 мг/кг) усиливало перекисное окисление липидов в печени (по уровню малонового диальдегида - МДА) и активность АЛТ в сыворотке. Применение 4-ГК (50 мг/кг, за 2 часа до Кон А) уменьшало эти показатели в 1,3 и 2,2 раза соответственно (P<0,01). Гистологические исследования сосудистого русла полукolicиcтвенным методом (оценивали отдельно расширение сосудов, их полнокровие, тромбообразование, повреждение сосудистой стенки и периваскулярные отеки) выявили, что ингибирование ПАРП снижало суммарный показатель повреждений с 13,1±0,5 (при КонА) до 9,0±0,5 (4-ГК), P<0,001 (в контроле 0,6±0,3). Суммарный показатель повреждений паренхимы (раздельно оценивали дистрофию и гибель гепатоцитов, нарушение балочной структуры, лейкоцитарную инфильтрацию и состояние клеток Купфера) снижался при введении 4-ГК с 15,6±0,5 (КонА) до 11,7±0,3 (4-ГК), P<0,001 (в контроле 2,2±0,4). Полученные данные свидетельствуют, что ПАРП играет существенную роль в развитии иммунного воспаления в печени, а ингибитор ПАРП 4-ГК оказывает выраженное гепатопротективное, противовоспалительное и антиоксидантное действие при КонА-индуцированном гепатите у мышей.

ВИРУСНЫЕ ГЕПАТИТЫ

ХАРАКТЕРИСТИКА СОСТОЯНИЯ ПЕРИФЕРИЧЕСКОЙ КРОВИ У БОЛЬНЫХ ХРОНИЧЕСКИМ ГЕПАТИТОМ С НЕ ПОЛУЧАВШИХ ПРОТИВОВИРУСНУЮ ТЕРАПИЮ

ХАРАКТЕРИСТИКА СОСТОЯНИЯ ПЕРИФЕРИЧЕСКОЙ КРОВИ У БОЛЬНЫХ ХРОНИЧЕСКИМ ГЕПАТИТОМ С НЕ ПОЛУЧАВШИХ ПРОТИВОВИРУСНУЮ ТЕРАПИЮ

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Цель. Определить различия выраженности фиброза печени у больных хроническим гепатитом С (ХГС), инфицированных 1-м генотипом вируса и метаболическим синдромом (МС) в сравнении с пациентами без МС/без ХГС.

Пациенты и методы исследования. Обследованы 289 больных, которые были разделены на 3 группы. Основная группа включала 73 пациента с ХГС (генотип 1) и наличием МС, соответствующего критериям IDF 2005 г. Группу сравнения 1 составили 117 больных ХГС (генотип 1) без МС, с нормальной массой тела. Группа сравнения 2 (99 человек) была представлена пациентами с МС, не инфицированные вирусом гепатита С (HCV). В исследование включались пациенты с шестимесячным анамнезом HCV-инфекции, подтвержденной стандартными тестами. Исключались другие заболевания печени (кроме НАЖБП). Среди пациентов с МС основанием для проведения биопсии печени было наличие как минимум одного из следующих критериев: диффузные изменения печени при УЗИ, дислипидемия, повышение уровней трансаминаз. Всем пациентам выполнена пункционная биопсия печени, оценка фиброза печени проводилась по шкале Ishak (1-6 баллов). В зависимости от ее результатов уровень фиброза был условно разделен на слабый (1-2 балла), умеренный (3-4 балла) и тяжелый (5-6 баллов).

Результаты. В основной группе (ХГС, генотип 1 и МС) слабый фиброз выявлен у 61 пациента (83,6%), умеренный – у 6 (8,2%), тяжелый – также у 6 пациентов (8,2%). В группе сравнения 1 (ХГС без МС) вышеозначенные показатели имели соответственно 109, 4 и 4 пациента (93%, 3%, 3%). В группе сравнения 1 (МС без ХГС) – 97 пациентов со слабым фиброзом (93%), по 4 пациента с умеренным (3%) и тяжелым фиброзом (3%).

Выводы. У больных ХГС, инфицированных 1-м генотипом HCV, в сочетании с МС значительно чаще выявляется более выраженный фиброз печени по сравнению с пациентами только с ХГС (генотип 1) или только с МС. Этот факт может служить основанием для рекомендации лечения МС с целью улучшения естественного течения ХГС и повышения эффективности противовирусной терапии.

ПРОГРЕССИРОВАНИЕ ЦИРРОЗА ПЕЧЕНИ У ПАЦИЕНТОВ С ПОЛИМОРФНЫМИ ВАРИАНТАМИ 1846G И 1846A ГЕНА ЦИТОХРОМА P450 2D6

ПРОГРЕССИРОВАНИЕ ЦИРРОЗА ПЕЧЕНИ У ПАЦИЕНТОВ С ПОЛИМОРФНЫМИ ВАРИАНТАМИ 1846G И 1846A ГЕНА ЦИТОХРОМА P450 2D6

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Фиброгенез является ответной реакцией на многие заболевания печени различной этиологии. Гепатоцит играет важную роль в этом процессе. Детоксикация – важная функция печени, реализуемая специализированной системой метаболизма ксенобиотиков, в которой ведущая роль принадлежит цитохрому P450. Роль этой системы в фиброгенезе изучена недостаточно, за исключением действия некоторых гепатотоксикантов, в том числе алкоголя, четыреххлористого углерода и некоторых лекарств. Полученные нами ранее данные по ускорению фиброгенеза под влиянием токсических воздействий указывают на необходимость таких исследований. В данной работе исследовалась связь полиморфных вариантов локуса 1846 G>A гена цитохрома P450 2D6 (CYP2D6) с развитием цирроза печени у 90 больных хроническими вирусными гепатитами. В группе больных вирусными гепатитами С, В и В+С такая связь не наблюдалась. Однако в группе больных, у которых циррозы вирусной этиологии (гепатит С, В и В+С) сочетались с дополнительным токсическим воздействием (алкоголь, профессиональные вредности) выявлена тенденция к более быстрому развитию цирроза у носителей генотипа CYP2D6*1846G/A, в сравнении с гомозиготами 1846G/G (отношение шансов 2,0, 95% ДИ 0,2 – 2,1).

СРАВНИТЕЛЬНЫЙ АНАЛИЗ ДИАГНОСТИЧЕСКОЙ ТОЧНОСТИ ФИБРОЭЛАСТОМЕТРИИ И БИОПСИИ ПЕЧЕНИ У БОЛЬНЫХ С ХРОНИЧЕСКИМ ВИРУСНЫМ ГЕПАТИТОМ С

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Цель работы. Оценка информативности эластометрии печени по сравнению с морфологическим исследованием печени у больных хроническим гепатитом С (ХГС).

Материалы и методы исследования. В 2010-2012 гг. на базе МБУЗ ГИКБ №8 и городской клинической больницы №3 г. Кемерово обследовано 152 пациента с ХГС (85 мужчин и 67 женщин) в возрасте 18-60 лет с длительностью заболевания от года до 15 лет. Всем больным выполнена фиброэластометрия на аппарате «Фиброскан» (EchoSens, Франция) и биопсия печени пистолетами с иглами G 16-18 под контролем УЗИ. Фиброэластометрия проводилась с измерением индекса эластичности в кПа. Допустимый интерквартильный коэффициент (IQR) – не более ¼ показателя эластичности. Стадии фиброза оценивали по шкале «Метавир».

Результаты. По результатам фиброэластометрии у 44 (28,9%) больных не выявлен фиброз, ранние стадии (F1-F2) диагностированы у 79 (51,9%) пациентов с ХГС. Поздние стадии фиброза (F3-F4) выявлены у 31 (20,3%) пациента, из них у 12 (7,8%) – отмечался цирроз печени, который подтверждался клинико-лабораторными данными. Совпадение результатов фиброэластометрии и биопсии печени на стадии F0 наблюдалось у 23 (52,2%) пациентов, на стадии F1 – у 10 (23,8%), F2 – у 6 (17,1%), F3 – у 16 (84,2%) и F4 – у 11 (91,6%) пациентов. Показатель диагностической точности совпадения результатов биопсии и фиброэластометрии для F0 составил 86,9%, для F1 – 40,0% для F2 – 66,0%, для F3 – 87,5%, для F4 – 90,0%.

Выводы. При сравнении результатов фиброэластометрии печени с морфологическим исследованием была выявлена достаточно высокая диагностическая точность. Наиболее высокая эффективность фиброэластометрии получена в определении 4-ой стадии фиброза с точностью метода 90,0%, что позволяет использовать этот метод в качестве альтернативы пункционной биопсии печени на поздних стадиях фиброза.

РАСПРОСТРАНЕННОСТЬ ГЕМОКОНТАКТНЫХ ВИРУСНЫХ ГЕПАТИТОВ У ВИЧ-ИНФИЦИРОВАННЫХ В САМАРСКОЙ ОБЛАСТИ И ПРОБЛЕМЫ ПРОФИЛАКТИКИ

РАСПРОСТРАНЕННОСТЬ ГЕМОКОНТАКТНЫХ ВИРУСНЫХ ГЕПАТИТОВ У ВИЧ-ИНФИЦИРОВАННЫХ В САМАРСКОЙ ОБЛАСТИ И ПРОБЛЕМЫ ПРОФИЛАКТИКИ

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Общие пути передачи гемоконтактных вирусных гепатитов и ВИЧ-инфекции способствовали колоссальной распространенности этих заболеваний в России во многом из-за отсутствия должной информации о путях распространения, методах защиты и профилактики. Сочетанное течение вирусных гепатитов и ВИЧ приобрело значимость демографической, политической и общечеловеческой проблемы.

Цель: оценить распространенность гепатитов В и С у пациентов с ВИЧ-инфекцией в Самарской области.

Материалы и методы: ф.25/у (840), результаты лабораторных исследований методом ИФА пациентов, состоящих на диспансерном учете в ГБУЗ «СОЦ СПИД и ИЗ», карты диспансерного наблюдения.

Результаты: обследовано 840 пациентов: 402 мужчин (47,9%) и 438 женщин (52,1%) от 20 до 76 лет. Средний возраст 33,9 ± 7,2 (M±SD). Диагноз ХГС установлен 197 (23,5%) (мужчин – 129, женщин – 68), диагноз ХГВ+С – 76 (9%) (мужчин – 59, женщин – 17), ХГВ - 4. Сочетание маркеров ВГВ и ВГС выявлено у 169 человек. Анти-HCV выявлены у 264 мужчин (65,8%) (95% ДИ: 61,0–70,5% по методу Клоппера-Пирсона), и 140 женщин (32%) (95% ДИ: 27,7–36,6%). Анти-HBcoAg исследованы у 452 пациентов, обнаружены у 235: мужчины – 157 (61,7%) (95% ДИ: 54,8–68,2%), женщины – 78 (47,9%) (95% ДИ: 41,4–54,5%). HBsAg определяется у 15 человек (13 мужчин и 2 женщины).

Заключение: Высокая распространенность гепатитов В и С среди ВИЧ-позитивных требует оптимизации мер профилактики. Правила соблюдения безопасного поведения и предотвращения заражения крайне важны как для ВИЧ-негативных, так и для пациентов с ВИЧ, в связи с тем, что заражение гепатитами может пагубно сказаться на качестве жизни. Оказание помощи в соответствии со стандартами лечения пациентам с коинфекцией является высоко затратным для государства, что должно быть принято во внимание при решении вопросов финансирования профилактических программ в регионах.

ХРОНИЧЕСКИЙ ГЕПАТИТ С И HELICOBACTER PYLORI

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Целью нашего исследования явилось изучение гастродуоденальной зоны (ГДЗ) при ХГ С, сопоставление показателей, характеризующих функциональное состояние печени и слизистой желудка (СОЖ) и 12 перстной кишки.

Материалы и методы. Обследовано 69 больных ХГ С у которых выполнены стандартные клинико-лабораторные и инструментальные исследования. Определяли антифосфолипидные антитела (АФ) в сыворотке крови Малоновый альдегид (МДА) и супероксидсмутазу (СОД).исследовали в сыворотке крови и в (СОЖ) и. одновременно изучали наличие в (СОЖ) НР и степень обсемененности, ФГС с морфологическим изучением биоптата. Обследованные пациенты с ХГ С были разделены на 2 группы: А гр–17 пациентов с минимальной, и В гр –69 с максимальной степенью инфицирования НР.

Результаты. В гр. В выявлен хрон. гастрит 72% (36), и хрон. дуоденит 65% (37). А гр- гастрит-28% (14), дуоденит 35% (13). В гр. А активность АЛТГ - (1,6±0,3 ммоль/ч/л) и АСТ – (0,6±0,2 ммоль/ч/л) была ниже, чем в гр. В-АЛТГ- (2,2±0,3 ммоль/ч/л и АСТ- 0,85±0,17 ммоль/ч/л) р≤0,01. В гр. В в сыворотке крови было выявлено повышение IgA (3,0±0,26 г/л), IgM (2,0±017 гл) АФ (21,8±0,65), МДА как в сыворотке крови так и в СОЖ был повышен (7,1±0,35 ммоль/мл, 26,55±0,8 ммоль/гр.тк.). При сопоставлении с показателями больных гр.А IgA- (2,0±0,3 г/л, Ig-M (1,7±0,15г.л) АФ 19,8±0,6, МДА в сыворотке 6,67±0,09 ммоль/л, и в СОЖ 20,8±0,4 ммоль/гр.тк.). В гр. В снижена активность СОД (СОЖ) – 2,5±0,11 ед/гр. тк., в сыворотке крови повышено 52,2±1,0 ммоль/мл., при сравнении с аналогичными показателями в гр. А (3,1±0,2 ед/гр.тк.мин, 47,8±0,8 ммоль/л).

Выводы. При ХГ С выявлена высокая частота заболеваемости ГДЗ Установлена достоверная связь между степенью инфицированности Нр и с частотой и тяжестью ГДЗ и функциональным состоянием печени.

ЭПИДЕМИОЛОГИЧЕСКАЯ И КЛИНИЧЕСКАЯ ИНТЕРПРЕТАЦИЯ РЕЗУЛЬТАТОВ СКРИНИНГА НА МАРКЕРЫ ГЕПАТИТОВ В И С ПАЦИЕНТОВ С НЕЙРОХИРУРГИЧЕСКОЙ ПАТОЛОГИЕЙ

ЭПИДЕМИОЛОГИЧЕСКАЯ И КЛИНИЧЕСКАЯ ИНТЕРПРЕТАЦИЯ РЕЗУЛЬТАТОВ СКРИНИНГА НА МАРКЕРЫ ГЕПАТИТОВ В И С ПАЦИЕНТОВ С НЕЙРОХИРУРГИЧЕСКОЙ ПАТОЛОГИЕЙ

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Работа выполнена в НИИ нейрохирургии им. академика Н.Н. Бурденко РАМН. Все пациенты, поступающие на оперативное лечение, обследованы на HBsAg и HCVAb в день госпитализации. В 2012 году обследовано 6700 пациентов на маркеры парентеральных вирусных гепатитов, 332 пациента с наличием этих маркеров в крови тестированы на активность аланин-аминотрансферазы (АлАТ). Исследования крови на HBsAg и HCVAb проводили с помощью систем ARCHITECT и Axsym (Эбботт Диагностика, США).Для выявления коровского антигена вируса гепатита С использовали тест «HCV Ag ARCHITECT system» (Эбботт Диагностика, США). Положительные результаты на HBsAg подтверждали автоматизированным тестом нейтрализации в этих же системах. Подтверждение положительных HCVAb осуществляли с помощью иммуноблоттинга (Inno-Lia, Innogenetics, Бельгия). Частота выявления HBsAg среди больных составила 1,2%±0,1. В динамике по годам отмечено снижение этого уровня, так в 2009 году уровень инфицирования пациентов вирусом гепатита В составлял 1,8%, в 2010 году - 1,5%. Частота выявления антител к вирусу гепатита С в этой же группе составила 3,7%±0,2 р<0,0001. Бесспорно, существенное влияние на частоту обнаружения HBsAg оказывает массовая вакцинопрофилактика гепатита В населения России. У половины (50,2%) лиц с наличием антител к вирусу гепатита С выявляли антитен к этому вирусу, что свидетельствует об активной репликации вируса и дает основание предполагать наличие высокого эпидемиологического риска при выполнении оперативных вмешательств таким пациентам. При исследовании активности АлАТ установлены достоверные отличия среди пациентов с HBsAg и HCVAb. У лиц с HBsAg частота гиперферментемии составила 7,4%±2,9, у лиц с HCVAb – 23,5%±2,7, р=0,011. Необходимо отметить, что частота гиперферментемии среди лиц с наличием как антител так и антигена вируса гепатита С была достоверно выше по сравнению с теми пациентами, в крови которых определяли только антитела к вирусу гепатита С и не определяли антиген (соответственно 42,8%±4,4 и 4,0%±1,6 р<0,0001). Учитывая эти данные, можно допустить, что увеличение активности АлАТ у этих больных ассоциировано с инфицированием вирусом гепатита С и является признаком хронической HС-вирусной инфекции, протекающей с репликацией вируса.

XVIII РОССИЙСКИЙ КОНГРЕСС «ГЕПАТОЛОГИЯ СЕГОДНЯ»	
<p>ПРЯМЫЕ МЕТОДЫ НЕИНВАЗИВНОЙ ДИАГНОСТИКИ ФИБРОЗА ПЕЧЕНИ У БОЛЬНЫХ ХРОНИЧЕСКИМ ГЕПАТИТОМ С</p> <p>Глазкова Е.Я., Малова Е.С., Рыбкина А.А., Морозов В.Г. <i>Медицинская компания «Гепатолог», Самара, Россия</i></p>	<p>в крови, позволявшим при уровне более 100 мкг/л с вероятностью около 95% дифференцировать цирроз печени с любой другой стадией фиброза при ХГС.</p> <p>Заключение. При ХГС ЭГ печени позволяет довольно четко регистрировать переход от одной стадии фиброзного процесса печени к другой, при этом наиболее точно граница между стадиями определяется на уровне F0/F1, F2/ F3, F3/F4. Уровень ГК в крови больных ХГС не позволяет диагностировать отдельные стадии фиброза печени, кроме цирроза (F4).</p>
<p>Материалы и методы.</p> <p>Обследовано 205 пациентов в возрасте от 18 до 60 лет с диагнозом ХГС в фазе репликации вируса. Все пациенты были разделены на 5 групп в соответствии со стадиями фиброза печени, установленными в ходе гистологического исследования биоптатов печени с оценкой по шкале METAVIR: (1) F0 – 17, (2) F1 – 96, (3) F2 – 26, (4) F3 – 22 и (5) F4 – 44 пациента. Контрольную группу составили 24 клинически здоровых человека. Прямые методы неинвазивной диагностики фиброза печени были представлены транзитной эластографией печени (ЭГ) и определением уровня гиалуриновой кислоты (ГК) в сыворотке крови. Статистическая обработка данных поводилась методами непараметрической статистики (SPSS 17.0), при этом оценивалась достоверность различий тестируемых показателей при переходе от каждой стадии фиброза к последующей, а также в сравнении с контролем.</p>	<p>Результаты.</p> <p>Результаты, полученные в ходе ЭГ у больных ХГС с отсутствием фиброза в печени (стадия F0), не имели значимых отличий от показателей в контрольной группе, но демонстрировали достоверный рост при переходе на стадию F1. Диапазон значений возрастал на стадии значимого фиброза (F2), но различия с предыдущей стадией (F1) не носили достоверного характера. Еще большее нарастание диапазона значений по данным ЭГ отмечалось на стадии выраженного фиброза (F3) и характеризовалось достоверными различиями с F2. Максимальные значения плотности печени регистрировались на стадии цирроза печени (F4), при этом различия со стадией F3 также были статистически значимыми.</p> <p>Результаты определения уровня ГК у больных на стадиях F0-F3, показывали его тенденцию к постепенному повышению, однако эти отклонения по сравнению с уровнем в контрольной группе не носили значимого характера. В то же время развитие цирроза печени сопровождалось достоверным ростом содержания ГК</p>
<p>РОЛЬ ТФР-β1 В ПАТОГЕНЕЗЕ ФИБРОЗА ПЕЧЕНИ, ВЫЗВАННОГО ВИРУСОМ ГЕПАТИТА С</p> <p>Горелова И.С., Склад Л.Ф., Журавлева А.С. <i>ГБОУ ВПО Владивостокский государственный медицинский университет Минздрава РФ, г.Владивосток, Россия</i></p>	<p>СЫВОРОТОЧНЫЕ МАРКЕРЫ ВПГ 1 ТИПА (HSV-1) ПРИ ХГ И ЦП (ХДЗП). СЫВОРОТОЧНЫЕ МАРКЕРЫ ВИРУСА ПРОСТОГО ГЕРПЕСА-HSV-1 (ВПГ) ПРИ ХРОНИЧЕСКОМ ГЕПАТИТЕ (ХГ) И ЦИРРОЗЕ ПЕЧЕНИ (ЦП)</p> <p>Дедов А.В., Панов А.А. <i>Астраханская Государственная Медицинская Академия, РФ, г. Астрахань</i></p>
<p>В настоящее время признано, что иммунологические механизмы являются ведущими в формировании фиброза печени при хронических гепатитах. По данным литературы последних лет, одним из ключевых факторов хронических воспалительных процессов с деструктивным потенциалом и морфологическими изменениями является активность ТФР-β1.</p> <p>Цель исследования: оценить роль сывороточного уровня ТФР-β1 в патогенезе фиброза печени, вызванного вирусом гепатита С.</p> <p>Материалы и методы: проведено комплексное клинико-лабораторное и инструментальное обследование 41 пациента (21 женщина и 20 мужчин) с хроническим вирусным гепатитом С (ХВГС). Противовирусную терапию пациенты не получали. Стадию фиброза печени регистрировали методом эластографии. Уровень ТФР-β1 в сыворотке крови определяли методом твердофазного ИФА с использованием диагностических наборов (R&D Diagnostics Inc., USA) с чувствительностью 1 пг/мл. В качестве контроля обследовали 14 практически здоровых добровольцев. Полученные результаты обрабатывали методом математической статистики при помощи компьютерного пакета обработки данных Statistica 6,0 для Windows.</p> <p>Результат: у всех пациентов ХВГС обнаружено значительное повышение содержания ТФР-β1 в сыворотке крови. При этом его средний уровень составил 24,2±1,8 пг/мл, достоверно превысив аналогичный показатель в группе здоровых лиц (10,5±1,1 пг/мл, р<0,01). Выявлена прямая корреляционная связь концентрации ТФР-β1 с выраженностью фиброза печени (г = 0,68). Так, средний уровень ТФР-β1 при отсутствии фиброза печени составил 22,2 ± 2,2 пг/мл, F1/2 – 25,0 ± 1,9 пг/мл, F3/F4 – 37,7 ± 3,3 пг/мл (р<0,01), что достоверно отличалось от нормы.</p> <p>Таким образом, полученные результаты могут подтверждать фиброгенную роль ТФР-β1 в иммунопатогенезе морфологических изменений в печени при ХВГС.</p>	<p>Повсеместность распространения (убиквитарность) ВПГ общеизвестна. Практически 100% человеческой популяции ВПГ-IgG позитивны. Вместе с тем довольно четкие тенденции к повышению маркера данной инфекции IgM у больных ХДЗП явно имеют место, реактивация вируса с его репликацией может иметь место у лиц с различными формами иммунного дефицита. Кроме того данную инфекцию следует исключать у больных гепатитами неясной этиологии. ВПГ может принимать участие в патогенезе ряда хронических заболеваний печени.</p> <p>Цель и задачи. Определить распространенность антител к ВПГ классов IgM и IgG среди больных ХГ и ЦП (ВПГ- IgM и ВПГ- IgG).</p> <p>Материал и методы. У 50 здоровых доноров и 89 больных ХГ и ЦП были определены уровни антител ВПГ- IgM и ВПГ- IgG методом ИФА.</p> <p>Результаты. Распространенность ВПГ- IgM и ВПГ- IgG у доноров составила 45,24% и 100%, тогда как в общей группе больных заболеваниями печени соответственно 67,42% и 100%. Таким образом, распространенность ВПГ- IgG была одинаковой как у больных, так и у здоровых и составляя 100%. Вместе с тем, имелаь тенденция к большей частоте ВПГ- IgM у больных общей группы с ХДЗП (р>0,05). У больных ХГ (n=40) серопозитивными по наличию ВПГ- IgM были 32,5% лиц с высоким титром антител и 17,5% с умеренным (всего 50% серопозитивных), а другие 50% больных были серонегативными. Среди больных ЦП (n=49) 59,2% были серопозитивными с высоким титром антител, 22,0% имели умеренный титр антител, а 18% были серонегативными по ВПГ- IgM (р<0,05 по сравнению с донорами).</p> <p>Выводы. Практически 100% доноров и больных ХДЗП являются серопозитивными по наличию ВПГ- IgG, что отражает повсеместное распространение ВПГ. При ХГ частота позитивности как по ВПГ- IgM, так и по ВПГ- IgG практически не отличается от донорской, тогда как у большинства больных ЦП имелось достоверное повышение уровня антител ВПГ- IgM. Наличие высоких титров IgM указывает на возможное наличие активной репликации ВПГ у значительной части больных ЦП. Это может быть свидетельством участия ВПГ в патогенезе ЦП, а также быть проявлением имеющегося в этой группе больных иммунного дефицита.</p>

ВИРУСНЫЕ ГЕПАТИТЫ	
<p>СЫВОРОТОЧНЫЕ МАРКЕРЫ ВИРУСА ЭПШТЕЙНА- БАРР (ВЭБ) ПРИ ХРОНИЧЕСКОМ ГЕПАТИТЕ (ХГ) И ЦИРРОЗЕ ПЕЧЕНИ (ЦП)</p> <p>Дедов А.В., Панов А.А.,Уразмухамбетова РИ., Вилявина Е.В. <i>Астраханская Государственная Медицинская Академия, РФ, г. Астрахань</i></p>	<p>СЫВОРОТОЧНЫЕ МАРКЕРЫ ЦИТОМЕГАЛОВИРУСА (ЦМВ) ПРИ ХРОНИЧЕСКОМ ГЕПАТИТЕ (ХГ) И ЦИРРОЗЕ ПЕЧЕНИ (ЦП)</p> <p>Дедов А.В., Панов А.А. <i>Астраханская Государственная Медицинская Академия, РФ, г. Астрахань</i></p>
<p>Хроническая вирусная инфекция Эпштейн-Барр (ВЭБ) характеризуется хроническими или рецидивирующими мононуклеозоподобными симптомами, такими как лихорадка, гепатоспленомегалия, гепатит и распространенная лимфаденопатия. Данную инфекцию следует исключать у больных гепатитом неясной этиологии, а также у лиц с иммунным дефицитом.</p> <p>Цель и задачи. Определить распространенность антител к ВЭБ классов IgM и IgG среди больных ХГ и ЦП (ВЭБ- IgM и ВЭБ- IgG).</p> <p>Материал и методы. У 50 здоровых доноров и 89 больных ХГ и ЦП были определены ВЭБ- IgM и ВЭБ- IgG методом ИФА.</p> <p>Результаты. Распространенность ВЭБ- IgM и ВЭБ- IgG у доноров составила 7,5% и 9,8%, тогда как в общей группе больных заболеваниями печени соответственно 31,03% и 32,58%. Это более чем в 3 раза превышало донорский уровень (р<0,05). В группе больных ХГ (n=40) серонегативными по наличию ВЭБ- IgM были 85%, 12,5% имели умеренный уровень антител и 2,5% - высокий уровень антител. Среди больных ЦП (n=49) 53,06% были серонегативными, а 46,97%- серопозитивными. У 28,57% имелся высокий уровень антител, а у 18,37% - умеренный. Распространенность антител ВЭБ-IgG при ХГ составила 20%, в том числе у 12,5% определялся высокий уровень антител и у 7,5%- умеренный. При ЦП имелось 57,14% ВЭБ- IgG- серонегативных лиц, 30,61% с высоким уровнем антител и 12,24% с умеренным.</p> <p>Выводы. Почти треть больных ХДЗП являются серопозитивными по наличию ВЭБ- IgM и ВЭБ- IgG, что статистически достоверно отличает их от группы контроля (доноры). При ХГ частота позитивности по маркерам составляет 15-20%, тогда как почти половина больных ЦП имели преимущественно высокие уровни ВЭБ- IgM и ВЭБ- IgG. Наличие высоких уровней IgM указывает на наличие активной репликации ВЭБ у значительной части больных ЦП. Это может указывать на участие последних в патогенезе заболеваний печени, в частности на возможную интерференцию с гепатотропными вирусами и модификацию клинической картины ХГ и ЦП.</p>	<p>Убиквитарность ЦМВ общеизвестна. Практически 100% человеческой популяции ЦМВ-IgG позитивны. Вместе с тем реактивация вируса с его репликацией может иметь место у лиц с различными формами иммунного дефицита. Данную инфекцию следует исключать у больных гепатитом неясной этиологии. ЦМВ может принимать участие в патогенезе ряда хронических заболеваний печени.</p> <p>Цель и задачи. Определить распространенность антител к ЦМВ классов IgM и IgG среди больных ХГ и ЦП (ЦМВ- IgM и ЦМВ- IgG).</p> <p>Материал и методы. У 50 здоровых доноров и 89 больных ХГ и ЦП были определены уровни антител ЦМВ- IgM и ЦМВ- IgG методом ИФА.</p> <p>Результаты. Распространенность ЦМВ- IgM и ЦМВ- IgG у доноров составила 47,62% и 95,24%, тогда как в общей группе больных заболеваниями печени соответственно 70,8% и 100%. Таким образом, распространенность ЦМВ- IgG была одинаковой как у больных, так и у здоровых и составляла практически 100%. Вместе с тем, имелаь тенденция к большей частоте ЦМВ- IgM у больных общей группы с ХДЗП (р>0,05). У больных ХГ (n=40) серопозитивными по наличию ЦМВ- IgM были 47,5% лиц, причем с высоким титром антител, а 52,5% были серонегативными. Среди больных ЦП (n=49) 79,6% были серопозитивными, а 20,1%- серонегативными по ЦМВ- IgM (р<0,05 по сравнению с донорами). У 69,4% из них имелся высокий уровень антител, а у 10,2% - умеренный.</p> <p>Выводы. Практически 100% доноров и больных ХДЗП являются серопозитивными по наличию ЦМВ- IgG, что отражает повсеместное распространение ЦМВ. При ХГ частота позитивности как по ЦМВ- IgM, так и по ЦМВ- IgG практически не отличается от донорской, тогда как у большинства больных ЦП имелось достоверное повышение уровня лишь антител ЦМВ- IgM, но не ЦМВ- IgG. Наличие высоких титров IgM указывает на возможное наличие активной репликации ЦМВ у значительной части больных ЦП. Это может быть свидетельством участия ЦМВ в патогенезе ЦП, а также быть проявлением имеющегося в этой группе больных выраженного иммунного дефицита.</p>
<p>ОЦЕНКА ЭФФЕКТИВНОСТИ КОМПЛЕКСНОЙ ТЕРАПИИ У БОЛЬНЫХ С ХРОНИЧЕСКИМ ГЕПАТИТОМ С В СОЧЕТАНИИ С САХАРНЫМ ДИАБЕТОМ 2 ТИПА</p> <p>Дербак М.А., Архий Э.Й., Розумик Н.В., Брич Н.И., Пичкарь Й.И., Крафчик О.М. <i>Ужгородский национальный университет, Украина</i></p>	<p>ГЕПАТИТ С: СОВРЕМЕННЫЕ ПРОБЛЕМЫ ДИАГНОСТИКИ, ЛЕЧЕНИЯ И ПРОФИЛАКТИКИ ИНФЕКЦИИ.</p> <p>П.Г. Дерябин <i>ФГБУ «НИИ вирусологии им. Д.И. Ивановского» Минздрава России</i></p>
<p>Цель работы. Изучить эффективность комплексной терапии хронического гепатита С (ХГС) у больных сахарным диабетом (СД) 2 типа.</p> <p>Материалы и методы. В исследование включено 58 больных ХГС в сочетании с СД 2 типа. Для подтверждения вирусной этиологии ХГС всем больным определяли антитела к HCV в сыворотке крови методом ИФА и РНК HCV с последующей вирусной нагрузкой методом ПЦР в режиме реального времени. Все больные имели 1 генотип HCV и вирусную нагрузку 4×105- 6×105МО/мл, а также СД 2 типа легкой или средней степени тяжести стадия компенсации. Больные были разделены на две группы: 1 группа (n=32) - пациенты получали только противовирусную терапию (ПВТ) в стандартных дозах и 2 группа (n=26)-ПВТ+ терапия сопровождения, которая состояла из приема препарата гептрал по схеме: по 800 мг 10 дней в/в, а затем в той же дозе в таблетках в течение месяца на 1-ом, 4-ом, 8-ом, 12-ом месяцах ПВТ и непрерывного приема препарата урсофальк по 15 мг/кг ежедневно. Срок лечения составлял 48 недель. Клинические синдромы, биохимические параметры и вирусная нагрузка оценивались перед началом лечения и через 1, 4, 12, 24 и 48 недель от начала терапии. Вид и дозы сахароснижающей терапии оставались без изменений на протяжении всего периода лечения.</p> <p>Результаты исследования. Быстрый вирусологический ответ получен в 9,4% больных 1 группы, и 11,5% - 2-ой. Ранний вирусологический ответ отмечен в 15,6% и 23,0% больных соответственно. В 1 группе побочные эффекты ПВТ имели 100% больных и поэтому 5 (15,6%) больных (1-депрессия, 2-анемии и 2-декомпенсации СД) прекратили лечение. Во 2-ой группе побочные эффекты были в 61,5% больных, но в медикаментозной коррекции не нуждались. Выраженной депрессии у больных 2-ой группы не наблюдалось ни у одного пациента. Стойкий вирусологический ответ получен в 31,25% и 38,5% больных соответственно.</p> <p>Выводы. Комплексный подход к терапии ХГС у больных СД 2 типа с включением в схему лечения препаратов гептрал и урсофальк, повышает эффективность ПВТ и уменьшает частоту ее побочных эффектов.</p>	<p>Среди вирусных гепатитов с парентеральным способом передачи гепатит С представляет собой наиболее значимую проблему здравоохранения. Прежде всего, это связано с глобальным распространением инфекции, высоким уровнем заболеваемости, склонностью к формированию хронических форм инфекции, приводящих к циррозу, первичному раку печени, вирус гепатита С способен поражать многие органы и ткани человека. В то же время, в практическом здравоохранении до сих пор нет вакцины против этой инфекции, а лечебные препараты, применяемые в настоящее время, все еще малоэффективны, дорогостоящи и не являются безвредными для здоровья человека. Таким образом, разработка и совершенствование необходимых для мониторинга новых методов диагностики инфекции, лечения и профилактики гепатита С является высоко актуальным для здравоохранения.</p> <p>В результате исследований по экспериментальному моделированию инфекции, вызванной вирусом гепатита С (HCV) in vivo и in vitro, из проб сывороток крови людей выделены инфекционные для культур клеток варианты HCV, характеризующиеся высокой продуктивной способностью. Сформирована коллекция штаммов разных субтипов HCV, пригодных для разработки диагностических и профилактических препаратов. Впервые созданы условия для доклинической апробации лечебных и профилактических средств. Получены данные, свидетельствующие о перспективе разработки культуральной инактивированной вакцины против гепатита С.</p>

XVIII РОССИЙСКИЙ КОНГРЕСС «ГЕПАТОЛОГИЯ СЕГОДНЯ»
<p>ВЛИЯНИЕ I/D ПОЛИМОРФИЗМА ГЕНА АПФ НА ТЕМПЫ ПРОГРЕССИРОВАНИЯ ХРОНИЧЕСКОГО ГЕПАТИТА С</p> <p>Мороз Л. В., Яцык И.В., Дудник В. М. <i>Винницкий национальный медицинский университет им. Н. И. Пирогова, г. Винница, Украина</i></p>
<p>Ключевым процессом в течении хронического гепатита С (ХГС) является фиброгенез в печени. Несколько недавних исследований показали, что ренин - ангиотензиновая система (РАС) играет важную роль в фиброзе печени и у пациентов с хроническими заболеваниями данного органа повышается уровень ее основного фермента – ангиотензин - превращающего фермента (АПФ). На активность АПФ влияет I/D полиморфизм его гена, который характеризуется наличием (insertion (I)) или отсутствием (deletion (D)) 287-основной пары ДНК последовательности в пределах гена АПФ. Учитывая вышеприведенные данные, можно предположить, что I/D полиморфизм гена АПФ влияет на характер прогрессирования фиброза печени при ХГС.</p>
<p>Цель. Целью нашего исследования было определение зависимости между I/D полиморфизмом гена АПФ и темпами прогрессирования заболевания у больных ХГС.</p>
<p>Материалы и методы. Обследовано 97 больных ХГС с 1-м генотипом вируса и 92 здоровых человека. Всем больным ХГС проводилось клинико-лабораторное обследование по общепризнанной методике, чрезкожная пункционная биопсия печени с оценкой по шкале METAVIR и определение I/D полиморфизма гена АПФ с помощью метода ПЦР на амплификаторе «Тердик». Больные были разделены на 2 группы в зависимости от темпов прогрессирования ХГС. В I группу вошли пациенты с медленным прогрессированием заболевания и наличием стадии фиброза F0-F2, во II - лица со стадией фиброза F3-F4 (срок инфицирования в обеих группах до 10 лет).</p>
<p>Результаты. Установлено, что среди больных ХГС генотип DD гена АПФ встречался в 1,7 раза чаще, чем среди здоровых лиц (65,98% против 39,13%). При этом аллель D в 1,4 раза чаще встречалась у больных I группы (85,59% против 61,84%) (протекторная), а аллель I в 2,7 раза больше у пациентов II группы (38,16% против 14,41%) (профибrogенная). Наличие аллели D (95,65%, p=0,0028) и генотипа DD (91,3%, p=0,0006) было характерно для женщин I группы, а алляли I (42,86%, p=0,0028), генотипов DI (42,86%, p=0,0103) и II (21,43%, p=0,0141) - для женщин II группы (у мужчин разница не достигла уровня достоверности). При медленном прогрессировании ХГС у большинства пациентов степень</p>

ПРОБЛЕМЫ МУЛЬТИВИРУСНОЙ ИНФЕКЦИИ ПРИ ХРОНИЧЕСКОМ ГЕПАТИТЕ

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В последние десятилетия XX века было обнаружено сразу несколько гепатотропных вирусов парентерального заражения. С позиций доказательной медицины считается, что вызывать хроническое поражение печени способны лишь вирусы В, С, D, что подтверждено многочисленными исследованиями. Однако эпидемиологический контроль и официальная регистрация заболеваемости касается только HBV и HCV. Кроме того, до сих пор не регистрируется HDV-инфекция, развивающаяся только при наличии HBsAg – основного маркера гепатита В. Такое положение может объясняться перспективной возможностью контроля за HDV-инфекцией с помощью внедряемой повсеместно вакцинации против гепатита В детей и лиц из групп риска. Спокойствие же большинства гастроэнтерологов в отношении вирусов HGV и TTV обосновывается отсутствием выраженного прогрессирования патологии печени и специфического этиотропного лечения при их моноинфекции. В последние пять лет нами с помощью молекулярно-биологических и иммуноморфологических исследований установлено, что отсутствие мониторинга всего спектра парентеральных гепатропных вирусов привело к стремительному росту сочетанных и мультивирусных хронических гепатитов, а моновирусные поражения печени стали большой редкостью. Такое положение усугубляет диагностические, терапевтические и прогностические проблемы, поскольку имеющиеся у больного гепатотропные вирусы не только оставляют свой след в иммунной системе, но и приводят к источнику всех ресурсов пораженного органа и всего организма. Несмотря на улучшение чувствительности диагностических тест-систем, продолжает увеличиваться количество случаев скрытой HBV-инфекции. Эти и другие проблемы мультивирусной инфекции при хронических гепатитах, а также возможные пути их решения будут изложены в докладе на примере конкретных клинических случаев после их углублённого диагностического изучения.

активности некровоспалительного процесса в ткани печени составляла A1 (66,1%), а при быстром прогрессировании - A2 (50%). Как при медленном, так и при быстром темпе прогрессирования ХГС аллель D была характерна для лиц с A1 (94,87% и 71,88%), а аллель I для пациентов с A3 (75% и 83,33%).

Вывод. Генотип DD гена АПФ доминирует у больных ХГС, а аллель D обладает протекторной ролью в прогрессировании ХГС, особенно у женщин.

УРОВЕНЬ ТРАНСФОРМИРУЮЩЕГО ФАКТОРА РОСТА -1В И ТКАНЕВОГО ИНГИБИТОРА МЕТАЛЛОПРОТЕАЗЫ 1 –ТИПА В СЫВОРОТКЕ КРОВИ У БОЛЬНЫХ ХРОНИЧЕСКИМ ГЕПАТИТОМ С

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Цель исследования – изучить клиническую информативность уровней трансформирующего фактора роста 1b (TGF-1b) и тканевого ингибитора металлопротеазы 1 типа (ТИМП-1) в сыворотке крови у больных хроническим гепатитом С (ХГ С).

Материал и методы исследования: Обследованы 63 больных ХГС в возрасте от 19 до 57 лет (средний возраст 35,6±10,5), из них мужчин 41 (36,6±9,9 лет), женщины 22 (37,2±11,3 лет). Диагноз установлен на основании общеклинического, биохимического, иммуноферментного и ПЦР-исследований. Стадию фиброза печени определяли посредством фиброэластометрии на аппарате «Фиброскан» (Echosens, Франция). Контрольную группу составили 35 здоровых лиц в возрасте от 19 до 46 лет (средний возраст 32,5±10,6). Концентрацию TGF-1b и ТИМП-1 в сыворотке крови определяли ИФА-методом с использованием коммерческих наборов (R@D, США).

Результаты: При изучении стадии фиброза установлено, что F0 по шкале Metavir выявлен у 22 (34,9%) больных, F1 –у 15 (23,8%), F2 –у 9 (14,4%), F3-у 7 (11,1%) и F4 –у 10 (15,8%). У больных ХГ С наблюдалось достоверное (p<0,001) повышение уровня TGF-1b и ТИМП-1 в сыворотке крови по сравнению с контрольной группой. Выявлена положительная достоверная (p<0,01) корреляционная связь между уровнем TGF-1b и ТИМП-1, с одной стороны, и активностью цитолитических ферментов, с другой (r=0,57, r=0,63, соответственно). Установлена положительная достоверная корреляционная зависимость между уровнем TGF-1b и ТИМП -1 и стадией фиброза по данным фиброэластометрии (r=0,76, p<0,01, r=0,69, p<0,01, соответственно).

Выводы: Трансформирующий фактора роста -1b и тканевой ингибитор металлопротеазы-1 сыворотки крови участвуют в иммунопатогенезе хронического гепатита С и, наряду с показателями фиброэластометрии могут служить неинвазивными параметрами, определяющими выраженность фибротических изменений в печени.

ВИРУСНЫЕ ГЕПАТИТЫ
<p>ОСНОВНЫЕ КОНЦЕПЦИИ ПАТОМОРФОГЕНЕЗА ХРОНИЧЕСКОГО ГЕПАТИТА С (HCV-ИНФЕКЦИЯ)</p> <p>Г.И.Непомнящих, М.А.Бакарев <i>ФГБУ НИИ региональной патологии и патоморфологии СО РАМН, Новосибирск, Россия</i></p>
<p>Цель исследования: Выявить основные закономерности патоморфогенеза хронического гепатита С (HCV-инфекции).</p>
<p>Материалы и методы: анализировано 112 клинических наблюдений с хронической HCV-моноинфекцией. Изучено сопоставление наличия репликации HCV в крови и ткани печени, уровня виремии, количества инфицированных гепатоцитов и генотипа HCV. Проведено исследование парафиновых, полутонких и ультратонких срезов биоптатов печени.</p>
<p>Результаты: при генотипировании HCV в 53% случаев выявлен генотип 1b, в 30% случаев – генотип 2, в 14% - генотип 3a. При генотипе 1b в 80% случаев преобладала слабо выраженная (70%), или минимальная (10%) степень активности инфекционного процесса. Установлено, что при достаточно высоком уровне виремии (от 106 до 108 копий РНК HCV в 1 мл плазмы) преобладали минимальные изменения структуры печени. Анализ показал, что распределение по степени активности HCV-инфекции не зависит от репликации вируса и уровня виремии – наличие РНК вируса гепатита С в образцах крови и/или ткани печени (по данным ПЦР) и число инфицированных гепатоцитов (по экспрессии NS3Ag HCV) не имеют достоверной связи со степенью активности инфекционного процесса, оцениваемой по структурным изменениям печени и клинико-биохимическим тестам. При исследовании полутонких срезов, нами впервые выделена мелковезикулярная субцитолеммальная липидная инфильтрация и сделан вывод, что она ассоциирована с фазой репликации вируса гепатита С.</p>
<p>Выводы: Репликация вируса гепатита С и число инфицированных гепатоцитов не оказывают значительного вклада в повреждение печени при хроническом гепатите С. Имеется достаточно данных, указывающих на то, что липидные капли принимают непосредственное участие в репродукции вирусных частиц, предоставляя им фактор, необходимый для их инфекционности, либо включая их в систему транспорта липидов и способствуя тем самым экспорту вируса из клетки.</p>

МАРКЕРЫ ИНФИЦИРОВАНИЯ ВИРУСОМ ГЕПАТИТА С У ПАЦИЕНТОВ РАЗНЫХ ВОЗРАСТНЫХ ГРУПП

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Вирусом гепатита С (ВГС) инфицированы около 3% населения РФ, включая все возрастные группы. Цель данного исследования – установить маркеры инфицирования ВГС в разных возрастных группах: от 2 до 14 лет (первая), от 18 до 29 лет (вторая) и от 30 до 55 лет (третья).

Исследовали образцы крови от 60 пациентов, составивших три группы по 20 человек. РНК ВГС выявляли методом ОТ-ПЦР с чувствительностью 50 МЕ/мл. Антитела к ВГС определяли иммуноферментным методом в коммерческих тест-системах «РекомбиБест анти-ВГС-IgM» и «РекомбиБест анти-ВГС–спектр» («Вектор-Бест», Россия). Статическую достоверность различий в группах пациентов определяли t-критерием Стьюдента.

Длительность инфицирования во всех группах была одинаковой (2-7 лет). Во всех группах преобладали мужчины (60%). Геном ВГС был выявлен у всех взрослых пациентов и у 80% инфицированных детей. Во всех группах доминировал субтип ВГС 1b. Однако доля вируса субтипа 3а в первых двух группах составила 40%, что в 2 раза больше, чем в третьей группе. Частота обнаружения и титры анти-ВГС IgM были почти одинаковыми во всех группах. Анти-core IgG обнаруживались в достоверно более низких титрах у детей (p<0,01). Аналогично, иммуноглобулины G к NS-антигенам (NS3, NS4ab, NS5a) были выявлены в более низких титрах у детей по сравнению с двумя взрослыми группами (p<0,01).

В заключение отметим, что у детей с хроническим гепатитом С серологические маркеры ВГС выявляются в более низких титрах, чем у взрослых пациентов. Вирус субтипа 3а чаще обнаруживался у детей и молодых взрослых пациентов, чем у больных старше 30 лет.

МОНИТОРИНГ ВЫЯВЛЕНИЯ МАРКЕРОВ ВИРУСА ГЕПАТИТА С У ПАЦИЕНТОВ ПОСЛЕ АНТИВИРУСНОЙ ТЕРАПИИ

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Эффективность противовирусной терапии (ПВТ) хронического гепатита С (ХГС) с использованием пег-интерферона и рибавирина составляет 50-70% в зависимости от генетических факторов вируса и пациента. Через 1-2 года после окончания ПВТ у 15-20% больных наблюдается рецидив. Цель данного исследования - установить особенности выявления маркеров ВГС-инфекции после окончания терапии. Анализировали образцы крови от 50 пациентов с устойчивым вирусологическим ответом (УВО) в течение 3-7 лет. РНК ВГС выявляли методом ОТ-ПЦР, используя коммерческую тест-систему «РеалБест РНК ВГС» с чувствительностью 15 МЕ/мл («Вектор-Бест», Россия). Антитела к ВГС определяли иммуноферментным методом в коммерческих тест-системах «РекомбиБест анти-ВГС-IgM» и «РекомбиБест анти-ВГС–спектр» («Вектор-Бест», Россия).

У 44% больных, завершивших терапию с УВО, была выявлена РНК ВГС. Наиболее часто геном ВГС обнаруживали через 2-4 лет после окончания ПВТ. На этот временной интервал пришлось 25% пациентов с вновь появившимся геномом ВГС. Вирусная нагрузка у этих пациентов была низкой 25-50 МЕ/мл. У них также часто отмечалось появление и стабильная детекция анти-ВГС IgM. У пациентов без РНК ВГС в течение всего периода наблюдения снижались титры антител к отдельным белкам ВГС, особенно к NS-антигенам. В заключение отметим, что длительное (до 7 лет) отсутствие РНК ВГС в крови пациентов после ПВТ сопровождается снижением титров антител к отдельным антигенам ВГС. Появление РНК ВГС часто происходит на 2-4 годы после окончания лечения.

МУЛЬТИЧАСТОТНАЯ БИОИМПЕДАНСОМЕТРИЯ БИОПТАТА ПЕЧЕНИ ПРИ ХРОНИЧЕСКИХ ВИРУСНЫХ ГЕПАТИТАХ

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Цель работы. Оценка информативности малоинвазивной импедансометрии биоптата печени в диагностическом алгоритме у пациентов с хроническими вирусными гепатитами.

Материалы и методы. Обследовано 76 пациентов с хроническими вирусными гепатитами В и С (29 женщин (38%) и 47 мужчин (62%)), средний возраст составил 37±2лет. Пациентам были проведены общеклинические обследования, УЗ – сканирование в В-и ЦДК-режимах, эластография печени . Выполнили биопсию печени под УЗ-навигацией с одновременным измерением мультичастотного биоимпеданса (in vivo) и полученного биопсийного материала (in vitro) с последующей оценкой коэффициента дисперсии импеданса печени.

Результаты. У 67% пациентов с ХВГ с уровнем АЛТ выше нормы регистрировался высокий уровень виремии, среди них при ХГС РНК HCV более 400тыс.МЕ/мл имел 61% исследуемых, при ХГВ ДНК HBV более 2тыс.МЕ/мл -39%. 34% пациентов имело минимальную гистологическую активность процесса в печени, у 21% обследованных отмечалась высокая активность и у 55% умеренная активность гепатита по данным биопсии печени. У 73% пациентов регистрировались высокие цифры импеданса на всех задаваемых частотах, в диапазоне 0,5-3,2кОм в зависимости от частоты переменного тока. Величина импеданса печени высоко коррелировала (r>0,62) в зависимости от активности гепатита. Коэффициент дисперсии зависел от тяжести поражения печени и был выше при отсутствии фиброза печени по данным морфологического исследования.

Выводы. При хронических вирусных гепатитах наблюдается расхождение клинико-лабораторных показателей и морфологических изменений в печени. Биоимпедансометрия биоптатов печени в стандартизированных условиях позволяет повышать оценку гистологических изменений в печени при рутинной биопсии печени.

ТЕЧЕНИЕ ХРОНИЧЕСКИХ ЗАБОЛЕВАНИЙ ПЕЧЕНИ ПРИ ГЕРПЕТИЧЕСКОЙ ИНФЕКЦИИ	ГЕПАТИТ С В РОССИЙСКОЙ ФЕДЕРАЦИИ
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Цель: оценить влияние вирусов герпеса (ВГ) – ВПГ-1, ВПГ-2, ВЭБ, ЦМВ на течение хронических заболеваний печени (ХЗП) различной этиологии.	В 2011 г. в РФ было зарегистрировано 2613 больных острым гепатитом С, протекавшим в основном с желтухой (1,83 на 100 тыс.населения , в то время как в 2000 году – 21,1о/оооо). Вместе с тем на один желтушный случай острого ГС приходилось 8 без этого оптического симптома, которых, как правило, в настоящее время не регистрируют. В 2011г. у 57028 чел. впервые диагностирован хронический ГС (39,92о/оооо), составивший в этом году в структуре хронических вирусных гепатитов 74,4% (в Москве – 80,9%). Имеет место отчетливый рост заболеваемости ХГС, заметно увеличение числа лиц с наличием антител к ВГС в крови (в 3-5 раз в отдельных регионах) у беременных женщин. Половину больных ХГС составляют сегодня лица младше 40 лет (в основном 20-29 и 30-39 лет), дети до 14 лет – 0,7%. Установлено заметное уменьшение в РФ в последние годы внутрибольничного заражения ВГС (по официальным данным до 2,7% в 2010г.), и инфицирования при внутривенном введении психоактивных препаратов (до 21%). Естественные пути передачи ВГС малоактивны (перинатальное заражение имело место лишь у 3,5-3,8% детей), а при сочетании с ВИЧ-инфекцией - у 14-16%. Способ родоразрешения и грудное вскармливание не влияло на частоту такой передачи вируса гепатита С. Внутрисемейное инфицирование отмечено у 0,7-1,0% мужей женщин с хроническим гепатитом С. У 22% больных ХГС выявлены в крови маркеры гепатита В. Оправданно проведение вакцинации против гепатита В больных ХГС, не имеющих маркеров HBV-инфекции. У привитых против ГВ таких больных не отмечена активизация патологических процессов в печени, увеличение частоты поствакцинальных реакций. В. У 83% ВИЧ-инфицированных лиц, выявляемых впервые, определяют маркеры гепатита С.
Материалы и методы. В сыворотке крови у 94 пациентов с ХЗП вирусной, алкогольной и алкогольно-вирусной этиологии определяли IgG и IgM к ВПГ-1, ВПГ-2, ВЭБ, ЦМВ (ИФА) и ДНК ВПГ-1, ВПГ-2, ВЭБ, ЦМВ (ПЦР).	
Результаты. Противогерпетические антитела (АТ) выявлены у 93/94 больных: IgG ВПГ-1 – в 91,5% случаев, IgG ВЭБ - в 89,4%, IgG ВПГ-2 – в 37,2%), IgG ЦМВ - в 48,9%. У 88/94 пациентов с ХЗП обнаружены АТ к нескольким видам ВГ. IgM ВПГ-1 были выявлены у 3 больных ХЗП, IgM ВПГ-2 - у 20, IgM ВЭБ - у 1, IgM ЦМВ – у 16. Частота обнаружения остальных маркеров ВГ при ХЗП достоверных различий не имела. ДНК ВГ не обнаружена. У большинства больных регистрировали микст-инфекцию ВПГ-1 и ВЭБ (n=60, 63,8%), преимущественно латентного и/или персистирующего течения. Реактивация ВГ-инфекции была установлена у 34 (36,2%) пациентов с ХЗП - в 28 (29,8%) случаях в виде моноинфекции, в 6 (6,2%) – микст-инфекции. При латентном и персистирующем течении ВГ-инфекции не отмечено влияния на клинико-биохимические и морфологические проявления ХЗП, а также на репликацию вирусов гепатитов В и С. У всех пациентов реактивация ВПГ-2-инфекции способствовала усилению некрозо-воспалительной активности. При алкогольном циррозе печени наиболее часто отмечена реактивация ЦМВ-инфекции (n=11, 44%), которая проявлялась нарастанием желтухи и прогрессированием геморрагического синдрома, а реактивация ВПГ-1-инфекции при хроническом алкогольном гепатите – наличием везикулярной сыпи и снижением альбумина (p<0,05).	
Выводы. При ХЗП выявлена высокая частота инфицирования ВГ (98,9%) с преобладанием микст-инфекций (94,6), что превышает распространенность ВГ в общей популяции (80-90%). Реактивация ВГ-инфекции чаще наблюдалась при алкогольной болезни печени. Это указывает на целесообразность проведения специфической противовирусной терапии.	

ЭФФЕКТИВНОСТЬ ПРОТИВОВИРУСНОЙ ТЕРАПИИ ХГС ПЕГ-ИФН-А И РИБАВИРИНОМ В КОМБИНАЦИИ С МЕТФОРМИНОМ У ПАЦИЕНТОВ С ИНСУЛИНОРЕЗИСТЕНТНОСТЬЮ, В ЗАВИСИМОСТИ ОТ УРОВНЯ ИНСУЛИНОРЕЗИСТЕНТНОСТИ(НОМА-1R-2-4 И НОМА-1R≥4) И ИМТ	
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Цель: оценить частоту излечения больных ХГС с инсулинорезистентностью при сочетании стандартной терапии (ПегИФНа-2b + рибавирин) и метформина в зависимости от уровня ИР и ИМТ.	
Материалы и методы: Работа основана на изучении 106 больных с ХГС и инсулинорезистентностью. НОМА-индекс (НОМА-1R) рассчитывался по формуле: НОМА-1R = уровень инсулина натощак (МкМЕ/мл) x глюкоза натощак (ммоль/л) / 22,5.Критерием наличия ИР считали значение НОМА-1R≥2.Для статистической обработки данных использовались MicrosoftExcel и Statistica 6.0 для Windows. Всем пациентам была назначена стандартная комбинированная терапия ПегИФН-α-2b в дозе 1,5мкг/кг/нед и рибавирин в дозе 15 мг/кг/сут. 48 из 106 пациентов с ИР был назначен метформин в дозе 20 мг/кг/сут.	
Результаты: Пациенты были разделены на группы в зависимости от уровня инсулинорезистентности (значения НОМА-индекса). Пациенты с НОМА-индексом от 2 до 4 (n=62), получающие метформин (n=26) и не получающие метформин (n=36) и пациенты с НОМА-1R≥4 (n=44), получающие метформин (n=22) и не получающие метформин (n=22). Так, при НОМА-индексе от 2 до 4, частота УВО среди пациентов, получающих метформин, составила 84% (n=22/26), а не получающих метформин, УВО достигли 69% (n=25/36), p=0,009. У пациентов с НОМА-1R≥4, получающих метформин – 81% (n=18/22), тогда как пациенты с НОМА-1R≥4, не получающие метформин, УВО достигли лишь 45% (n=10/22), p=0,0001. Пациенты обеих групп были разделены на подгруппы в зависимости от массы тела: 41 пациент с ИМТ<25кг/м ² и 65 пациентов с ИМТ≥25кг/м ² .	
Так, среди пациентов, получающих метформин (n=48), было 25 пациентов с ИМТ≥25кг/м ² и 23 пациента с нормальной массой тела (ИМТ<25кг/м ²), а среди пациентов, не получающих метформин (n=58), было 40 пациентов с повышенной массой тела (ИМТ≥25кг/м ²) и 18 пациентов с нормальной массой тела (ИМТ<25кг/м ²). Пациенты с повышенной массой тела, получавшие метформин, достигли УВО в 80% (n=20/25), тогда как пациенты с повышенной массой тела без метформина, достигли УВО лишь в 55% (n=22/40), p=0,0001. Пациенты с	

L-СЕЛЕКТИН И ХРОНИЧЕСКАЯ ПАТОЛОГИЯ ПЕЧЕНИ	МАРКЕРЫ ИНФИЦИРОВАНИЯ ВИРУСАМИ ГЕПАТИТОВ В И С У БОЛЬНЫХ И МЕДИЦИНСКОГО ПЕРСОНАЛА ОТДЕЛЕНИЙ ГЕМОДИАЛИЗА
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Цель. Целью исследования явилось изучение плазменного содержания L-селектина при хронических заболеваниях печени.	Пациенты и медицинский персонал отделений гемодиализа относятся к группам повышенного риска инфицирования вирусами парентеральных гепатитов
Материал и методы. Обследовано 198 больных (125 мужчин, 73 женщины) в возрасте от 18 до 60 лет: 28 – с хроническим вирусным гепатитом (ХВГ) В, 93 – ХВГ С, 62 – вирусным циррозом печени (ЦП) и 15 пациентов с ЦП алкогольной этиологии. У 7 больных алкогольным циррозом печени определялись признаки острого алкогольного гепатита. К классу А по Child-Pugh были отнесены 39 пациентов с циррозом печени, к классу В – 28 больных, к классу С – 10 обследованных. Контрольную группу составили 54 здоровых добровольца в возрасте от 22 до 55 лет. Концентрацию L-селектина в крови определяли методом ИФА.	Цель: эпидемиологический анализ результатов тестирования на наличие маркеров инфицирования ВГВ и ВГС у пациентов и персонала отделений гемодиализа, распространенность «окультурных» и HBsAg-мутантных форм ВГВ.
Результаты. Плазменные уровни L-селектина были увеличены как при хроническом гепатите, так и при циррозе печени без каких-либо межгрупповых различий. Тип, генетические и фенотипические особенности гепатотропных вирусов, а также степень виремии HBV и HCV не влияли на содержание медиатора в крови. Этиология цирроза печени не была взаимосвязана с повышенными плазменными значениями L-селектина. В случаях сочетания алкогольного цирроза печени с острым алкогольным гепатитом отмечалось более высокое содержание молекулы адгезии в крови. У пациентов с хронической патологией печени выявлено нарастание плазменных показателей L-селектина с усилением выраженности цитолитического синдрома. Прогностические индикаторы цирроза печени (классы В и С по Child-Pugh, декомпенсированная портальная гипертензия, варикозное расширение вен пищевода 2-3 степени, гиперспленизм) не влияли на концентрацию L-селектина в крови.	Пациенты и методы: образцы сывороток крови от 145 больных и 63 сотрудников отделений гемодиализа ГКБ им. С.П.Боткина исследовали с помощью тест-систем ЗАО «Вектор-Бест» (Россия), «Abbott Diagnostics» (США). Определение нуклеотидных последовательностей участка S-гена проводили с использованием секвенатора «ABI-3100 PRISM Genetic Analyzer» (США).
Заключение. При хронической патологии печени наблюдается увеличение содержания L-селектина в крови, наиболее выраженное в случаях высокой биохимической активности заболевания, что свидетельствует о патогенетической значимости медиатора в развитии воспалительного процесса в печени.	Результаты: HBsAg выявлен у 2(1,4%) больных и 1 (1,6%) сотрудника отделения. У каждого из них определялась ДНК ВГВ. «Окультурные» формы гепатита В и анти-ВГС были обнаружены у 2 (1,4%) и у 13 (9,0%) пациентов, соответственно. Установлено наличие суммарных антител к HBsAg у 13 (20,6%) сотрудников и увеличение частоты их обнаружения до 31,4% среди работавших в отделении более 10 лет. У носителей HBsAg при секвенировании выявлены 3 изолята ВГВ с заменами S-гена, которые имели генотип D, субтип ауw3 и вирусную нагрузку в диапазоне 10^2-10^3 МЕ/мл. Во всех изолятах оказалась серологически значимая замена по 118 аминокислотному остатку HBsAg.
Работа выполнена в рамках гранта Президента Российской Федерации № МД-934.2012.7.	Заключение: частота «окультурных» и HBsAg-мутантных форм ВГВ среди диализных пациентов оказалась достаточно высокой, что свидетельствует о необходимости углубленных молекулярно-биологических исследований у инфицированных лиц в этой популяции.

**ЛЕКАРСТВЕННЫЕ
ПОРАЖЕНИЯ ПЕЧЕНИ**



ПОЛИМОРФНЫЕ ВАРИАНТЫ ГЕНОВ СYP2E1 И NAT2 И ПОБОЧНЫЕ ЭФФЕКТЫ ЛЕКАРСТВЕННОЙ ТЕРАПИИ ТУБЕРКУЛЁЗА

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Лекарственная терапия туберкулеза лёгких, характеризующаяся длительным применением комбинаций препаратов в высоких дозах, часто сопровождается гепатотоксическими реакциями. Реакции с умеренно выраженным повышением уровней аланин- или аспартат аминотрансфераз в сыворотке крови развиваются у 10-20 % пациентов, у 0, 5 - 4% пациентов – с пятикратным повышением их уровня. Среди таких пациентов смертность достигает 5 % вследствие функциональной несостоятельности печени. Большое значение в развитии гепатотоксических реакций имеет метаболизм лекарств. Это обусловлено тем, что в результате метаболизма могут возникать токсичные метаболиты. Так, изониазид подвергается как ацелированию N-ацетилтрансферазой 2 (NAT2) с образованием нетоксичного ацелизониазида, так и гидролизу амидазой с образованием токсичного гидразина. Далее гидразин может ацелироваться и окисляться цитохромом P450 (CYP2E1) в конечные токсичные метаболиты, которые повреждают белки, ДНК, липиды мембран. Нами исследованы изменения уровней АЛТ при лечении больных туберкулёзом легких в зависимости от носительства аллелей, обусловливающих низкую скорость ацелирования (генотипы NAT2*5, *6, *7) и высокую активность цитохрома P450 2E1 (генотип CYP2E1*7632T/A). Во всей группе (n = 54 чел) без учета генотипов повышение активности АЛТ выше границы нормы на первом месяце лечения наблюдалось у 29% пациентов. Однако увеличение отмечалось у 47% пациентов с генотипами NAT2*5, *6, *7, у 50% пациентов с высокой активностью цитохрома P4502E1 (генотип CYP2E1*7632T/A) и у 75% пациентов с комбинацией этих генотипов. В соответствии с метаболическими закономерностями, возрастание активности АЛТ составило 1,53 раза во всей группе, 2,0 и 3,0 у пациентов с генотипами NAT2*5, *6, *7 и CYP2E1*7632T/A, и 5,18 раза у пациентов с комбинацией этих генотипов.

ЭФФЕКТИВНОСТЬ ТЕРАПИИ ЛЕКАРСТВЕННОГО ГЕПАТИТА У БОЛЬНЫХ С ТУБЕРКУЛЕЗОМ ЛЕГКИХ ГЕПАТОПРОТЕКТОРАМИ НА ОСНОВЕ ПРОДУКТОВ ПЧЕЛОВОДСТВА

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Апитерапия с древности использовалась в гепатологии.

Цель: изучить эффективность современной терапии препаратами на основе продуктов пчеловодства в лечении лекарственного гепатита, развившегося в результате полихимиотерапии туберкулеза легких.

Материалы и методы. Обследованы 60 больных, 30 из которых (основная группа) в течение месяца получали препарат Гепазил композитум (JVI Innovation, Австрия), основным компонентом которого является маточное молочко. Затем в течение 5 месяцев эти пациенты получали препарат Гепазил того же производства, основным компонентом которого является цветочная пыльца. В его состав также входят силимарин, кверцетин, чернитин, экстракт артишока. 30 больных группы сравнения получали препарат силимарина. До и после лечения проводили биохимическое исследование крови, сонографию печени и желчного пузыря. Пяти больным основной группы выполнена пункционная биопсия печени до и после лечения.

Результаты. При лечении препаратами Гепазил композитум и Гепазил удалось достичь существенного снижения выраженности цитолиза гепацититов, холестаза, улучшения синтетической и детоксикационной функций печени, уменьшения атерогенности липидного спектра крови. По результатам ультразвуковой гистогграфии печени лечение этими препаратами способствовало уменьшению выраженности ее стеатоза, снижению частоты выявления билиарного сладжа в желчном пузыре. По результатам пункционной биопсии печени оказалось, что препараты Гепазил композитум и Гепазил способствовали уменьшению выраженности гистологических изменений печени: дистрофии гепацититов, внутриклеточного холестаза, отмечалось усиление регенераторных процессов.

Вывод: препараты на основе продуктов пчеловодства Гепазил композитум и Гепазил эффективны в комплексной терапии лекарственного поражения печени у больных с туберкулезом легких.

ЛЕКАРСТВЕННЫЙ ГЕПАТИТ И БЕРЕМЕННОСТЬ

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Одной из наименее изученных областей клинической фармакологии остается изучение влияния лекарственных препаратов на течение и исходы беременности. Однако, по данным статистики не менее 80-90 % женщин принимают различные лекарственные средства во время беременности, многие из которых могут быть потенциально опасными и приводить к лекарственному поражению печени у беременных, что является серьезной угрозой для здоровья женщины, течения беременности и состояния плода.

В этой связи целью нашего исследования явилось изучение лекарственного поражения печени у беременных женщин, наблюдавшихся на базе перинатального центра республики Мордовия в период с 2011 по 2012 гт. Всего за это время было выявлено 20 пациенток с клинико–лабораторной картиной лекарственного гепатита. Количество наименований лекарственных препаратов, назначаемых данным пациенткам в течение беременности, составило от 3 до 11. Представляем спектр данных препаратов: витаминно-минеральный комплекс «Витрум Пренатал» на протяжении беременности принимало 16 женщин, «Элевит» - 3, «Курантил» - 8, «Сорбифер» - 5, «Магне В6» - 4, витамин Е – 3, «Фенюльс» - 2, «Йодомарин» – 3, «Дюфастон» до 20 недель беременности принимали10 женщин, «Утрожестан» -6. Кроме того, 5 пациенток в последний триместр беременности принимали препарат «Флебодиа». Также практически все беременные периодически принимали спазмолитики (но-шпа, дротаверин), фитотерапию (бруснивер).

По полученным результатам выявлена, прямая зависимость между количеством принимаемых препаратов и активностью лекарственного гепатита. Так наиболее высокий уровень печеночных трансаминаз, превышающих 10 норм, отмечался у женщин, которые принимали 9-11 наименований лекарственных средств. Особенно высокими оказались печеночные пробы, у пациенток, в схемы лечения которых, входили такие препараты как «Дюфастон» и «Утрожестан», особенно в сочетании с препаратом «Витрум».

Таким образом, беременность требует чрезвычайной осторожности при назначении лекарственной терапии, а ее ожидаемый эффект должен превалировать над возможным риском для здоровья самой женщины и плода.

ПОЛИМОРФНЫЕ ВАРИАНТЫ ГЕНОВ АНТИОКСИДАНТНОЙ ЗАЩИТЫ (GSTM1, GSTT1, GSTP1, GSTA2) ЯВЛЯЮТСЯ МАРКЁРАМИ ГЕПАТОТОКСИЧНОСТИ ЛЕКАРСТВЕННОЙ ТЕРАПИИ ТУБЕРКУЛЁЗА ЛЁГКИХ

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Туберкулёз лёгких – одно из наиболее значимых социальных заболеваний. В процессе медикаментозного лечения туберкулёза лёгких часты побочные реакции, особенно гепатотоксические (до 47%). В процессе метаболизма противотуберкулёзных препаратов образуются реактивные метаболиты и ими вызывается окислительный стресс в клетках печени, большую роль в защите от гепатотоксичности могут играть глутатион S-трансферазы (GST), как ферменты антиоксидантной защиты. У 75 пациентов с ежедневным режимом приёма противотуберкулёзных препаратов определялись полиморфные варианты 63G>C5 экзона и 83A>C7 экзона гена GSTA2, 313A>G и 314C>T гена GSTP1, также делеционные полиморфизмы генов GSTM1 и GSTT1. Определение маркёров гепатотоксичности – сывороточных активностей аланинаминотрансферазы (АЛТ) и аспартамаминотрансферазы (АСТ) проводилось при поступлении и через один месяц после начала лечения. Показано, что полиморфный locus 63G>C 5 гена GSTA2 оказывает наиболее существенное влияние на увеличение уровня сывороточных активностей АЛТ и АСТ в процессе лечения. У пациентов, с генотипом 63GG гена GSTA2, уровень АЛТ возрастал с 14,5 до 68 ед/л (p=0051), тогда как во всей исследованной группе, независимо от генотипа, с 18 до 27,5 ед/л за первый месяц лечения (p=0,0051). Также значимыми являются и исследованные полиморфные локусы гена GSTP1: у пациентов с генотипом 313AA уровень АЛТ возрастал с 17,5 до 32,5 ед/л (p=0,0005), у пациентов с генотипом 341CC с 16,5 до 28,5 ед/л (p=0,000004). Роль делеционных полиморфизмов генов GSTM1 и GSTT1 была не однозначной. Если у пациентов с делецией гена GSTM1 уровень АЛТ возрастал с 16 до 28 ед/л (p=0,0009), то и для GSTT1 наличие гена было более значимым (19 - 36 ед/л (p=0.0011)), чем его отсутствие (15 -21 ед/л (p=0.093)).

ЭФФЕКТИВНОСЬ СУКЦИНАТСОДЕРЖАЩИХ ПРЕПАРАТОВ И АДЕМЕТИОНИНА ПРИ ПОРАЖЕНИЯХ ПЕЧЕНИ У БОЛЬНЫХ ТУБЕРКУЛЕЗОМ ЛЕГКИХ

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Цель. Сравнительное изучение эффективности гепатопротекторного действия и оценка относительного риска неблагоприятного исхода (RR) при применении реамберина, ремаксолоа и эзогенного адеметионина у больных с лекарственными поражением печени (ЛПП) на фоне противотуберкулезной химиотерапии.

Материалы и методы. Обследовано 180 пациентов впервые выявленным туберкулезом органов дыхания, разделенных на 4 группы (n=45 в каждой группе): основная группа 1 (ОГ1) - пациенты, получавшие реамберин, основная группа 2 (ОГ2) – пациенты, получавшие ремаксол, основная группа 3 (ОГ3) – пациенты, получавшие адеметионин и группа сравнения (ГС) - пациенты, получавшие 5% раствор глюкозы. Изучаемые препараты назначали внутривенно капельно 1 раз в сутки курсом 10 дней. Произведена оценка лабораторного индекса (ЛИ) тяжести по Т.Н. Калачнюк и RR с расчетом NNT (число больных, которых необходимо пролечить).

Результаты. ЛИ статистически значимо (в 1,7-1,8 раза) повышался при развитии ЛПП, вызванном воздействием противотуберкулезных препаратов. На фоне терапии изучаемыми препаратами определялось статистически значимое снижение (в 1,3-1,5 раза) ЛИ по сравнению с раствором глюкозы, при этом наиболее выраженное снижение отмечено на фоне применения ремаксолоа. При оценке RR и отношения шансов установлена большая вероятность наступления благоприятного исхода (снижение ЛИ) при применении каждого из трех изучаемых препаратов в сравнении с раствором глюкозы, наибольший относительный риск (RR) и отношение шансов (OR) выявлены также при использовании ремаксолоа (1,87 и 2,31 соответственно). Коэффициент NNT при использовании ремаксолоа был в 1,6 и 4,4 раза ниже в сравнении с реамберином и адеметионином соответственно.

Заключение. Изучаемые препараты эффективны в терапии ЛПП у больных туберкулезом. Наибольший положительный эффект на величину лабораторного индекса тяжести с учетом показателей RR и NNT достигнут при использовании ремаксолоа.

ОСОБЕННОСТИ ЛЕКАРСТВЕННОГО ПОРАЖЕНИЯ ПЕЧЕНИ ПРИ СПЕЦИФИЧЕСКОЙ ТЕРАПИИ ТУБЕРКУЛЁЗА ЛЁГКИХ

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Цель: разработать современный метод мониторинга состояния печени у больных туберкулезом легких, получающих специфическую терапию.

Материалы и методы: Первый этап: ретроспективное исследование 250 историй болезней 250 больных туберкулёзом лёгких. Второй этап: сравнительное проспективное исследование в параллельных группах 50 больных туберкулезом легких. Для оценки функционального состояния печени ежемесячно исследовались: общие анализы крови и мочи, биохимические тесты.

Результаты: Проанализированы 250 историй болезни: 165 мужчин (66%) и 85 женщин (34%) в возрасте от 15 до 73 лет, преобладали впервые выявленные – 231 (92,4%), получавшие лечение по стандартным режимам химиотерапии. Установлено, что для контроля проводимой терапии наиболее показательно исследование динамики АСТ и АЛТ. В проспективном исследовании участвовали 35 мужчин и 15 женщин, средний возраст – 39,7 лет. Группу сравнения составили 30 здоровых лиц (18 мужчин и 12 женщин). Установлено исходное превышение в 1,2 раза уровней АСТ и щелочной фосфатазы (ЩФ). По окончании терапии достоверно снизилась только ЩФ. Анализ коагулограмм показал превышение в 1,1 раза исходного уровня протромбинового индекса и международного нормализованного отношения. После лечения достоверно изменилось на 17,6% активированное частичное тромбопластиновое время. Меньшую вариативность в группах «здоровые», «до лечения», «после лечения» имели CD4 (39, 33 и 33%) и CD16% (38, 36 и 44%). Наиболее значимо с возрастом увеличивался уровень CD16% (+64%). В результате лечения у и мужчин, и у женщин снижался уровень CD4 и увеличивался D16%. Однако, эти изменения у мужчин были менее выражены.

Выводы: Для контроля безопасности химиотерапии туберкулеза легких целесообразно исследовать АСТ и АЛТ. Профилактику гепатотоксических реакций необходимо начинать с момента поступления. Для оценки эффективности терапии необходимо исследовать CD4 и CD16.

КЛИНИЧЕСКОЕ НАБЛЮДЕНИЕ: ЛЕКАРСТВЕННО-ИНДУЦИРОВАННЫЙ ГЕПАТИТ У БОЛЬНЫХ ЛЕГочНЫМ ТУБЕРКУЛЕЗОМ НА ФОНЕ СОЧЕТАННОЙ ГЕПАТОТРОПНОЙ ТЕРАПИИ

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Актуальность. Несмотря на существенный прогресс, достигнутый во многих странах с высоким бременем туберкулеза, в регионе остаются существенные проблемы. Лекарственно-индуцированный гепатит (ЛИГ) на противотуберкулезные препараты – наиболее тяжелая и потенциально фатальная побочная реакция, которая варьирует от 2 % до 28 % и негативно влияет на клиническое излечение. Клиническая тактика в таких случаях остается несовершенной.

Цель. Оценить эффективность применении комбинации аминокислот-содержащего гепатопротектора глутаргина и магнитозаеротерапии (МЛТ) для профилактики ЛИГ, спровоцированного приемом противотуберкулезных препаратов.

Материалы и методы. Пациенты с активным туберкулезом легких были разделены на контрольную 1-ю группу (43 пациента) и 2-ю группу наблюдения (38 пациентов), лечение которых дополнено комбинацией глутаргина и МЛТ. Изониазид, рифампицин, пиразинамид и этамбутол в течении 2 месяцев продолжен лечением в фазе продолжения 4 месяца.

Результаты. Наши наблюдения свидетельствуют о снижении частоты ЛИГ за 6 месяцев во 2-й группе (p<0,05) в сравнении с 1-й группой. При этом, токсические реакции отмечены в 2,4 раза реже (p<0,05), и токсико-аллергические – в 3,5 раза реже (p<0,05), чем в 1-й группе. Среди них клинические и клинико-лабораторные проявления поражения печени выявлены в 2,5 раза реже (p<0,05), чем в 1-й группе. В обеих группах они, преимущественно, были в течение первых 2 месяцев лечения. При применении глутаргина с МЛТ не выявлены случаи ЛИГ, тогда как в контроле выявлены в 2 (4,6%) случаев на 3 и 4 неделе от начала лечения. Лабораторные признаки цитолиза, мезенхимального воспаления и нарушения пигментного обмена были выражены значительнонее, чем во 2-й группе.

Выводы. Применение комбинации глутаргин и магнитозаеротерапии предупреждает возникновение лекарственно-индуцированных эффектов противотуберкулезных препаратов, снижает тяжесть их клинических проявлений, сохраняя приверженность больных к лечению туберкулеза легких.

МЕТАБОЛИЧЕСКИЕ НАРУШЕНИЯ ПЕЧЕНИ



РАК ТОЛСТОЙ КИШКИ И ГЕПАТОБИЛИАРНЫЕ ДИСФУНКЦИИ

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Актуальность. В структуре смертности от онкологических заболеваний в большинстве развитых стран, в том числе в России, колоректальный рак занимает второе место. Основная доля (до 50%) летальных исходов при данном заболевании приходится на лиц старческого возраста. Наличие у таких больных сопутствующих заболеваний (коморбидность) часто в декомпенсированной форме, а также возрастная астенизация являются основными прогностическими факторами неблагоприятного исхода хирургического вмешательства.

Цель. Изучить частоты, локализации, морфологических характеристик, тактику лечения рака толстой кишки, наличие сопутствующей патологии.

Материалы исследования. В отделении колопроктологии РБ №2 ЦЭМП изучены 95 историй болезни (за 2011г) с диагнозом рак толстой кишки. Проведен структурный и статистический анализ результатов исследования.

Результаты. Выявлены следующие частоты встречаемости рака: в прямой кишке-36,8%, в толстой кишке-62,1% (из них: в слепой кишке-9,47%, печеночного угла-7,36%, селезеночного угла-8,42%, в сигмовидной кишке-36,8%), ануса-1,1%. У мужчин – 41,1%, у женщин-58,9%. По национальной принадлежности у коренных – у 41 (43,1%), у некоренных – у 54 (56,8%). По возрасту у мужчин и женщин в процентах соответственно в интервалах 20-30 лет – у 2 (2,1%), 31-40 лет – у 2 (2,1%), 41-50 – у 16 (17%), 51-60 – у 20 (21%), 61 и старше – у 55 (57,8%). У 53 (55,8%) больных структура опухоли носила характер умеренно-дифференцированной аденокарциномы, у 15 (15,8%) больных имели слизистую и мало-дифференцированную аденокарциному, 9 (9,4%) – тубулярно-ворсинчатую аденому, 11 (11,6%) – хорошо дифференцированную аденокарциному и 7 (7,4%) – перстневидно-клеточный рак. Оперативное вмешательство проведено у 78 (82,1%) больных. Из них: гемиколэктомия-13 (16,7), операция Гартмана-15 (19,2%), аппаратный анастомоз - 8 (9,8%), сигмостомия-11 (14,1%), трансверзостомия-5 (6,4%), экстирпация прямой кишки - 13 (16,7%). У 10 (12,8%) больных полипы удалены методом эндоскопической полипэктомии. Летальность составляет – 7,36% (7 человек). Из сопутствующих заболеваний ЖКБ выявлено у 20 (21%) человек, с проявлением механической желтухи – у 5 (5,26%). Из них женщины составляют-12 (60%), мужчины - 8 (40%) человек, коренные - 15 (75%),

некоренные - 5 (25%). Трудоспособного возраста-10 (50%), молодого - 2 (10%), старческого - 8 (40%). По УЗИ выявлены следующие гепатопанкреатобилиарные дисфункции : механическая желтуха – у 5 (5,26%) пациентов, калькулезный холецистит – у 20 (21%), хронический панкреатит – у 90 (94,7%), диффузные изменения паренхимы печени – у 85 (89,4%), гепатомегалия – у 2 (2,1%).

Выводы. Таким образом, преобладает рак толстой кишки – 62,1%, из них наиболее распространен рак сигмовидной кишки – 36,8%, чаще болеют женщины – 58,9%, некоренные – 56,8%, в возрастной группе 61 и старше – 57,8%. У большинства больных выявлена умеренно-дифференцированная аденокарцинома (55,8%). У 10 (12,8%) больных полипы удалены методом эндоскопической полипэктомии, остальным – абдоминальные операции. Из сопутствующей патологии ЖКБ диагностируется у каждого четвертого больного колоректальным раком, в клинической картине преобладают диспепсические проявления.

МОЛЕКУЛЯРНАЯ И КЛЕТОЧНАЯ БИОЛОГИЯ

ВЛИЯНИЕ ИНГИБИТОРА ПОЛИ(АДФ-РИБОЗО) ПОЛИМЕРАЗЫ (ПАРП) 4-ГИДРОКСИКВИНАЗОЛИНА НА НЕКРОЗ И АПОПТОЗ ИММУНОКОМПЕТЕНТНЫХ КЛЕТОК (ИКК) ПРИ КОНКАНАВАЛИН А -ИНДУЦИРОВАННОМ ГЕПАТИТЕ У МЫШЕЙ

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Путь клеточной гибели может играть ключевую патогенетическую роль, особенно при аутоиммунных заболеваниях. Достаточный уровень апоптоза ИКК необходим для поддержания толерантности и ограничения воспаления и иммунного ответа, а некроз является источником внутриклеточных аутоантигенов и может провоцировать аутоиммунитет. Повреждение клеточной мембраны, основной признак некроза, приводит также к выходу в ткани цитотоксичных молекул, которые индуцируют и усиливают воспаление. Вероятно, что при массивной лейкоцитарной инфильтрации поврежденной ткани некроз ИКК может вносить существенный вклад в инициацию и усиление аутоиммунных заболеваний, а его ослабление могло бы оказывать протективное действие. Есть данные, что ПАРП-1, фермент репарации ДНК, может индуцировать некроз. Он активируется при разрывах ДНК и синтезирует из НАД+ полимеры АДФ-рибозы. Чрезмерная активация ПАРП приводит к исчерпанию НАД и АТФ в клетках, следствием чего является их некроз. Роль ПАРП-1 при аутоиммунных заболеваниях печени изучена мало. Конканавалин А (КонА) - индуцированный гепатит у мышей является широко используемой моделью повреждения печени Т-клеточного генеза. Мы изучали влияние ингибитора ПАРП 4-гидроксиквиназолина (4-ГК) на некроз и апоптоз клеток лимфоузлов и селезенки в условиях КонА-гепатита. КонА снижал жизнеспособность ИКК и усиливал как апоптотическую, так и некротическую их гибель. Введение 4-ГК оказывало выраженное гепатопротективное и противовоспалительное действие, а также значительно снижало некроз клеток лимфоузлов и селезенки (в 1,8 и 2,0 раза соответственно, P<0.001), не влияя на уровень их апоптоза. Таким образом, ПАРП-1 участвует в патогенезе иммунного повреждения печени, усиливая некроз клеток, в том числе и ИКК. Ингибирование ПАРП эффективно предотвращало гибель клеток по провоспалительному и иммуногенному некротическому пути. Это свидетельствует о перспективности применения ингибиторов ПАРП для лечения аутоиммунных заболеваний печени.

СВОБОДНОРАДИКАЛЬНЫЕ ПРОЦЕССЫ И ЭКСПРЕССИЯ ГЕНА REG1A В ГЕПАТОЦИТАХ КРЫС ПРИ ДЛИТЕЛЬНОЙ ЖЕЛУДОЧНОЙ ГИПОХЛОРИДРИИ

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Длительная желудочная гипохлоридрия и последующая гипергастринемия являются причинами развития патологических процессов в желудочно-кишечном тракте, в том числе и в гепатобилиарной системе (Jensen R., 2006).

Цель. Целью работы было определить интенсивность свободнорадикальных процессов и экспрессию гена Reg1a в гепатоцитах крыс при длительном гипоацидном состоянии.

Материалы и методы. Исследования проводили на белых нелинейных половозрелых крысах-самцах. Гипоацидное состояние моделировали внутрибрюшинным введением 14 мг/кг омепразола 1 раз в сутки 28 дней. В гепатоцитах определяли содержание пероксида водорода с использованием ксиленола оранж и диеновых конъюгатов в гептан-изопропанольном экстракте – спектрофотометрическими методами, шиффовых оснований – флуориметрическим методом, ТБК-активных соединений – по реакции с тиобарбитуровой кислотой. Экспрессию гена Reg1a определяли методом полуколичественной ОТ-ПЦР.

Результаты. Показано, что у крыс при длительном снижении желудочной секреции гидрохлоридной кислоты, в гепатоцитах содержание пероксида водорода возрастало в 2 раза, при этом количество продуктов перекисного окисления липидов также увеличивалось: диеновых конъюгатов – в 2,2 раза, ТБК-активных соединений – в 1,7 раза и шиффовых оснований – в 1,6 раза относительно контроля. При длительном гипоацидном состоянии в гепатоцитах была обнаружена экспрессия гена Reg1a по сравнению с контролем.

Выводы. При длительной желудочной гипохлоридрии в печени активируются свободнорадикальные процессы, что свидетельствует о развитии оксидативного стресса. Рассматривается возможность неоплазии гепатоцитов вследствие возникновения экспрессии гена Reg1a.

ПЛАЗМОЦИТОИДНЫЕ ДЕНДРИТНЫЕ КЛЕТКИ И ИХ РОЛЬ В ПАТОГЕНЕЗЕ ХГС У ВЗРОСЛЫХ И ДЕТЕЙ

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С описанием, в 1999 году, плазмацитоидных дендритных клеток (ПДК), открыта новая страница в иммунном ответе человека.

Цель работы: установить роль ПДК в патогенезе ХГС у детей и взрослых.

Пациенты и методы: обследован 161 человек - 133 пациента в различные фазы ХГС(58 детей и 75 взрослых), 28 человек(16 детей и 12 взрослых) - здоровые лица. Определение количества ПДК в крови проводилось методом проточной цитофлуориметрии с помощью моноклональных антител к специфическим маркерам ПДК(CD303 и CD123). Определение ИФН - продуцирующей функции ПДК методом ИФА ELISA, с предшествующей стимуляцией ODN2216 и IL3.

Результаты: У больных ХГС выработка ИФН в ПДК достоверно выше, чем у здоровых, оставаясь по всем основным параметрам, определяющим течение ХГС, более высокой у взрослых пациентов, чем у детей. Количество ПДК у больных ХГС выше у детей, чем у взрослых, однако у всех достоверно более низкие, чем у здоровых. Выявлена закономерная обратно пропорциональная связь между уровнем выработки ИФН и вирусной нагрузкой. При низкой вирусной нагрузке уровень ИФН в ПДК как у взрослых, так и у детей высок (461,1±262,2пг\мл у взрослых, 153,5±38,07пг\мл у детей),а высокой виремии соответствует низкий ИФН-генез (147,1±59,77пг\мл и 75,76±20,72пг\мл, p<0,05). Показана взаимосвязь выработки ИФН в ПДК и цитолиза. Увеличение выработки ИФН у взрослых связано с повышением уровня трансаминаз (132,8±42,72пг\мл при нормальных показателях АлТ, АсТ, 314,9±137,7 пг\мл при АлТ, АсТ выше нормы, p<0,05), но имеет обратную направленность у детей (146,7±36,73пг\мл и 86,19±23,64пг\мл соответственно, p<0,05). Продемонстрировано,что показатели ПДК у взрослых больных тесно соотносятся со стадией фиброза печени. Количество ПДК резко снижается с 8,4±0,9 кл\млк при F0-1 баллов, до 3,9±0,9 кл.\млк при F4 балла по шкале METAVIR (p<0,05), а выработка ИФН увеличивается пропорционально стадии фиброза (от 68,32±33,21 пг\мл при F0-1 до 291,3±195,9 пг\мл при F4, p<0,05).

Заключение. Полученные данные впервые демонстрируют тесную связь количества и функции ПДК с основными параметрами, определяющими течение ХГС, свидетельствующую о важной роли этих новых иммунных клеток в его патогенезе у взрослых и детей.

ВЗАИМОДЕЙСТВИЕ T1+ С SH-ГРУППАМИ БЕЛКОВ МИТОХОНДРИЙ ПЕЧЕНИ КРЫСЫ

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Активные центры многих митохондриальных ферментов содержат SH-группы. Кроме того, эти группы играют важную роль в сохранении пространственной конфигурации белков. Окисление SH-групп во внутренней митохондриальной мембране (BMM) способствует открытию в ней кальций-зависимого неспецифического канала (КЗНК). Ранее было показано, что T1+ индуцировал открытие КЗНК во BMM митохондрий печени крысы, нагруженных Ca2+ (Kogotkov, Saris, 2011). Ионы тяжёлых двухвалентных металлов Me(т)2+ (Cd2+, Hg2+, Pb2+, Zn2+) обладают высоким химическим сродством к SH-группам, что является одной из причин токсичности этих металлов. Напрортив, сродство T1+ к SH-группам оказалось существенно ниже по сравнению со сродством Me(т)2+ (Perrin, 1979). Реакция T1+ с SH-группами белков митохондрий практически не изучена. Мы оценивали взаимодействие ионов T1+ с SH-группами белков митохондрий печени крысы по их реакции с 5,5'-дитиобис-(2-нитробензойной кислотой) (Kowaltowski, Castillo, 1997). Опыты проводили в 400 мОсм средах, содержащих 0-75 мМ T1NO3 и 250-400 мМ сахарозу или 0-75 мМ T1NO3, 125 мМ KNO3 и 0-150 мМ сахарозу, а также 100 мкМ Ca2+ (в некоторых случаях). Митохондрии были энергизованы глутаматом с малатом или сукцинатом - субстратами I и II дыхательного комплекса, соответственно. При увеличении концентрации T1NO3 в среде до 50-75 мМ было обнаружено заметное увеличение концентрации SH-групп во фракции BMM и одновременное снижение этой концентрации во фракции матрикса. Этот эффект был заметно сильнее в среде, содержащей KNO3. Он проявлялся независимо от наличия в среде ионов Ca2+ или того или иного дыхательного субстрата. Полученные результаты дают основание предположить, что взаимодействие T1+ с SH-группами белков матрикса снижает их растворимость в водной фазе и способствует сосаждению части этих белков с фракцией BMM. Усиление сосаждения в солевой среде с KNO3 может быть связано с большей доступностью R-групп аминокислот митохондриальных белков для реакции с ионами T1+.

ВЛИЯНИЕ СОРБЕНТОВ НА ПОКАЗАТЕЛИ СВОБОДНОРАДИКАЛЬНОГО ОКИСЛЕНИЯ ПРИ ОСТРОМ ОТРАВЛЕНИИ ЭТАНОЛОМ

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Цель работы: оценить влияние сорбентов на показатели свободнорадикального окисления в периферической крови крыс при остром отравлении этанолом.

Материалы и методы. Этанол в дозе 0,5 LD50 вводили 78 крысам внутрижелудочно. Исследуемые сорбенты (полисорб, литовит, сапропель) в дозе 3000 мг/кг вводили однократно, внутрижелудочно через 30 минут после введения ксенобиотика. Для оценки состояния процессов свободнорадикального окисления был использован хемилюминесцентный анализ эритроцитов и плазмы крови. Забор крови производился через 24 часа после введения этанола. Содержание этанола в цельной крови определяли методом газовой хроматографии. Содержание церулоплазмينا (ЦП) в плазме крови определяли по методу В.С. Камышникова (2003).

Результаты. Через 24 часа после введения животным этанола не установлено достоверных изменений интенсивности хемилюминесценции эритроцитов и плазмы крови. Введение животным этанола в сочетании с энтеросорбентами не оказало влияния на показатели хемилюминесцентного анализа плазмы крови. При хемилюминесцентном анализе эритроцитов установлено, что введение животным этанола в сочетании с полисорбом или литовитом приводит к достоверному снижению максимального значения интенсивности хемилюминесценции, тенденции к снижению светосуммы хемилюминесценции и светосуммы после максимального значения хемилюминесценции. Содержание церулоплазмينا при остром отравлении этанолом увеличивается почти в 1,5 раза по сравнению с контролем (P<0,01). При использовании исследуемых сорбентов (полисорба, литовита, сапропеля) содержание ЦП в крови не отличается от контроля.

Выводы. Выявлено корректирующее влияние энтеросорбентов на содержание основного антиоксиданта плазмы крови ЦП при остром отравлении этанолом. Энтеросорбенты являются эффективным средством детоксикации при острых отравлениях этанолом

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ВЗАИМОСВЯЗЬ МЕЖДУ АБДОМИНАЛЬНЫМ ОТЛОЖЕНИЕМ ЖИРА И ПОРАЖЕНИЕМ ПЕЧЕНИ ПРИ МЕТАБОЛИЧЕСКОМ СИНДРОМЕ

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Цель исследования. Выявить корреляции между выраженностью абдоминального отложения жира и наличием жирового гепатоза при метаболическом синдроме.

Материалы и методы. Обследовано 138 больных от 40 до 90 лет (64 женщины и 74 мужчины). Проводилось антропометрическое исследование (рост, вес, окружность талии (ОТ), индекс массы тела (ИМТ)), лабораторные исследования (липидный спектр, показатели углеводного обмена, биохимический анализ крови). При ультразвуковом исследовании брюшной полости измерялась толщина подкожного жира (ПКЖ) и интраабдоминального жира (ИАЖ) на середине расстояния между пупком и мечевидным отростком. Статистический анализ полученных данных осуществляли при помощи пакета прикладных программ Statistica 6.0.

Результаты. У всех пациентов имели место ИБС и артериальная гипертензия. Нарушения углеводного обмена выявлены у 50,7% больных. ОТ у женщин составила 102,6±1,7 см, у мужчин 100,6±1,4 см, ИМТ составил 28,8±0,4 кг/м². Толщина ИАЖ колебалась от 10,5 до 106 мм, в среднем 53,5±1,64 мм. Толщина ИАЖ была достоверно выше у мужчин (p<0,001). Диапазон измерений толщины ПКЖ составил от 3,7 до 30 мм, в среднем 12,7±0,38 мм, причем показатель был недостоверно выше у женщин. Гепатомегалия выявлена у 36,2% больных, у 52% больных – диффузное уплотнение и повышение эхогенности печени.

Выявлены корреляционные связи между толщиной ИАЖ и ИМТ (r=0,44, p=0,000001), ОТ (r=0,56, p=0,000001), уровнем HbA1c (r=0,57, p=0,03) с уровнем ЛПВП (r= -0,19, p=0,02), уровнем ТГ (r=0,17, p=0,05). Толщина ПКЖ коррелировала с ИМТ (r=0,3, p=0,00016), с ОТ (r=0,27, p=0,0014), уровнем ОХ (r=0,18, p=0,02), с косо-вертикальным размером (КВР) правой доли печени (r=0,19, p=0,02). У мужчин КВР правой доли печени прямо коррелировал с толщиной ИАЖ (r=0,28, p=0,016).

Выводы. Увеличение толщины подкожного и интраабдоминального жира является предиктором поражения печени у больных с метаболическим синдромом.

КОМПЛЕКСНАЯ КУРОРТНАЯ ТЕРАПИЯ НЕАЛКОГОЛЬНОЙ ЖИРОВОЙ БОЛЕЗНИ ПЕЧЕНИ С ПРИМЕНЕНИЕМ БАД МЕТАБОЛИТ ПЛЮС

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Цель исследования: изучить эффективность комплексной курортной терапии НАЖБП с использованием питьевой минеральной воды Ессентуки-Новая в сочетании с приемом БАД Метаболит Плюс.

Материал и методы исследования. Обследовано 52 больных с НАЖБП в возрасте 49,8±5,7 лет. Из них – 20 (38,5%) больных с неалкогольным стеатогепатитом и 32 (61,5%) – со стеатозом печени. Все больные получали курортную терапию, включающую лечебное питание, лечебную физкультуру и внутренний прием минеральной воды Ессентуки-Новая и БАД Метаболит Плюс по 1 чайной ложке во время еды 3 раза в день.

Результаты исследования. После проведенного лечения у большинства больных улучшились клинические показатели, у 87,5% достоверно снизились масса тела и ИМТ, у 77,3% нормализовались печеночные пробы, у 77,5% отмечено снижение уровня общего холестерина, триглицеридов, липопротеидов низкой и очень низкой плотности (соответственно с 6,42±0,1 до 5,52±0,17, с 2,25±0,05 до 1,88±0,11, с 4,17±0,15 до 3,51±0,18 и с 0,98±0,05 до 0,8±0,05 ммоль/л (p<0,05)). У больных с гиперинсулинемией уровень инсулина снизился с 17,8±0,9 до 11,5±0,7 мкМЕ/мл, индекс инсулинорезистентности НОМА-IR - с 4,11±0,19 до 2,58±0,16, (p<0,05). Отмечено улучшение показателей перекисного гомеостаза: повышенный уровень малонового диальдегида снизился у 77,5% больных с 6,12±0,11 до 3,83±0,12 ммоль/л, а сниженная концентрация каталазы увеличилась у 75% больных от 11,18±0,54 до 20,21±0,62 мккат/л (p<0,05).

Заключение. Комплексная курортная терапия с применением питьевой маломинерализованной воды «Ессентуки-Новая» и БАД Метаболит Плюс способствует уменьшению клинических симптомов заболевания, улучшению функционального состояния печени, липидного обмена, снижению инсулинорезистентности, а также нормализации окислительного гомеостаза у больных с неалкогольной жировой болезнью печени.

ЧАСТОТА СТЕАТОЗА ПЕЧЕНИ У БОЛЬНЫХ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ В СОЧЕТАНИИ С СУБКЛИНИЧЕСКИМ ГИПОТИРЕОЗОМ

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Цель исследования. Оценить частоту стеатоза печени у больных первичным субклиническим гипотиреозом (СГ) в сочетании с артериальной гипертензией (АГ).

Материалы и методы. Проведен сравнительный анализ у 101 пациента с первичным СГ в сочетании с АГ (средний возраст 52,74±8,47 лет) и больных гипертонической болезнью (111 больных, средний возраст 50,04±10,12 лет). Индекс массы тела в группах был сопоставим - 32,88±5,44 и 32,71±4,19 кг/м². Всем больных выполнено лабораторное обследование и ультразвуковое исследование (УЗИ) щитовидной железы, общих сонных артерий и печени. Оценивали размеры печени, эхогенность и эхоплотность паренхимы, архитектуру сосудистого рисунка, состояние внутри и внепеченочных желчных протоков, диаметр воротной и нижней полой вен. Статистические данные представлены в виде M±SD.

Результаты. У больных СГ в сочетании с АГ выявлена достоверно более высокий уровень дислипидемии по сравнению с больными ГБ (общий холестерин - 5,97±0,96 и 5,61±0,97 ммоль/л, p<0,01, триглицериды -1,65±1,00 и 1,2±0,62 ммоль/л, p<0,001, ЛПНП - 3,57±0,78 и 3,31±0,82 ммоль/л, p<0,02), выявлена положительная корреляция средней силы между уровнем ТГП и степенью нарушения липидного обмен (r=0,49). Уровень трансаминаз у больных СГ с АГ был достоверно выше (АЛТ - 40,07±22,06 и 25,28±6,64 ммоль/л, p<0,001, АСТ - 29,79±8,53 и 22,50±4,54 ммоль/л, p<0,001). У пациентов с СГ и АГ атеросклеротические бляшки в области сонных артерий выявлялись в 2,7 раз чаще, чем у больных с ГБ (16,8% и 6,3%). Сагитальный размер печени у больных СГ с АГ был достоверно выше, чем у больных ГБ (170,53±17,36 и 161,61±15,98 мм, p=0,001). УЗИ признаки стеатоза печени (повышение эхогенности и эхоплотности, обеднение сосудистого рисунка паренхимы в сочетании с гепатомегалией) у больных СГ с АГ выявлялись в 2 раза чаще (74% против 38%). Таким образом, дислипидемия и стеатоз печени у больных СГ с АГ встречается достоверно чаще, чем у больных ГБ.

ОПУХОЛИ ПЕЧЕНИ

ХИМИОТЕРАПИЯ АЛЬВЕОКОККОЗА ПЕЧЕНИ

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Альвеококкоз печени – серьезная проблема хирургической гепатологии. Характеристики паразита: медленное, скрытое течение, инфильтрующий рост, инвазия вдоль клетчатки сосудисто-секреторных ножек к воротам печени. Сложности при лечении больных с альвеококкозом печени: большой дефицит непораженной паренхимы печени, наличие желтухи, фоновый цирроз, высокий удельный вес паллиативных операций.

Цель исследования: обосновать необходимость адьювантной и неoadьювантной химиотерапии альвеококкоза печени.

Материалы и методы: 125 оперированных пациентов: мужчин – 95, женщин – 30. Возраст: 16–79 лет. Локализация: правая половина – 92(73,6%), левая – 29(23,2%), билобарная – 4. Два этапа в хирургическом лечении: без неoadьювантной терапии и с дооперационным назначением немозола.

I этап (n=76): правосторонняя гемигепатэктомия – 48, двухэтапные операции – 6, циторедукция – 17, вскрытие и дренирование полости паразита – 5. II этап (n=49): правосторонняя гемигепатэктомия – 30, двухэтапные операции – 1, циторедукция – 2, бисекментэктомии – 9, левосторонняя лобэктомия – 7.

Схема применения немозола (альбендазол): до операции 400–800 мг в сутки 28 дней, 14 дней перерыв, курс терапии 3–6 месяцев. После операции 800 мг 3–6 месяцев, затем 400 мг до 1 года, а при паллиативной операции до 3х лет.

Результаты: I группа: осложнения – 9 (11,84%), летальность – 4 (5, 26%), рецидивы – 7 (9,21%), 5-летняя выживаемость – 56 (73,68%). II группа: осложнения – 5 (10,2%), летальность – 2 (4,08%), рецидивы – 3 (6,12%), 5-летняя выживаемость – 40(81,63%).

Выводы: полученные результаты позволяют рекомендовать не только адьювантную, но и неoadьювантную терапию альвеококкоза печени. Эффективность дооперационного использования немозола подтверждена морфологически.

ГЕПАТОЦЕЛЛЮЛЯРНАЯ КАРЦИНОМА В ИСХОДЕ ХРОНИЧЕСКОЙ ДЕЛЬТА-ИНФЕКЦИИ

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Цель: представить клиническую характеристику пациентов с гепатоцеллюлярной карциномой (ГЦК) в исходе хронической дельта-инфекции, проживающих в эндемичном регионе по этой инфекции (Республика Тыва, Россия).

Материал и методы. С помощью иммунологических и молекулярно-генетических методов обследовали 318 пациентов 4-77 (39,1±10,6) лет с хронической дельта-инфекцией. Из них: мужчин было 123 (38,7%), женщин - 195 (61,3%), 68 пациентов наблюдали в динамике с 2009 г. по 2012 г.

Результаты. В 77,4% (246/318) случаев диагностирован хронический гепатит D (ХГD), в 22,6% (72/318) – цирроз печени D (ЦП D). У всех больных инфицирование вирусом гепатита D (ВГD) было зарегистрировано на фоне уже имеющегося ХГВ (суперинфекция). При динамическом наблюдении в течение 4-х лет у 14,7% (10/68) пациентов отмечено прогрессирование ХГD в ЦПD, у 14,7% (10/68) - декомпенсация ЦПD и у 11,8% (8/68) – развитие ГЦК. Показано, что ГЦК формируется у небольшой части пациентов, что обусловлено быстрым прогрессированием инфекции, развитием декомпенсированного ЦП и его осложнений (кома, кровотечение) с высокой частотой летальных исходов. Средняя длительность заболевания от момента предполагаемого инфицирования ВГD до развития ГЦК составила – 15-20 лет, а средний возраст пациентов с ГЦК – 43,5±8,4 лет. Диагноз ГЦК у всех больных установлен на поздней стадии заболевания – уже при наличии нескольких очагов в печени (по данным УЗИ). Средний уровень активности АЛТ составил 48±16,6 Е/л, содержание билирубина не превышало 11,8±1,8 мкмоль/л. Репликация вирусов гепатитов установлена в 4 из 8 случаев ГЦК: РНК ВГD обнаружена у 2 пациентов, ДНК ВГВ - у 1. Одна пациентка с ГЦК погибла вследствие кровотечения из варикозно расширенных вен пищевода и желудка. В данном наблюдении выявлена репликация обоих вирусов.

Заключение. В эндемичном регионе (Республика Тыва, Россия) хроническая дельта-инфекция преимущественно выявляется среди лиц молодого и трудоспособного возраста и характеризуется прогрессирующим течением, быстрым развитием ЦП, ГЦК и высоким уровнем летальности.

СИСТЕМНЫЙ ПОДХОД В ГЕПАТООНКОПРЕВЕНЦИИ

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Цель. В рамках составления индивидуальных программ гепатоонкопревенции, выявить наличие экзогенных, системно-органных и локальных туморогенных факторов в гепатоканцерогенезе.

Материалы и методы. У 80 больных с верифицированным гепатоцеллюлярным раком (ГЦР) ретроспективно изучены коморбидные факторы возникновения опухоли (117 заболеваний), а также морфологические изменения в паратуморальных тканях печени. Контроль составили 40 пациентов с непаразитарными кистами печени (НКП). Статистическая валидность полученных данных верифицировалась с помощью индекса OR.

Результаты: приведены в таблице.

Факторы	ГЦР	НКП	OR
	n %	n %	
Органно-системные процессы:			
Сахарный диабет	11 (13,7%)	1 (2,5%)	5,5
Гипералиментация	41 (51,2%)	16 (40,0%)	1,3
Метаболический синдром	19 (23,7%)	3 (7,5%)	3,2
Желчнокаменная болезнь	18 (22,5%)	2 (5,0%)	4,5
Хронический панкреатит	13 (16,2%)	1 (2,5%)	6,5
Заболевания печени:			
Вирусные гепатиты -HBV, HCV	23 (28,7%)	2 (5,0%)	5,8
Циррозы печени - Child A,B,C	16 (20,0%)	1 (2,5%)	8,0
Гепатостеатоз	15 (18,7%)	3 (7,5%)	1,9
Алкогольные гепатиты	8 (10,0%)	1 (2,5%)	4,0

Структура печени вне опухолевых очагов характеризовалась наличием фиброза – 40%, воспалительной лимфоцитарной инфильтрации – 53,3% (OR 5,2 и 6,6 соответственно).

Выводы: Выявлены системные и локальные факторы, ведущие к воспалительно-фибротическим изменениям печени с последующей канцер-трансформацией, что диктует необходимость назначения урсодезоксихолевой кислоты (урсофальк), обладающей комплексными воздействиями на основные звенья гепатоканцерогенеза.

ВНУТРИПРОСВЕТНАЯ ЛУЧЕВАЯ ТЕРАПИЯ В СОСТАВЕ КОМБИНИРОВАННОГО ЛЕЧЕНИЯ РАКА ВНЕПЕЧЕНОЧНЫХ ЖЕЛЧНЫХ ПРОТОКОВ

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Цель исследования: оценить возможности внутрипросветной лучевой терапии (ВЛТ) в составе комбинированного лечения больных раком внепеченочных желчных протоков. **Материалы и методы:** 68 пациентам со злокачественными стриктурами внепеченочных желчных протоков, осложненных механической желтухой, проведено комбинированное лечение, включающее в себя чрескожное чреспеченочное дренирование желчных протоков, ВЛТ с последующей реконструкцией билиарной системы. ВЛТ на область внепеченочных желчных протоков проводилась с использованием аппарата микроселектрон HDR на расстоянии 10мм от центра источника. Суммарная очаговая доза составила 60иГр. Последующая реконструкция желчных протоков осуществлялась тремя способами: стентированием желчных протоков, оставлением транспеченочного дренажа, формированием холангиогастротомы. **Результаты:** разработанная методика комбинированного лечения рака внепеченочных желчных протоков была выполнена 68 пациентам. 43 пациентам проведена только ВЛТ в СОД = 60иГр. 4 – ВЛТ (СОД= 42иГр) дополнена дистанционной гамма-терапией (СОД = 30-35Гр). 22 больным выполнена операция в объеме резекции гепатикохоледоха с последующей ВЛТ зоны культей долевых протоков печени (СОД=60иГр). 49 пациентам в последующем оставлен постоянный транспеченочный катетер, 16 больным произведена установка эндопротезов wallstent, транспеченочный катетер удален, 2 выполнена реконструктивная операция, 1 – пункционная холангиогастротомия. В группу контроля (n=34) вошли больные, которым было выполнено только паллиативное дренирование билиарной системы. Выживаемость в группе анализа (n=68) составила 100%, 85%, 66%, 46%, 22% за 3, 6, 9, 12 и 24 месяца соответственно. Выживаемость в группе контроля составила соответственно 96%, 67%, 23%, 4%, 0%.

Заключение: разработанная методика комбинированного лечения рака внепеченочных желчных протоков позволила достоверно увеличить продолжительность жизни больных.

КЛИНИКО-ЛАБОРАТОРНЫЕ ОСОБЕННОСТИ ГИПОГРАНУЛЯРНОГО ВАРИАНТА ОСТРОГО ПРОМИЕЛОЦИТАРНОГО ЛЕЙКОЗА

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Современной клинической гематологией достигнуты несомненные успехи в лечении острого промиелоцитарного лейкоза (М3 по классификации ФАБ). Однако большую резистентность к терапии проявляет гипогранулярный вариант (ГТВ) промиелоцитарного лейкоза. Целью настоящей работы было выявление клинико-лабораторных особенностей данного варианта М3. Проанализированы все случаи М3, зарегистрированные в течение года в практике гематологического отделения Краевой клинической больницы. Всего за год зарегистрированы 6 случаев впервые выявленного острого промиелоцитарного лейкоза, в двух случаях морфологически описан гипогранулярный вариант. Для 4 случаев классического М3 были характерны лейкопения, выраженная тромбоцитопения (количество тромбоцитов менее 10 тыс. в мкл). В обоих случаях с гипогранулированными бластами наблюдался лейкоцитоз (20-30 тысяч лейкоцитов в мкл), количество тромбоцитов в пределах 25 -50 тыс. в мкл. Геморрагический синдром был менее выражен у больных с ГТВ М3, вероятно, цитоплазма бластных клеток у данной группы больных содержала меньше гранул с гепариноподобным веществом. У одного больного с ГТВ наблюдалась генерализация лейкоемии с поражением многих органов: печени, кишечника, легких. Мы сочли интересным для исследования иммуноцитохимических особенностей бластов клиническое наблюдение М3 с двумя морфологически отличающимися бластными субпопуляциями. В препаратах костного мозга наблюдались как гипогранулированные, так и гипергранулированные бластные клетки, в препаратах, приготовленных из периферической крови наблюдались исключительно бласты с малой гранулированностью. Вероятно, данная популяция в меньшей степени «удерживалась» микроокружением костного мозга. Иммунофенотип субпопуляций был идентичен: CD34-, HLA-DR-, CD13+, CD33+, МРOсуt+. Цитохимическое исследование мембранной миелопероксидазы выявило ее высокую активность на бластах костного мозга и почти полное отсутствие активного фермента на бластных клетках крови.

**ТРАНСПЛАНТАЦИЯ
ПЕЧЕНИ, ПЕЧЕНОЧНАЯ
НЕДОСТАТОЧНОСТЬ**



ВЕДЕНИЕ ЛИСТА ОЖИДАНИЯ НА ТРАНСПЛАНТАЦИЮ ПЕЧЕНИ И ПОСЛЕОПЕРАЦИОННЫЙ МОНИТОРИНГ ПАЦИЕНТОВ, ПОЛУЧИВШИХ ДОНОРСКИЙ ОРГАН, В НИЖНЕМ НОВГОРОДЕ

УСТОЙЧИВЫЙ ВИРУСОЛОГИЧЕСКИЙ ОТВЕТ В ЛЕЧЕНИИ HCV-ИНФЕКЦИИ ПОСЛЕ ТРАНСПЛАНТАЦИИ ПЕЧЕНИ

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В Нижнем Новгороде с 2009 года осуществляется трансплантация печени (ТП) от посмертного донора. Лист ожидания (ЛО) на ТП ведется с 2007 года, число больных в нем постоянно меняется (от 15 до 74). В ЛО в декабре 2012 году находится 55 пациентов, из них 34 женщины и 21 мужчина, средний возраст 46,3±22,6 лет (от 19 до 60 лет). Количество больных с вирусными циррозами печени (ЦП) составляет 16 (29,1%) человек.

За период с 2009 по 2012 год от посмертного донора выполнено 26 ТП (в т.ч. 3 пациентам с вирусными ЦП и одному - ТП и почки). Летальность в раннем послеоперационном периоде составила 19,2% (5 человек). Причины летальности: ТЭЛА, фульминантная печеночная недостаточность, сепсис, панкреонекроз. В ЛО с 2007 года летальность пациентов составила 36 человек.

После ТП все больные 1 раз в три месяца выполняют биохимические анализы, исследование концентрации иммуносупрессивных препаратов в крови, УЗИ+УЗДГ трансплантата.

Пациенты получают следующие схемы иммуносупрессии: препараты такролимуса или циклоспорина (6 пациентов)+микофенолаты (17 пациентов)+ГКС (4 пациента). Трехкомпонентная схема иммуносупрессии связана с аутоиммунными причинами ЦП. Однокомпонентную схему получают пациенты с развитием лейкопении или язвенного колита. В общей структуре иммуносупрессии принимают препараты циклоспорина 6 (23,1%) пациентов, препараты такролимуса 20 (76,9,8%). Конверсий иммуносупрессивных препаратов не было.

Таким образом, только полное комплексное обследование больных позволяет тщательно осуществить отбор пациентов для постановки в ЛО на ТП, выявить показания и противопоказания, значительно снизить осложнения в посттрансплантационном периоде. Детальный мониторинг пациентов после ТП помогает выявить возможные осложнения на раннем этапе, предупредить их дальнейшее развитие и прогрессирование.

Рост числа HCV-положительных реципиентов, тяжелое и непредсказуемое течение возврата HCV-инфекции требуют проведения ПВТ после ортотопической трансплантации печени (ОТП), в зависимости не от срока после ОТП, а от общего статуса пациента, тяжести течения возврата гепатита С, стадии фиброза, наличия хирургических и/или инфекционных осложнений, состояния почечной функции, выраженности цитопении. В период 12/2004-12/2012 в нашем центре 31 HCV-положительному реципиенту выполнены ОТП. Из 14 пациентов, кому проводилась ПВТ ПЕГ ИФН+рибавирин, 9 (64,3%) достигли устойчивого вирусологического ответа (УВО). ПВТ у больных, достигших УВО, была начата на сроке 2, 7,12,15 месяцев после ОТП на фоне монотерапии такролимусом или циклоспорином А. Течение возврата варьировалось от мягкого до тяжелого (1 случай фиброзирующего холестатического гепатита С). У четырех больных зарегистрировано быстрое прогрессирование фиброза F0-F 2 за 6 месяцев. На момент начала ПВТ инфекционные и хирургические осложнения отсутствовали. Ни у одного больного не было сахарного диабета, у 5 присутствовала артериальная гипертензия. Скорость клубочковой фильтрации (СКФ), как показатель функции почек , находилась в диапазоне 61-105 мл/мин, гематологические показатели: Hb 87-144г/л, RBC 2,9-5,07, WBC 1,4-3,7, NEU 30-68%,PLT 57000-341000. У трех больных был генотип 3а, у 6-1в. В одном случае ПВТ продолжалась 72 недели в виду развития медленного вирусологического ответа (МВО), в другом лечение было прекращено на 6 неделе лечения в виду стойкого повышения уровня сывороточного билирубина вопреки отрицательной HCV RNA со второй недели лечения. У остальных больных лечение соответствовало протоколу относительно генотипа вируса гепатита С(24-48 недель). В одном случае ПВТ была остановлена после достижения раннего вирусологического ответа (РВО) на 15 неделе, из-за абсцесса правой доли печени. Спустя 3 месяца уровень виремии составлял 2,8*10⁷ МЕ/мл. Повторная попытка спустя 8 месяцев привела к достижению РВО и УВО. Среди НЯ у больных с УВО с наибольшей частотой (100%) встречались тромбоцитопения и нейтропения, анемия была зарегистрирована у 78%, психические расстройства развились у двух больных, инфекционное осложнение было диагностировано в одном случае.

ОПЫТ ЛЕЧЕНИЯ ВОЗВРАТА HCV-ИНФЕКЦИИ В ПОСТТТРАНСПЛАНТАЦИОННОМ ПЕРИОДЕ

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Возврат вирусного гепатита С (ВГС) после ОТП у HCVРНК – положительных реципиентов универсален и результаты таких пациентов хуже, чем в HCV –негативных. Широко известно, что цирроз трансплантата печени формируется почти у четверти этих реципиентов в течение 5 -10 лет после ОТП. Лечение возврата гепатита С комбинированной противовирусной терапией (ПВТ) является единственным вариантом в настоящее время, но он ограничен противоречивой частотой устойчивого вирусологического ответа (УВО). Дискутабельными остаются время начала лечения и модификация иммуносупрессии. Увеличение числа пациентов с HCV - ассоциированным циррозом печени (ЦП HCV), тяжелое и непредсказуемое течение возврата ВГС и неблагоприятный исход HCV – положительных реципиентов по-прежнему остается драматической проблемой на поле трансплантации печени. За 8 лет (12/2004-12/2012) в нашем центре выполнено 138 ОТП 132 реципиентам. Наиболее частым показанием является ЦП HCV – 31(23,5%), причем в 6 случаях осложнившийся развитием гепатоцеллюлярной карциномы (ГЦК). 19,4% больных погибли:3 реципиента- в раннем посттрансплантационном периоде, 3-на отдаленных сроках наблюдения.14 больным (45,2%) проведена ПВТ ПЕГ ИФН+рибавирин. Сроки начала ПВТ – от 40 суток до 28 месяцев после ОТП. Общая частота УВО составила 64,3%. 4 пациента с 3а генотипом развили быстрый вирусологический ответ(БВО), ранний вирусологический ответ (РВО) и впоследствии УВО был зарегистрирован у 3 больных. У 1 реципиента с 1в генотипом был зарегистрирован БВО, РВО присутствовал в 4 случаях, частичный ранний вирусологический ответ(чРВО) – у 3-х, медленный вирусологический ответ(МВО) – у 2 больных. Непосредственный вирусологический ответ (НВО) на момент завершения ПВТ достигнут у 7 пациентов, в то время как УВО – только у 6. У всех пациентов ПВТ проводилась на фоне иммуносупрессивной монотерапии:10 – такролимус, 4 – циклоспорин А. Ни в одном случае реакции отторжения трансплантата не было. Нежелательными явлениями ПВТ после ОТП были анемия,тромбоцитопения,ле йкопения, в 2-ух случаях на фоне лечения у больных развились инфекционные осложнения(холангиогенный абсцесс печени – 1,правосторонняя пневмония), у 1-ого больного зарегистрирован острый психоз. Полученные результаты свидетельствуют , что ПВТ после ОТП может изменить прогноз HCVРНК-положительных реципиентов, быть эффективной и безопасной, однако требует определения оптимальных сроков начала лечения.

СЕМИЛЕТНИЙ ОПЫТ ОРТОТОПИЧЕСКОЙ ТРАНСПЛАНТАЦИИ ПЕЧЕНИ (ОТП) В ФЕДЕРАЛЬНОМ НАУЧНОМ ЦЕНТРЕ ТРАНСПЛАНТОЛОГИИ И ИСКУССТВЕННЫХ ОРГАНОВ ИМ. В.И. ШУМАКОВА (ФНЦ ТИО).

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больных после ретрансплантации оказалась существенно ниже-не более 50% по сравнению с до 90% у перенесших одну ОТП. Выживаемость HCV-положительных реципиентов через 1 и 3 года была значительно ниже таковой у HCV-положительных реципиентов и составила 70 и 76% против 93,1% и 93%, соответственно. С 2008 года стандартная противовирусная терапия проводится реципиентам с целью предотвращения прогрессирования фиброза трансплантата.

Вступление: За период с 2006 по 2011 г. в 38 медицинских центрах Российской Федерации выполнено 918 ОТП, из них 503 (54,8%) трупных трансплантаций, 395 (45,2%) – живых родственных доноров. Абсолютный прирост показателя за пятилетний период наблюдения составил +116 ОТП (+131,8%).

Восьми пациентам ОТП была выполнена по поводу ГЦК на фоне ЦП вирусной этиологии. (средний возраст - 56,75±11 лет). Выживаемость через 1 и 3 года составила 86 и 68%, соответственно. Рецидив констатирован у 2 больных, выживших за пределы Миланских критериев. Смерть наступила через 11 и 13 месяцев, соответственно.

Цели и задачи: изучить динамику количества ортотопической трансплантации печени (ОТП), спектр показаний к операции, выживаемость реципиентов и трансплантата за 2004-2011 годы в ФНЦ ТИО.

Выводы: за период с 2004 по 2011 год количество ОТП в России значительно возросло продемонстрированы хорошие отдаленные результаты операций: выживаемость реципиентов, трансплантата, количество послеоперационных осложнений, ретрансплантаций, сравнимых с мировым опытом. Показано, что выживаемость HCV-положительных реципиентов и больных с ГЦК, не соответствующих Миланским критериям, значительно ниже.

Материалы и методы: В период с декабря 2004 по июнь 2011 года в Федеральном научном центре трансплантации и искусственных органов им. В.И. Шумакова было выполнено 100 ОТП 94 пациентам в возрасте от 11 от 71 года. Средний возраст реципиентов составил 43,8±13,3 года. Сроки наблюдения составили 6-84 месяцев, в среднем 45,6±2,4 месца. Показания к ОТП листе ожидания были следующей: хронический гепатит С – 24%, хронический гепатит В – 15% (суммарно вирусные гепатиты – 29%), гепатоцеллюлярная карцинома – 8%, первичный билиарный цирроз – 21%, первичный склерозирующий холангит – 6%, алкогольный цирроз печени – 9%, цирроз печени в исходе аутоиммунного гепатита – 9%, поликистоз печени 1%, синдром Бадда-Киари 4%, нейроэндокринная опухоль – 1%, другие заболевания- 6%. Преобладали пациенты с ЦП класс В по Child-Turcotte-Pugh [46 человек (49%)], среднее значение по шкале MELD составило 17±7 (от 9 до 41,5). Ретрансплантация выполнена 6 (6,4%) пациентам (4-в раннем послеоперационном периоде).

Суммарный показатель выживаемости пациентов через 1, 3 и 5 лет после ОТП составил 89, 87 и 87%, соответственно. Показатель выживаемости трансплантата в течение 1, 3 и 5 лет составил 85, 82 и 70%, соответственно. Случаев интраоперационной летальности не наблюдалось. В раннем послеоперационном периоде умерло 5 (5,3%) реципиентов. Выживаемость

ХОЛЕСТАТИЧЕСКИЕ ЗАБОЛЕВАНИЯ ПЕЧЕНИ



ЦИРРОЗ ПЕЧЕНИ И ЕГО ОСЛОЖНЕНИЯ



ОПЫТ РАБОТЫ С ГРУППОЙ БОЛЬНЫХ ЦИРРОЗОМ ПЕЧЕНИ, ИМЕЮЩИХ ПОКАЗАНИЯ ДЛЯ ЕЕ ТРАНСПЛАНТАЦИИ

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Одной из важных задач ведения больного с декомпенсированным циррозом печени является тщательная оценка пациента при включении в лист ожидания трансплантации, поскольку ее успешный исход требует оптимального выбора реципиента и оптимального выбора времени операции. Изучение структуры патологии, являющейся противопоказанием для включения в лист ожидания пациентов с циррозом печени, а также анализ движения пациента в листе ожидания является важной задачей и опыт подобной работы в России пока небольшой.

Материалы и методы: В исследование включались больные с терминальной стадией хронического заболевания печени и показаниями для ее трансплантации, госпитализированные в областной гепатологический центр с 2005 г. по 2010 г. (n=618).

Результаты: После проведения обследования всех пациентов, имевших показания для пересадки в соответствии с протоколом, в лист ожидания было включено 196 больных (31,7%). Число отказавшихся от операции составило 57 больных (9,2%). Группа больных, у которых при обследовании были выявлены те или иные противопоказания для проведения пересадки печени, составила 365 чел. (59,1%). Среди наиболее часто выявляемых заболеваний, препятствующих включению в лист ожидания потенциальных реципиентов, был алкоголизм - 79 чел.(21,6%) и заболевания сердечно – сосудистой системы 51 чел. (14,0%). Крайне тяжелое состояние пациентов, как следствие позднего обращения, не позволившее включить их в лист ожидания, было у 19 чел. (5,2%). Кроме того, течение заболевания у этих больных сопровождалось инфекционными осложнениями. Еще 93 чел. (25,5%) не были включены в лист ожидания в связи со стабилизацией процесса, когда, несмотря на то, что они поступали в отделение в крайне тяжелом, декомпенсированном состоянии, и по классификациям Чайлд-Пью и MELD объективно имели все показания для трансплантации, проводимая консервативная терапия дала стабилизацию процесса и, в ряде случаев, его регресс.

КЛИНИЧЕСКОЕ НАБЛЮДЕНИЕ: ТЕЧЕНИЕ ТРОМБОЗА ПОРТАЛЬНОЙ ВЕНЫ У ПАЦИЕНТА С ЦИРРОЗОМ ПЕЧЕНИ

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Тромбоз воротной вены - частое осложнение цирроза печени, его частота варьирует по разным данным от 7 до 16%, и увеличивается по мере прогрессирования заболевания. У пациентов, находящихся в листе ожидания трансплантации печени, данная патология составляет до 30% случаев. При локализации тромба в воротной вене или в ее внутрипеченочных ветвях трансплантация возможна лишь после всестороннего обследования больного и оценки степени распространенности процесса.

Пациент В. 48 лет наблюдается в Свердловском областном гепатологическом центре с 2010 г. с диагнозом: Цирроз печени вирусной этиологии в исходе НСV инфекции, Child С (11баллов), MELD - 17, порталная гипертензия (асцит, спленомегалия), гиперспленизм. С этого же времени включен в лист ожидания трансплантации печени. Постоянно получал терапию: мочегонные, гепатопротекторы, ингибиторы протонной помпы, ферменты, римфаксимин, дюфалак, периодически по показаниям альбумин. Ухудшение самочувствия с августа 2011г, отметил появление болей в животе, повышение температуры до 37,7С, увеличение живота в объеме, госпитализирован в гепатологический центр. В анализах определялось повышение уровня общего билирубина до 134 мкмоль/л, гипоальбуминемия 28 г/л, повышение уровня МНО до 1,45 и тромбоцитопения до 62х109/л. При компьютерной томографии брюшной полости в сентябре 2011 г. был впервые выявлен тромбоз воротной, селезеночной и верхнебрыжеечной вен. В связи с этим пациенту был назначен сулодексид в дозе 1 капс (250 ед) 2р в сутки. При контрольной КТ в январе 2012 г. была выявлена положительная динамика, заключававшаяся в уменьшении распространенности тромбоза с определением лишь пристеночных тромбов селезеночной и воротной вен.

Заключение – максимально раннее назначение антикоагулянтной терапии при возникновении тромбоза воротной вены, как осложнения цирроза печени, даже в условиях имеющейся коагулопатии, вероятно создает возможность лизиса тромба и/или его реканализации. Данный эффект крайне важен для продления жизни пациента и сохранения возможности трансплантации печени в будущем.

Заключение: Решение о включении больного в лист ожидания является сложной задачей, требующей всесторонней оценки больного и должно приниматься после определенного периода наблюдения за пациентом, который позволяет провести полное обследование и оценить степень обратимости декомпенсации процесса на фоне проводимой терапии.

ДИНАМИКА ПОРТАЛЬНОГО КРОВОТОКА ПРИ ЦИРРОЗЕ ПЕЧЕНИ

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Цель исследования – оценка влияния комбинации стандартной терапии цирроза печени с гипотензивными средствами на динамику портального кровотока.

Обследовано 24 больных ЦП в возрасте от 29 до 58 лет, с длительностью заболевания от 11 месяцев до 10 лет. Диагноз был подтвержден данными клинических, лабораторных, инструментальных исследований. Контрольная (I группа) - базисная терапия ЦП, II группа – базис+кардиорм(2,5 мг/сут), III группа – базис+рамприл(5 мг/сут). У больных определяли изменение линейной (ЛС), объемной(ОС) скоростей в воротной (ВВ), селезеночной(СВ) венах для 3-х групп пациентов.

Результаты: ЦП наиболее часто, по данным нашего исследования, встречался у мужчин (37,5%) в возрасте от 30 до 50 лет (60%). ЛСВВ увеличивалась относительно данных при поступлении для I группы на 2,4%, II группы на 7,4%, III группы на 11,2%, относительно данных контрольной группы – увеличение этого показателя на 3,5% у II группы и на 4,9% у III группы, соответственно. ЛССВ увеличивалась относительно данных при поступлении для I группы на 4,3%, II группы на 9,6%, III группы на 15,4%, относительно данных контрольной группы – наблюдалось увеличение этого показателя на 4,1% у II группы и на 6,1% у III группы, соответственно. ОСВВВ увеличивалась относительно данных при поступлении для I группы на 5,1%, II группы на 9,7%, III группы на 16,2%, относительно данных контрольной группы – увеличение на 4,5% у II группы и на 3,7% у III группы, соответственно. ОССВ увеличивалась относительно данных при поступлении для I группы на 6,1%, II группы на 8,3%, III группы на 16,1%, относительно данных контрольной группы – увеличение у 3,6% у II группы и на 3,6% у III группы.

Выводы: при включении гипотензивных препаратов (кардиорм (2,5 мг/сут), рамприл (5 мг/сут)) в схему стандартной терапии ЦП отмечалось значительное улучшение скоростных показателей кровотока в системе ВВ и СВ. Кардиорм (2,5 мг/сут) увеличивал ЛСВВ на 7,4%, в СВ – 9,6%, ОСВВ – на 9,7%, в СВ – 10,3%. Рамприл (5 мг/сут) увеличивал ЛСВВ на 11,2 %, в СВ-15,4%, ОСВВ – на 16,2%, в СВ – 18,4%. Более выраженный эффект на скоростные показатели портального кровотока оказывал рамприл (5 мг/сут), что свидетельствует о целесообразности комбинации стандартной терапии с гипотензивными средствами при лечении больных ЦП.

ЦИРРОЗ ПЕЧЕНИ И ЕГО ОСЛОЖНЕНИЯ

НОВЫЕ ПОДХОДЫ К КОРРЕКЦИИ ПОРТАЛЬНОЙ ГИПЕРТЕНЗИИ У БОЛЬНЫХ ЦИРРОЗОМ ПЕЧЕНИ

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Цель работы: изучить влияние препаратов групп β-адреноблокаторов и и - АПФ на коррекцию синдрома ПГ у больных ЦП.

Обследовано 24 больных ЦП в возрасте от 29 до 58 лет, с длительностью заболевания от 11 месяцев до 10 лет. Диагноз был подтвержден данными клинических, лабораторных, инструментальных исследований. Контрольная (I группа)-базисная терапия ЦП, II группа–базис+кардиорм(2,5 мг/сут), III группа–базис+рамприл(5 мг/сут). У больных определяли степень ПГ, стадию компенсации, изменение размеров печени, селезенки, динамику скоростных показателей воротной и селезеночной вен.

Результаты: У3-признаки ПГ обнаруживались у 87,5% больных. Больные ЦП с ПГ класса В составили 25%, класс С – 75%. Размеры печени больных были увеличены в 91,7% случаев, уменьшены – в 8,3%, нормальных размеров не обнаружено. ПЗР правой доли: у II группы увеличился на 6,8% относительно данных при поступлении, на 4,2% относительно I группы, у III группы увеличение на 12,4% относительно данных при поступлении, на 8,5% относительно I группы. ВНР правой доли печени – для III группы – увеличился на 7,1% относительно данных при поступлении и на 4,1% относительно I группы. Длинник селезенки увеличен относительно данных при поступлении для I группы на 2,9%, II группы на 3,7%, III группы на 5,9%, относительно данных I группы – увеличение на 3,1% у II группы и на 3,9% у III группы, соответственно. Поперечник селезенки: для III группы увеличен на 2,6% относительно данных при поступлении и на 2,9% относительно I группы. Кардиорм (2,5 мг/сут) увеличивал ЛСВВ на 7,4%, в СВ – 9,6%, ОСВВ – на 9,7%, в СВ – 10,3%. Рамприл (5 мг/сут) увеличивал ЛСВВ на 11,2 %, в СВ-15,4%, ОСВВ – на 16,2%, в СВ – 18,4%.

Выводы: преобладание пациентов с ПГ класса С свидетельствует о том, что необходимость в госпитализации и проведении неотложной интенсивной терапии происходит при осложненном течении ЦП. При включении гипотензивных препаратов в схему лечения ПГ у больных ЦП отмечается значительная коррекция размеров печени и селезенка, что свидетельствуют об усилении процессов микроциркуляции в исследуемых органах. Более выраженный эффект на коррекцию ПГ оказывал рамприл (5 мг/сут), способствующий улучшению почечного кровотока как фактора участвующего в формировании ПГ при ЦП.

НОВЫЕ ПОДХОДЫ К КОРРЕКЦИИ ПОРТАЛЬНОЙ ГИПЕРТЕНЗИИ У БОЛЬНЫХ ЦИРРОЗОМ ПЕЧЕНИ

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Цель работы: изучить влияние препаратов групп β-адреноблокаторов и ингибиторов - АПФ на коррекцию синдрома портальной гипертензии (ПГ) у больных циррозом печени (ЦП).

Материалы и методы: обследовано 24 больных ЦП в возрасте от 29 до 58 лет, с длительностью заболевания от 11 месяцев до 10 лет. I группа (контрольная), где пациенты получали базисную терапию (БТ) ЦП, II группа – БТ +кардиорм (2,5 мг/сут), III группа – БТ +рамприл (5 мг/сут). У больных определяли степень ПГ, стадию компенсации ПГ, наличие и частоту осложнений, изменение размеров печени и селезенки.

Результаты: ЦП наиболее часто, по данным нашего исследования, встречался у мужчин (38%) в возрасте от 30 до 50 лет (60%). У3-признаки ПГ обнаруживались у 88% больных. Больные ЦП с ПГ класса В составили 25%, класса С – 75%. Частые осложнения: отечно-асцитический синдром – 100%, печеночная энцефалопатия II-III ст – 95 %, кровотечения из варикознорасширенных вен пищевода и желудка – 67 %, синдром гиперспленизма – 62%. У 92% больных наблюдалось увеличение размеров печени, нормальных размеров не обнаруживалось, в оставшихся случаях размеры уменьшались. Достоверных изменений ПЗР правой доли: у пациентов I группы не отмечалось, во II и III группах он увеличился на 7% и 12% соответственно. Относительно контрольных значений данный показатель возрастал на 4% во II группе и на 9% в III группе. Достоверное увеличение ВНР правой доли (на 7% относительно данных при поступлении и на 4% по отношению к контрольной группе) наблюдалось лишь у больных в III группе. ПЗР и ВНР левой доли печени достоверно не изменялись. Длинник селезенки–увеличивался для I группы на 3%, II группы на 4%, III группы на 6%, относительно данных I группы – увеличение на 3% у II группы и на 4% у III группы, соответственно. Увеличение размеров поперечника были не достоверны.

Выводы: при включении гипотензивных препаратов в схему лечения ПГ у больных ЦП отмечается значительная коррекция размеров печени и селезенки. Более выраженный эффект на коррекцию ПГ оказывал рамприл (5 мг/сут).

ДИНАМИКА ПОРТАЛЬНОГО КРОВОТОКА ПРИ ЦИРРОЗЕ ПЕЧЕНИ

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Цель исследования – оценка влияния комбинации стандартной терапии цирроза печени (ЦП) с гипотензивными средствами на динамику портального кровотока.

Материалы и методы: обследовано 24 больных ЦП в возрасте от 29 до 58 лет, с длительностью заболевания от 11 месяцев до 10 лет. I группа (контрольная), где пациенты получали базисную терапию (БТ) ЦП, которая включала в себя гепатопротекторы, антиоксиданты, мочегонные, витаминные препараты, II группа – БТ +кардиорм (2,5 мг/сут), III группа – БТ +рамприл (5 мг/сут). У больных определяли изменение линейной (ЛС), объемной (ОС) скоростей кровотока в воротной вене (ВВ) и селезеночной вене (СВ).

Результаты: ЦП наиболее часто, по данным нашего исследования, встречался у мужчин (37,5%) в возрасте от 30 до 50 лет (60%). На фоне проводимой терапии при помощи УЗ - диагностики и доплерографии были выявлены следующие динамические изменения: у пациентов получающих базисные средства (I группа) ЛСВВ и ЛССВ увеличивалось на 2% и 4% соответственно, ОСВВ в данной группе поднималась на 5%, а ОССВ на 6%. При включении гипотензивных препаратов в схему стандартной терапии ЦП отмечалось значительное улучшение скоростных показателей кровотока в системе ВВ и СВ. Кардиорм (2,5 мг/сут) увеличивал ЛСВВ на 7,4%, в СВ – 9,6%, ОСВВ – на 9,7%, в СВ – 10,3%. Рамприл (5 мг/сут) увеличивал ЛСВВ на 11,2 %, в СВ-15,4%, ОСВВ – на 16,2%, в СВ – 18,4%. Таким образом, по сравнению с данными контрольной группы, ЛСВВ и ЛССВ увеличивались во II группе на 3,5% и 5% соответственно, в III группе – на 5% и 6%. ОСВВ и ОССВ при добавлении к терапии кардиорма и рамприла, также имели тенденцию к росту по сравнению с контрольными данными, во II группе на 4,5% и 3,6% соответственно, а в III группе на 4% и 3,6%.

Выводы: Более выраженный эффект на скоростные показатели портального кровотока оказывал рамприл (5 мг/сут), что свидетельствует оцелесообразности комбинации стандартной терапии с гипотензивными средствами при лечении больных ЦП.

КОНЦЕНТРАЦИЯ ФЕТАЛЬНОГО ГЕМОГЛОБИНА У БОЛЬНЫХ ЦИРРОЗОМ ПЕЧЕНИ С ЛЕГОЧНОЙ ГИПЕРТЕНЗИЕЙ

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Цель исследования: изучить изменения уровня фетального гемоглобина (HbF) при циррозах печени (ЦП) в зависимости от наличия легочной гипертензии (ЛГ).

Материалы и методы. Концентрация HbF в крови исследовали у 98 больных ЦП (56 мужчин и 42 женщин в возрасте от 35 до 60 лет). Контрольная группа (КГ) - 30 доноров. Для количественного анализа HbF разработан и запатентован способ ракетного электрофореза в агаровом геле. Всем больным проводилось определение диаметра легочной артерии (ДЛА) и среднего давления в легочной артерии (СрДЛА) с помощью ультразвукового сканера «АЛОКА-5500 Prosaund» (Япония).

Результаты: содержание HbF в крови в группе больных ЦП составило в среднем 2,98±0,07% от общего Hb (p<0,001 по сравнению с контролем), причем превышение нормальной концентрации HbF имелось у 72 пациентов. Сравнение значений HbF у больных ЦП по половому признаку показало, что содержание HbF% у мужчин было с высокой степенью достоверности (p<0,001) ниже, чем у женщин (соответственно 2,8±0,09% и 3,35±0,1%). Повышение средних значений показателей концентрации HbF% у женщин, по-видимому, можно объяснить более высокими компенсаторными возможностями женского организма, сохраняющимися, несмотря на развитие ЦП и его осложнений. У 49 больных ЦП отмечены признаки ЛГ, т.е. увеличение ДЛА и СрДЛА выше 25 мм.рт.ст., из них в 12 случаях – в пределах от 30 до 35 мм.рт.ст. В этой подгруппе показатель HbF составил в среднем 3,02±0,03%. У 49 больных СрДЛА было ≤25 мм.рт.ст., а уровень HbF - в среднем 2,86±0,01% от общего Hb. Выявленные различия между сравниваемыми подгруппами были статистически достоверными.

Заключение. Увеличение уровня HbF в крови как маркера тканевой гипоксии у взрослых при ЦП связано с наличием ЛГ. Повышение давления в легочной артерии является следствием гемодинамических изменений в малом круге кровообращения при патологии печени. ЛГ может приводить к нарушению оксигенации крови и к развитию тканевой гипоксии. HbF, являясь маркером тканевой гипоксии, способствует лучшей адаптации, чем Hb взрослого организма к хронической гипоксии

КЛИНИКА ЦИРРОЗОВ ПЕЧЕНИ ГОСПИТАЛЬНЫХ БОЛЬНЫХ

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Цель: анализ клинико-anamnestических особенностей циррозов печени (ЦП) у пациентов в динамике стационарного этапа лечения.

Материал и методы. В условиях терапевтического отделения городского стационара в течение календарного года было пролечено 1726 пациентов. С патологией пищеварительной системы было госпитализировано 138 человек. Заболевания желудочно-кишечного тракта были на третьем месте после сердечно-сосудистых и бронхолегочных. По поводу ЦП получили стационарное лечение 24 пациента: 15 мужчин и 9 женщин в возрасте от 28 до 75 лет (средний возраст 48 лет). Был проведен анализ анамнестических и объективных данных госпитализированных больных.

Результаты. 24 пациента (т.е. 100%) имели анамнестическое злоупотребление алкоголем, у 1 – ЦП развился на фоне хронического вирусного гепатита С. 9 пациентов были госпитализированы по скорой помощи, 6 – переведены из других больниц, 9 – поступали в плановом порядке. Ухудшение состояния развивалось в среднем за 12 дней до госпитализации. В структуре сопутствующей патологии наиболее значимыми были хронические панкреатиты и холециститы (23%) и артериальная гипертензия (13%). Большинство пациентов (26%) были злостными курильщиками, 29% – курили в прошлом. 1 пациент был ВИЧ-инфицированным и страдал наркозависимостью. Ведущими жалобами на момент госпитализации были нарушения стула (27%), слабость (16%), увеличение живота (13%), желтушность кожи и снижение аппетита (по 12%), остальные жалобы – с частотой менее 10%. При объективном осмотре увеличение живота определялось в 83%, расширение подкожных вен передней брюшной стенки – в 68%, боли при пальпации живота – в 40%. К выписке наиболее актуальной оставалась слабость (31%), прочие жалобы уменьшались до частоты менее 10%, увеличение живота сохранялось лишь у 5% больных (лапароцентез выполнялся только 2 больным из 24).

Выводы. Алкоголизм является одним из ведущих факторов риска развития ЦП. Потребность в госпитализации определяется, в первую очередь, выраженностью диспептического, астеновегетативного синдромов, холестаза и портальной гипертензии.

ПРОЧИЕ

XVIII РОССИЙСКИЙ КОНГРЕСС «ГЕПАТОЛОГИЯ СЕГОДНЯ»

ИССЛЕДОВАНИЕ ЗАБОЛЕВАЕМОСТИ ЖКБ ПРИ САХАРНОМ ДИАБЕТЕ НА ПРИМЕРЕ ПОЛИКЛИНИКИ №1 Г. ЯКУТСКА

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Актуальность. Всемирная организация здравоохранения сообщает, что сейчас в мире 6% населения болны сахарным диабетом, это примерно 284,7 миллиона человек. Прогнозы на будущее неутешительны, по мнению специалистов, количество больных будет неуклонно расти, и к 2030 году их станет уже 438,4 миллиона. Известно, что заболевание ЖКБ встречается в любом возрасте, у женщин в 2- 7 раза, чаще чем у мужчин. В 51,7% желчные камни появляются во время беременности и у 25% после родов (Himal H. S., 1996), а так же является сопутствующей патологией при сахарном диабете.

Цель. Изучить заболеваемость желчекаменной болезнью (ЖКБ) при сахарном диабете на примере поликлиники №1 г. Якутска.
Материалы исследования. В качестве материалов исследования взяты амбулаторные карты эндокринологического кабинета поликлиники №1 г. Якутска.
Проработаны 264 амбулаторных карт больных с сахарным диабетом, находящихся на диспансерном учете (2012): из них выявлено 20 (7.6%) больных с ЖКБ (19 женщин и 1 мужчина) в возрасте от 35 -40 лет 1 (5%) человек, от 50 – 60 лет 10(50%) человек, 60- 70 лет 5 (25%) человек, 70- 80 лет 4 (20%) человека. У всех больных сахарный диабет II типа. Коренные жители- 6 (30%), некоренные - 14 (70%). Длительность заболевания ЖКБ свыше 10 лет.
Результаты. При ультразвуковом исследовании выявлены механическая желтуха - 1 (5%) пациента, калькулезный холецистит - 20 (100%), хронический панкреатит – 10 (50%), диффузные изменения паренхимы печени - 6 (30%), гепатомегалия - 3 (15%), жировой гепатоз – 4 (20%). Клиническими проявлениями ЖКБ в виде болевой синдром у 18 (90%) пациентов, проявления билиарной диспепсии у 10 (50%) пациентов, нарушение моторики толстой кишки диагностирована у 16 (80%) больных. Избыточная масса тела и ожирение у 15 (75%) человек. При лабораторном исследовании определяется повышение уровня ГТТП, ЩФ, глюкозы. Содержание АЛТ, АСТ - в пределах нормы. Было проведено

<p>ОЦЕНКА СОСТОЯНИЯ БОЛЬНЫХ В ОТДАЛЕННЫЙ ПЕРИОД ПОСЛЕ ХОЛЕЦИСТЭКТОМИИ ПО ПОВОДУ ЖЕЛЧНОКАМЕННОЙ БОЛЕЗНИ</p> <p>Макарова Ю.В., Волошина Н.Б., Осипенко М.Ф., Литвинова Н.В. <i>ГБОУ ВПО НГМУ Минздрава России, Новосибирск, Россия</i></p> <p>Частота разнообразных клинических проявлений в отдаленный период после холецистэктомии по поводу желчно – каменной болезни составляет от 20 до 86 %, что совпадает с литературными данными. Выявлено достоверное снижение частоты билиарных болей и синдрома диспепсии. Достоверно возросла частота запоров и изжоги.</p> <p>Подобная динамика симптомов сопровождается возрастанием качества жизни больных (опросник SF-36).</p> <p>Значимых различий в показателях качества жизни у лиц, перенесших холецистэктомию по поводу желчнокаменной болезни в сравнении с группой не оперированных пациентов нет.</p>	<p>ОСОБЕННОСТИ ТЕЧЕНИЯ ТОКСИЧЕСКИХ ГЕПАТИТОВ ПРОФЕССИОНАЛЬНОЙ ЭТИОЛОГИИ</p> <p>Мерзликин Л.А.¹, Северов М.В.², Северова М.М.². <i>1ФГБУ ИППО ГНЦ «ФМБЦ им.А.И.Бурназяна» ФМБА России, Москва, 2Кафедра терапии и профболезней медико-профилактического факультета ГБОУ ВПО Первый МГМУ им. И.М.Сеченова Минздравсоцразвития, Россия, Москва</i></p> <p>Количество веществ способных поражать печень в производственных условиях исчисляется десятками тысяч. Выделена группа гепатотропных ядов. Показано, что клинические проявления при профессиональных отравлениях зависят как от сопутствующего соматических заболеваний, вредных привычек, так и от, предшествующего интоксикации, поражения печени. При некоторых интоксикациях (свинцом, бензолом, фтором) признаки поражения печени развиваются параллельно с появлением другой тяжёлой клинической симптоматики. В других случаях преобладающее в клинической картине заболевания поражение других органов может отодвигать на второй план симптомы патологии печени. Если симптоматика заболевания печени не доминирует, то тяжесть клинических проявлений зависит от избирательного действия токсического химического вещества.</p> <p>Термин «токсический гепатит» общепринят в профессиональной патологии, хотя понятие «гепатит» употребляется несколько условно, поскольку при поражении токсическими веществами часто нет выраженных лабораторных и морфологических признаков воспаления органа. Поэтому иногда применяют термин «токсико-химическое поражение печени». Отдельными авторами используется термин «токсическая гепатопатия», под которым понимается поражение печени при острых отравлениях так называемыми печеночными ядами (дихлорэтан, четыреххлористый углерод и пр.), некоторыми растительными ядами (бледная поганка, мужской папоротник), медикаментами (парацетамол, акрихин и пр.). Дальнейшее изучение токсических гепатитов профессиональной этиологии имеет большое практическое значение при решении вопросов о связи заболевания с профессией, экспертизе трудоспособности и разработке лечебно-профилактических меропрятий.</p>
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лечение по поводу ЖКБ: лапароскопическая ХЭ – 3 пациента, консервативная литолитическая терапия препаратами желчных кислот - 12 человек, отказ от лечения – 5 человек.

Выводы. ЖКБ диагностируется у каждого седьмого больного с сахарным диабетом, в клинической картине преобладают диспепсические проявления, позднее выявление требует целенаправленной диагностики, способствующей своевременному выявлению ЖКБ, проведению дифференцированной адекватной терапии больным.

<p>ФУНКЦИОНАЛЬНАЯ ДИСПЕПСИЯ, АССОЦИИРОВАННАЯ С HELICOBACTER PYLORI НА ФОНЕ ИЗБЫТОЧНОЙ МАССЫ ТЕЛА И ОЖИРЕНИЯ И ИХ НЕМЕДИКАМЕНТОЗНАЯ КОРРЕКЦИЯ</p> <p>Мырзабаева Н.А. <i>Казахский Национальный медицинский университет им. С.Д. Асфендиярова, Алматы, Казахстан</i></p> <p>Цель. Целью нашей работы было исследование результативности немедикаментозных методов лечения, а именно рефлексотерапии у пациентов с функциональной диспепсией (ФД), ассоциированной с Helicobacter pylori на фоне избыточной массы тела (ИМТ) и ожирения. Исследование проведено у 46 пациентов с верифицированным диагнозом ФД, ассоциированной с Helicobacter pylori, из них у 73,9% больных была ИМТ, у 26,1% - ожирение. Синдром боли наблюдался у 58,7% лиц с ФД, ассоциированной с Helicobacter pylori на фоне ИМТ и ожирения. Постпрандиальный дистресс-синдром имел место в 41,3% случаях. Возраст пациентов был от 16 до 45 лет. Длительность заболевания составляла от 12 месяцев до 4 лет. В основную группу вошли 26 пациентов, которым была назначена эрадикационная терапия согласно рекомендациям Маастрихского консенсуса-3 и, дополнительно назначали индивидуальную для каждого пациента гипокалорийную диету, затем проводили аурикулупунктуру: по две точки на один сеанс на основные точки (АР 18,17) в течение 30 мин, а на остальные дополнительные точки (АР 22, 28, 51, 55, 87) по 10-12 мин. Одновременно осуществляли терапию сканирующим лазерным лучом на проекцию солнечного сплетения, ширина сканирования 4´4 см, на болевую точку пяточм, на протяжении 4 минут, на паравертбральную зону Th5-Th8, ширина сканирования 6 см, воздействовали продолжительностью - 7 мин, а КВЧ-пунктуру проводили на отдаленные точки общего действия G1 4, G1 11, E 36, C 7, TR 5, MC 6, RP 6, RP 9, F2, F 3, время воздействия в каждом конкретном случае было индивидуальным и составляло 10-20 мин на одну ТА. Суммарное время воздействия на одну процедуру от 20 до 40 мин. Курс лечения составлял 10 -15 процедур. Контрольную группу составили 20 обследованных, которые получали в зависимости от клинического варианта ФД симптоматическое лечение и эрадикационную терапию.</p> <p>В результате лечения было отмечено позитивное влияние и высокая клиническая эффективность рефлексотерапии в снижении массы тела и успешной эрадикации Helicobacter pylori у больных с ФД на фоне ИМТ и ожирения.</p>	<p>АМИНОКИСЛОТНЫЙ ДИСБАЛАНС У БОЛЬНЫХ С ХРОНИЧЕСКИМ ПАНКРЕАТИТОМ</p> <p>Русин В.И., Сирчак Е.С., Курчак Н.Ю. <i>Ужгородский национальный университет, г.Ужгород, Украина</i></p> <p>Цель работы: Изучить изменения уровней свободных аминокислот сыворотки крови у больных с хроническим панкреатитом.</p> <p>Материалы и методы: В клинике ЗОКБ г.Ужгород нами обследовано 24 больных с хроническим панкреатитом. Среди обследованных пациентов преобладали мужчины - 16, возрастом 43,1±2,8 лет, женщин было - 8, возрастом 44,7±4,6 лет. Больным кроме стандартных методов исследования проводили определение свободных аминокислот сыворотки крови по методу одномерной нисходящей хроматографии на бумаге (И.М.Хайс, К.Мацек, 1962, Т.С.Пасхина, 1964).</p> <p>Результаты и обсуждения. При обследовании больных с хроническим панкреатитом у всех пациентов наблюдали разной степени выраженности боли в верхних отделах живота, а также признаки диспепсического (тошнота, рвота, отрыжка, метеоризм) и астеновегетативного синдромов. Больные также жаловались на увеличение частоты акта дефекации (в среднем до 3-4 раз в день).</p> <p>У больных с хроническим панкреатитом в крови наблюдали признаки диспротеинемии, что проявлялось уменьшением количества альбуминов (до 35,9±2,7%) и увеличением уровней γ- и α2-глобулинов (до 33,5±2,1% и до 9,3±0,9% соответственно).</p> <p>Эти изменения сопровождались нарушением уровней свободных аминокислот сыворотки крови, с преимущественным увеличением показателей глутамина, треонина, лизина, гистидина, тирозина, триптофана, метионина, валина, что объясняется снижением индивидуальной деградации аминокислот. Параллельно диагностировали снижение показателей серина, аспарагина, глицина, аланина.</p> <p>Изменения белкового обмена у больных с хроническим панкреатитом развиваются на фоне выраженной трофологической недостаточности.</p> <p>Выводы: У больных с хроническим панкреатитом наблюдается диспротеинемия в сыворотке крови, что сопровождается нарушение уровней свободных аминокислот.</p>	<p>ЭФФЕКТИВНОСТЬ СОЧЕТАНИЯ ЗАМЕСТИТЕЛЬНОЙ ГОРМОНОТЕРАПИИ И ПРЕПАРАТА УРСОСАН ПРИ ЭСТРОГЕНОДЕФИЦИТНЫХ СОСТОЯНИЙ У ЖЕНЩИН ВМЕНОПАУЗЕ</p> <p>Нурмухамедов А.И., Абдуллаев А.Х., Тургунова М.Ш., Юсупова И.Ш., Исмаилова Ж.А. <i>Республиканский специализированный научно-практический медицинский центр терапии и медицинской реабилитации, Ташкент, Узбекистан</i></p> <p>Заместительная гормонотерапия (ЗГТ) натуральными эстрогенами в комбинации с прогестеронами в настоящее время получила значительное распространение для лечения синдрома дефицита эстрогенов (ДЭ), обусловленного естественной или искусственной менопаузой. Вместе с тем длительное применение эстроген-прогестеронных комбинаций в качестве ЗГТ помимо положительных сдвигов в гомеостазе может вызвать нередко нежелательные побочные нарушения функции печени. Учитывая это, у женщин с ДЭ, патогенетически обоснованным было бы применение препаратов, обладающих цито – и гепатопротекторным, антиоксидантным действием. В этом отношении препаратом выбора является урсосан. Хорошо всасываясь в кишечнике, при приёме внутрь, он встраивается в мембрану гепатоцита, стабилизирует её структуру и защищает гепацит от повреждающих факторов. Замещая неполярные желчные кислоты, формирует нетоксичные смешанные мицеллы, уменьшая синтез холестерина в печени и его всасывание в кишечнике, образование цитотоксических Т – лимфоцитов. В исследование включены 70 женщин с ДЭ, нуждавшиеся в длительной ЗГТ. Больные были разделены на 2 группы по 35 человек. Обе группы были идентичны по возрасту (41+7,5 лет), терапевтическим и гинекологическим заболеваниям, длительностью заболевания. В обеих группах больные от 6 до24 месяцев принимали ЗГТ. Больные первой группы дополнительно к ЗГТ получали препарат урсосан по 2 капсулы на ночь. Пациенты, принимавшие урсосан, переносили ЗГТ более благоприятно, а у большинства пациенток второй группы отмечались тяжесть в правом подреберье, горечь во рту и другие диспепсические расстройства, что служило причиной отказа от гормонотерапии. Проводили биохимические анализы – контроль крови для определения активности печёчных трансаминаз. урсосан рекомендуется использовать у лиц с патологией печени и желчных путей и нуждающихся в длительной ЗГТ.</p>
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ЭКСПЕРИМЕНТАЛЬНЫЙ БИОХИМИЧЕСКИЙ АНАЛИЗ ГЕПАТОПРОТЕКТОРНОГО ЭФФЕКТА ПРЕПАРАТА ИЗ БИОМАССЫ КЛЕТОЧНОЙ КУЛЬТУРЫ ЖЕНЬШЕНЯ

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Цель данной работы - изучение влияния препарата из биомассы клеточной культуры женьшеня на биохимические проявления экспериментального токсического гепатита, вызываемого затравкой половозрелых нелинейных крыс-самцов токсическими дозами тетрахлорметана (трехдневное внутримышечное введение 50%-го масляного раствора в дозе 0,2 мл/100 г). На предварительном этапе из биомассы клеточной культуры женьшеня методом перколяции готовили спиртовую настойку. Затем ее деалкоголизировали на роторном испарителе выпариванием до каломельного состояния с последующим восстановлением исходного объема дистиллированной водой. Полученный водный препарат женьшеня вводили подопытным животным внутрь через желудочный зонд в течение трех дней до их затравки гепатотоксином и в течение трех дней наряду с ним в дозах 2,5, 5 и 10 мл/кг (в пересчете на настойку).

Выраженность патологического процесса в печени в контрольной и препаратной сериях оценивалась по значениям динамики активности ряда ферментов – аспаратаминотрансферазы, аланинаминотрансферазы и гамма-глутамил-транспептидазы сыворотки крови, определяемых с использованием стандартных наборов фирмы «LАСHEMА» (Чехия).

Полученные результаты свидетельствуют о наличии у препарата из биомассы клеточной культуры женьшеня умеренного гепатопротекторного эффекта к воздействию на печеночную ткань тетрахлорметана. Это проявилось меньшей степенью гиперферментемии, особенно по значениям аспаратаминотрансферазы и гамма-глутамилтранспептидазы. При этом более значимо анализируемый эффект проявился при применении доз 5 и 10 мл/кг. Учитывая патогенетическую особенность гепатотоксического действия тетрахлорметана, обусловленную инициацией свободнорадикальных процессов при его биотрансформации, вполне вероятно, что установленный гепатопротекторный эффект базируется на выраженной антиоксидантной активности женьшеня, что расширяет фармакодинамическую характеристику данного препарата.

ПРОЧИЕ

СРАВНИТЕЛЬНАЯ ОЦЕНКА АНТИОКСИДАНТНЫХ СВОЙСТВ РАЗЛИЧНЫХ ОБРАЗЦОВ МОНОФЛЕРНОЙ ПЫЛЬЦЫ НА МОДЕЛИ ТЕТРАХЛОРМЕТАНОВОГО ГЕПАТИТА

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В настоящей работе проведена сравнительная оценка выраженности антиоксидантного эффекта монофлерной пыльцы различного ботанического происхождения. Для этого использована классическая экспериментальная «свободнорадикальная» модель тетрахлорметанового гепатита, характеризующаяся значительным ростом количественных параметров активности перекисного окисления липидов, что и позволяет проводить корректный сравнительный анализ выраженности антиоксидантного действия.

Эксперименты выполнены на взрослых нелинейных крысах-самцах, токсический гепатит у которых вызывали трехдневным внутримышечным введением 50%-го масляного раствора тетрахлорметана в дозе 2 мл/кг. В препаратных сериях крысам за 10 дней до введения тетрахлорметана и в течение трех дней наряду с ним внутрь назначали свежеприготовленные суспензии пыльцы одуванчика, василька, клевера и кипрея в дозе 250 мг/кг каждая. Оценку интенсивности липопероксидации проводили в гомогенате печеночной ткани путем определения концентрации малонового диальдегида, активности НАДФ-Н-индуцируемого и аскорбат-индуцируемого перекисного окисления липидов.

Все оцениваемые образцы монофлерной пыльцы способствовали уменьшению степени интенсификации свободнорадикального процесса в печеночной ткани, индуцируемого тетрахлорметаном. При этом максимальная степень антиоксидантной активности отмечена в случаях применения пыльцы одуванчика и клевера, несколько меньшая – у животных, получавших пыльцу василька и минимальный протекторный эффект был определен в серии, где вводили пыльцу кипрея. Полученные результаты позволяют рекомендовать использование именно пыльцы одуванчика и клевера в качестве пищевых добавок при «свободнорадикальных» патологиях в целом и токсических гепатитах, близких по механизму развития к тетрахлометановому, в частности.

ВОЗМОЖНОСТЬ НЕИНВАЗИВНОЙ СКРИНИНГОВОЙ ОЦЕНКИ У ПАЦИЕНТОВ С ЗАБОЛЕВАНИЯМИ ЖЕЛЧЕВЫВОДЯЩИХ ПУТЕЙ НАЛИЧИЯ ИНФЕКЦИИ HELICOBACTER PYLORY В УСЛОВИЯХ ЦЕНТРАЛЬНОЙ РАЙОННОЙ БОЛЬНИЦЫ

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В последние годы отмечен рост пациентов с сочетанными заболеваниями желчевыводящих путей и желудка. Поэтому актуальной становится ранняя неинвазивная скрининговая диагностика этих патологий.

За период с января 2011 г. по март 2012 г. на базе ГБУЗ НО «Уренская ЦРБ» было обследовано 73 пациента с патологией желчевыводящих путей (дискинезия желчевыводящих путей и хронический холецистит), из них 17 мужчин (средний возраст 48,4±13,6 лет) и 56 женщин (средний возраст 56,6±7,7 лет). Всем пациентам выполнялись: УЗИ органов брюшной полости на аппарате «Siemens Sonoline G40» и ФГДС аппаратом «Fujinon FG-1Z» по стандартным методикам.

При УЗИ органов брюшной полости дополнительно проводили УЗ-обследование желудка без наполнения водой, измеряли толщину мышечного слоя. При ФГДС выполнялась щипцевая биопсия слизистой желудка с последующим проведением экспресс-теста на уреазную активность Helicobacter pylory (Hр).

Также была обследована группа лиц («здоровые») в количестве 30 человек (мужчин 8 (средний возраст 44±10,7 лет), женщин 22 (средний возраст 53±5,3 лет)) без патологии желчевыводящих путей и отсутствием инфекции Hр.

Получено, что в группе «здоровые» толщина мышечного слоя желудка по данным УЗИ составляла 3,8±0,14 мм, при ФГДС диагностирован гастрит без признаков атрофии слизистой, уреазный тест – отрицательный.

В группе пациентов с наличием заболеваний желчевыводящих путей величина мышечного слоя желудка равнялась 5,002±1,74 мм. Во всех случаях при ФГДС у пациентов был диагностирован гастрит без признаков атрофии слизистой. Отмечено, что чем толще мышечный слой желудка, тем выше уреазная активность Hр.

Таким образом, наличие у пациента с заболеванием желчевыводящих путей увеличения толщины мышечного слоя желудка по данным УЗИ-обследования. свыше 3 мм позволяло в условиях центральной районной больницы заподозрить наличие инфекции Hр и своевременно направить пациента на выполнение ФГДС с последующей щипцевой биопсией слизистой желудка и проведением экспресс-теста на уреазную активность.

ТЯЖЕЛАЯ ПЕЧЕНОЧНАЯ НЕДОСТАТОЧНОСТЬ, КАК ОДНО ИЗ ПРОЯВЛЕНИЙ СИСТЕМНОГО АСПЕРГИЛЛЕЗА

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Введение и цель. Острые афлатоксикозы редко диагностируются у человека. Однако следует учитывать возможность его развития у пациента с желтухой. Представляем случай системного аспергиллеза, протекающего под «маской» декомпенсированного цирроза печени (ЦП) с развитием сепсиса.

Описание случая. Больная М., 47 лет. Длительность болезни 6 мес. Острое начало заболевания - с желтухи, диспепсии, выраженной слабости, гектической лихорадки. При госпитализации - кома I, интенсивная желтуха, одышка, анасарка. В легких дыхание ослаблено, тахикардия, гипотония. Перкуторно печень не увеличена, селезенка не пальпировалась. В анализах: анемия (эритроциты - 2,62 х 106/м), лейкопения (1,2 х 103/м.), гранулоциты (91%), тромбоцитопения (19 х 103/м.), гиперферментемия (2,5 нормы), гипербилирубинемия до 26 норм (прямой билирубин > 10 норм), общий белок – 41 г/л, альбумин – 23,3 г/л, протромбин - 26,3%, МНО – 2,43. По данным КТ - двухсторонняя полисегментарная пневмония, гидроторакс, портальная гипертензия, асцит. Посев крови отрицательный. Бронхоскопия: на задней стенке трахеи выявлен язвенный дефект до 2 см. Установлен сепсис без выявленного первичного очага с развитием тяжелой полиорганной недостаточности, вторичной гепатопатии, завершившийся летальным исходом. При аутопсии - признаки септицемии, с поражением внутренних органов (мозга, сердца, почек, легких) - некроз сосудистой стенки и кровоизлияния в окружающие ткани. При электронной микроскопии аутопсированной ткани печени в полях мицелия обнаружены герминативные формы гриба, а также типичного строения гифы Aspergillum fumigatus (A.f.). В посевах смывов бронха, полученных после смерти пациентки, в большом количестве (A.f.).

Заклчение. У пациентов при наличии клинической картины декомпенсированного криптогенного ЦП, в дифференциально-диагностический алгоритм целесообразно включать системные микозы.

ЧАСТОТА ВСТРЕЧАЕМОСТИ ЗАБОЛЕВАНИЙ ОРГАНОВ ПИЩЕВАРЕНИЯ ПРИ АТЕРОСКЛЕРОЗЕ СОСУДОВ

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Атеросклероз – одно из самых актуальных заболеваний XXI века, которая является одним из четырех наиболее частых заболеваний и причин смерти. Известно, что более чем в 90% случаев смерть от сердечно-сосудистых заболеваний обусловлена ИБС и мозговым инсультом, в развитии которых основная роль принадлежит атеросклерозу.

Цель работы: выявить частоту встречаемости поражения ЖКТ при атеросклерозе сосудов головного мозга, коронарных сосудов и аорты.

Материалы исследования: проведен анализ 358 протоколов (194 женщин и 164 мужчин в возрасте 29-83 лет) вскрытый лиц городского населения (314) 84,4% и сельского населения (44) 12,2%, умерших от разных форм атеросклероза (атеросклероз сосудов головного мозга – (182) 50,8%, атеросклероз коронарных сосудов –(238) 66,4%, атеросклероз аорты – (294) 82,1%, что составило 26% от общего числа вскрытый (1373), проведенных в патологоанатомическом отделе РБ №1 – НЦМ г. Якутска за 2010-2012 гг.

Результаты: поражения пищеварительного тракта из числа общих умерших больных от разных форм атеросклероза, представлены следующими заболеваниями: такие, как опухоль кардиального отдела желудка с переходом на пищевод – у (19)5,3% случаев, хронический гастрит – у (38)10,6%, острая язва и эрозия желудка – у (44)12,2% больных, ЖКБ – у (130)36,3% случаев. Изменения со стороны печени и панкреатобилиарной зоны встречаются в виде цирроза печени - у (14) 3,9% больных, гепатита В или С - у (37) 10,3%, хронического панкреатита - у (213) 59,4% случаев. Чаще они выявлены у женщин в возрасте 51- 83 лет и количество их максимально возрастало после 60 лет. Лица некоренной национальности ЗАБОЛЕВАЛИ в 2 раза чаще, чем коренные пациенты.

Основными причинами смерти явилось кардиогенный шок – у (66)18,4% случаев, острая сердечная недостаточность – у (67)18,7%, отек и набухание головного мозга – у (112) 31,2% случаев.

КЛИНИЧЕСКОЕ ТЕЧЕНИЕ ДОБРОКАЧЕСТВЕННЫХ СТРИКТУР ЖЁЛЧНЫХ ПРОТОКОВ

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Актуальность: Доброкачественные стриктуры внепеченочных желчных протоков (ВЖП) являются, как правило, следствием травмы желчного дерева во время холецистэктомии. Травмы ВЖП происходят в 0,5-1,4% случаев. Принимая среднюю частоту травмы ВЖП за 1%, в России ежегодно от подобного осложнения страдают 600-1000 человек, в республике Саха (Я) ежегодно встречается у 11-20 человек, большинства из них в послеоперационном периоде развиваются стриктуры, нередко требующие длительного лечения, многократных лечебно-диагностических мероприятий, зачастую приводящие к серьезной инвалидизации пациентов.

Цель исследования: изучение клинического течения доброкачественных стриктур внепеченочных желчных протоков.

Материалы и методы: Проведен анализ клинического течения 119 больных с доброкачественными рубцовыми стриктурами внепеченочных желчных протоков за период с 1993г по 2003г. Женщин всего было:-89, мужчин всего:-30. Из них в возрасте: до 39лет-8, 40-49лет-25, 50-59лет-63, 60-69лет-22, 70-79лет-1, 80 и старше. Коренных -86, некоренных-33.

Результаты: У 86 (72%) человек стриктуры выявлены после «открытой» холецистэктомии, еще у 33 (28%) - после лапароскопической холецистэктомии. По результатам УЗИ выявлено: развитие фиброза наблюдалось у 13(11%) больных, билиарный цирроз у 6(5%), увеличение и уплотнение печени у 48(40,3%), билиарная гипертензия у 18(15%) пациентов. Клинические проявления: послеоперационная анорексия, тошнота, рвота наблюдались у 36(30%) больных, боли в животе были у 78(65,5%). Холестатическая желтуха наблюдалась у 32 (26,8%) пациентов, зуд кожи у 24(20%). Подпеченочный абсцесс выявлен у 3(2,5%) пациентов.

Рецидивирующий холангит (интермиттирующая билиарная лихорадка Шарко) развился у 5(4,2%) человек. Биохимическое исследование сыворотки крови выявило у 68(57%) больных повышение активности щелочной фосфатазы, ГТТФ и уровня жёлчных кислот.

Вывод: Таким образом, сопутствующие поражения пищеварительного тракта при атеросклерозе сосудов головного мозга, коронарных сосудов и аорты встречаются в виде острых язвенно-эрозивных поражений желудка в (44) 12,2% случаев, желчекаменной болезни в (130) 36,3% случаев и хронического панкреатита в (213) 59,4% случаев.

ПЕЧЕНОЧНО-КЛЕТОЧНАЯ НЕДОСТАТОЧНОСТЬ КАК ОСЛОЖНЕНИЕ ЗАБОЛЕВАНИЙ ПЕЧЕНИ

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Термин «печеночная недостаточность» (ПН) является часто употребляемым понятием, не имеющим четкого определения. Он объединяет различные нарушения функции печени: от легких отклонений,дотяжелых,заканчивающихся печеночной комой, является функциональным, а не анатомическим понятием. Постоянные морфологические признаки отсутствуют. Выделяют малую ПН, или гепатодепрессию (гепатодепрессивный синдром) и «большую», или явную ПН с симптомами «печеночной энцефалопатии». Большую ПН делят на печеночно-клеточную и портально-кавальную. Клиническая картина печеночно-клеточной недостаточности при различных заболеваниях печени в целом одинакова и не зависит от этиологии. Характерны неврологические нарушения (печеночная энцефалопатия), слабость, анорексия, желтуха, асцит, нарушения азотистого и электролитного обмена, свертывания крови, кожные и эндокринные изменения и др. Клинические проявления хронической ПН обычно сочетаются с симптомами болезни печени, которая и привела к недостаточности ее функции. В сыворотке крови обнаруживают повышение билирубина, трансаминаз. Повышение показателей креатинина, электролитные нарушения свидетельствует о вовлечении почек в патологический процесс (гепаторенальный синдром).

Лабораторные исследования показывают гипоальбуминемию, низкое содержание холинэстеразы в сыворотке крови, натрия, протромбина, холестерина, умеренную анемию, удлинение времени кровотечения и времени свертывания крови.

В развитии печеночной комы выделяют стадии прекомы, угрожающей комы и собственно кому. Комплексную терапию необходимо начинать при появлении первых признаков ПН.

XVIII РОССИЙСКИЙ КОНГРЕСС «ГЕПАТОЛОГИЯ СЕГОДНЯ»
<p>ГАСТРОДУОДЕНАЛЬНЫЕ ЯЗВЫ ПОСЛЕ ПЕРЕНЕСЕННОЙ ХОЛЕЦИСТЭКТОМИИ, ЕЕ КЛИНИЧЕСКИЕ ПРОЯВЛЕНИЯ</p>
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<p>Актуальность: Язвенная болезнь желудка и 12-перстной кишки, равно как и рак желудка на протяжении последнего столетия остаются наиболее социально значимыми заболеваниями во всем мире. Начавшееся в условиях кризиса снижение уровня жизни неизбежно вызовет дальнейший рост заболеваемости и увеличение количества угрожающих жизни осложнений, таких как кровотечение и перфорация язвы.</p>
<p>Цель: изучить особенности клинических проявлений у пациентов с гастродуоденальными язвами в сочетании с патологией желчевыводящих путей (основная группа), обострением язвенной болезни желудка и двенадцатиперстной кишки (контрольная группа).</p>
<p>Материалы исследования: В качестве материалов исследования взяты истории болезни I хирургического отделения за 2011 г. Проведен сравнительный анализ клинических проявлений у 16 (20%) пациентов основной группы (14-мужчин (87,5%), 15-женщин (12,5%)), которые перенесли в анамнезе холецистэктомиию по поводу острого и хронического калькулезного холецистита и 64 (80%) пациента контрольной группы (49-мужчин (87,5%), 15-женщин (12,5%). Пациенты обеих групп были статистически однородны по возрасту и полу. Возраст пациентов от 31 до 60 лет, средний возраст-48 3.2 года. Коренные жители составляют- 31,25%, некоренных –68,75%. Продолжительность заболевания от 1 года до 5 лет в обеих исследуемых группах.</p>
<p>Результаты исследования: У больных с гастродуоденальными язвами в сочетании с патологией желчевыводящих путей (ЖКБ, холестероз) значительно чаще встречаются явления диспепсии по сравнению с пациентами контрольной группы. Среди диспептических проявлений у больных основной группы значительно чаще встречалась тошнота- у 14(87,1%) пациентов по сравнению с 36% контрольной группы, вздутие живота –у 12 (75%) пациентов по сравнению с 54% контрольной группы. Запоры часто наблюдались в контрольной группе в 46% случаев. Частота возникновения диареи не отличалась в обеих группах. Новющий и тупой характер боли, тяжесть в эпигастрии, которая возникала сразу после приема пищи, значительно чаще встречалась у пациентов основной группы у 12 (75%) по сравнению с 42,3% пациентами контрольной группы.</p>

ИССЛЕДОВАНИЕ ЖЕЛЧЕКАМЕННОЙ БОЛЕЗНИ У БОЛЬНЫХ С ВАРИКОЗНОЙ БОЛЕЗНЬЮ НА ПРИМЕРЕ ПОЛИКЛИНИКИ №1 Г. ЯКУТСКА
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<p>Цель: изучить заболеваемость ЖКБ у больных с хронической венозной недостаточностью (ХВН) на примере поликлиники №1 г. Якутска.</p>
<p>Материалы исследования. В качестве материалов исследования взяты амбулаторные карты диспансерных больных на 2012 год хирургического кабинета поликлиники №1 г. Якутска.</p>
<p>Проработаны 162 амбулаторных карт, больных с варикозной болезнью, из них выявлено 21 (12,9%) больных с ЖКБ (20 женщин и 1 мужчина) в возрасте от 35 -40 лет, коренные жители составили - 47 (30%) человек, некоренные - 115 (70%).</p>
<p>Результаты. Варикозная болезнь наблюдается у 56% женщин трудоспособного возраста, 12% - нетрудоспособных. Мужчины составили: трудоспособные - 26% и нетрудоспособные - 6%. Тромбофлебит нижних конечностей встречаются у 62% взрослого населения, у лиц старше 65 лет частота трофических язв возрастает в 3 раза и более, достигая 3-6%. Примерно у четверти диспансерной группы старше 60 лет и трети - старше 70 лет определяются на УЗИ желчные камни. В клинической картине преобладают диспепсические проявления -11% в виде отрыжки, тошноты, запоров, неустойчивого стула. Проявлениями ХВН служат телеангиоэктазии 3%, варикозно-расширенные подкожные венозные сосуды 46%, отечность нижних конечностей 24%, появления синдрома «тяжелых ног» у 16% больных. У больных с ХВН значительно чаще развиваются деструктивные формы острого холецистита, характеризующиеся высокой частотой осложнений и летальности. Основными причинами осложнений являлись – сердечно-сосудистая недостаточность (10-15%), печеночно-почечная недостаточность (3-5%), тромбозмболи (14-16%).</p>
<p>Заключение. Таким образом, ЖКБ диагностируется у 12,9% больных с варикозной болезнью, в клинической картине преобладают диспепсические проявления в 11% случаев. Учитывая, что у больных с ХВН значительно чаще развиваются деструктивные формы острого холецистита, характеризующиеся высокой частотой осложнений и летальности, необходимо раннее выявление ЖКБ, при клиническом обследовании больного с варикозной болезнью</p>

В исследуемых группах чаще заболевают больные с I группой крови крови- 37,5%. В основной группе были проведены оперативные вмешательства по поводу язвенного кровотечения в виде - иссечение перфоративной язвы ДПК с пилорипластикой по Джадду-Танока -у 1 больного (6,25%), резекция желудка по Бильрот – 1 - 1 больного (6,25%), гастротомия – у 1 больного (6,25%), а остальным консервативное лечение - 13 больных (81,25%). Во второй группе всем больным проведена симптоматическая терапия. В основном локализация язвенного процесса в ДПК - 62,5%, в желудке встречается – в 37,5% случаев.

Заключение: Таким образом, клиническими особенностями гастродуоденальных язв в сочетании с патологией желчевыводящих путей являются проявления функциональной диспепсии, чаще встречающиеся у мужчин (87,5%), трудоспособного возраста (50%), некоренной группы (68,75%).при частой локализации в ДПК (62,5%).

ПРОЧИЕ
<p>ОСЛОЖНЕНИЯ ДИФFUЗНЫХ ЗАБОЛЕВАНИЙ ПЕЧЕНИ И ГЕНДЕРНЫЕ РАЗЛИЧИЯ В ИХ РАЗВИТИИ</p>
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<p>Современный образ жизни, характер питания и частые употребления алкоголя значительно повреждают печеночную ткань, из-за чего и развиваются диффузные изменения паренхимы печени. Не последнее место занимает и вирусные поражения, которые часто остаются без внимания и благодаря этому передаются от человека к человеку. Существует очень большое количество различных методов, направленных на диагностику различных патологических состояний печени. В настоящее время прижизненное морфологическое исследование ткани печени получило широкое распространение в клинической практике.</p>
<p>Цель работы: изучить гендерные различия в развитии осложнений диффузных заболеваний печени среди женщин (Ж) и мужчин (М).</p>
<p>Материалы и методы. Нами изучено морфологическое исследование ткани печени у180 больных с хроническими диффузными заболеваниями печени (ДЗП). Мужчин было 66,7%, женщин -33,3%. Все больные прооперированы по поводу желчекаменной болезни в условиях РБ №2 Центра экстренной медицинской помощи г.Якутска. В возрасте 16-20 лет – 19 человек, 21-40 лет – 51, 41-60 лет – 57, 61-70 лет – 37, старше 70 лет – 16.</p>
<p>Результаты. В группу больных с ДЗП вошли больные с гепатитами- 100чел. и билиарным циррозом- 80 пациентов. Предварительный диагноз хронического гепатита при морфологическом исследовании был подтвержден лишь у 40% пациентов. У 43% больных с морфологически подтвержденным хроническим гепатитом в клинический диагноз были внесены изменения по части оценки степени активности процесса: у 25% была диагностирована более легкая, а у 15% - более выраженная стадия поражения печени от всего количества больных. В анамнезе у 9,4% Ж и у 15% М имеется перенесенный ранее вирусный гепатит (44чел). Хронический лекарственный гепатит встретился у 8 женщин. У остальных 48 больных выявлен алкогольный гепатит-26,7% от всех ДЗП, в том числе у М- 16,7% и Ж- 10%. Билиарный цирроз печени мы выявили у 80 больных (44,4% от всех ДЗП): Ж –17 (9,4%), М – 63 (35%). Страдали холециститом более 6 лет – 27 человек, от 10-15 лет – 29 человек и более 15 лет – 24 человек. Осложнения при диффузных заболеваниях печени с развитием портальной гипертензии</p>

РАСПРОСТРАНЕННОСТЬ ЭХИНОКОККОЗА В РЕСПУБЛИКЕ САХА (ЯКУТИЯ).
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<p>Актуальность: Эхинококкоз – опасное паразитарное заболевание человека. В России наиболее высокая заболеваемость населения эхинококкозом регистрируется в Башкортостане, Татарстане, в Республике Саха (Якутия), на территории республик Северного Кавказа, Краснодарском, Алтайском, Красноярском и Хабаровском краях, Томской, Омской, Магаданской, Амурской областях и Чукотском автономном округе.</p>
<p>Высокая частота распространения заболеваемости, трудности активного выявления заболевания на ранней стадии, связанные со стертой клинической картиной и высокий процент стойкой утраты трудоспособности обуславливают актуальность проблемы эхинококкоза для здравоохранения.</p>
<p>Цель исследования: Изучение распространенности эхинококкоза в РС (Я).</p>
<p>Материалы и методы исследования: Проведен анализ статистических данных Республиканского паразитологического кабинета Республиканской больницы №3 и историй болезни больных, находившихся на стационарном лечении в отделении хирургической гастроэнтерологии Республиканской больницы № 1 НЦМ за период с 2004 по 2012 гг.</p>
<p>Результаты исследования: На 01.01.2012г. на диспансерном учете состоит 140 больных эхинококкозом. Из них 30 человек(21,4%) – жители города Якутска. Остальные 110(78,6%) зарегистрированы в 22 районах республики: 13 человек в Сунтарском районе, 11 человек в Усть-Майском районе, 10 человек в Алданском районе, 9 человек в Намском районе, по 8 человек в Верхневилуйском, Кобяйском, Нюрбинском районах, по 7 человек в Олекминском, Оленекском, Чурапчинском районах, по 5 человек в Амгинском, Усть-Алданском районах, по 4 человека в Вилуйском, Горном районах, по 3 человека в Таттинском, Верхнеколымском районах, 2 человека в Нижнеколымском районе, по 1 человеку в Верхоянском, Ленском, Мирнинском, Момском, Томпонском районах.</p>
<p>За исследуемый период с 2004 по 2012 гг. эхинококкоз встречался во всех возрастных группах: 18-19 лет-4 человека, 20-29 лет-14 человек, 30-39 лет-13 человек, 40-49 лет-14 человек, 50-59 лет-20 человек, 60 лет и старше-45 человек. Анализ возрастной структуры заболеваемости показал, что наиболее часто</p>

и отечно-асцитического синдрома выявлены: варикозное расширение вен пищевода (ВРВП) Iстепени у М- 10,6% и у Ж-32,7%, 11 степени- у М-40,8% и у Ж-13,8%, 111 степени- у М-48,6% и у Ж- 22,7%. Наличие в анамнезе кровотечения из ВРВП: среди М- 9,9% и среди Ж-4,08%. Рефрактерный асцит встречается у 36,6% М и у 14,2% Ж. Гепатомегалия выражена у М-32,8%, среди Ж-16,4%. Нарушения белково-синтетической функции печени: гипоальбуминемия среди М отмечена у 27,6%, а среди Ж- у 48,9%. Снижение протромбинового индекса (ПТИ) выявлено у 32,1% М и у 70,4% Ж, фибриногена – у 27,8% М и 57,9% Ж. Гипербилирубинемия встречается у 50,6 % М и у 89,8% Ж, в том числе билирубин более 100 мкмоль/л отмечается у 36,4% М и у 60,8% Ж.

Выводы. 1. У мужчин в 2 чаще возникают осложнения в виде портальной гипертензии и кровотечения из ВРВП. 2. Нарушения белково-синтетической функции печени и гипербилирубинемия чаще встречаются у женщин (48,9% против27,6%).

данное заболевание встречалось в возрастных группах от 50 до 59 лет и старше 60 лет.

Распределение:

-по полу: женщин-76(54,3%), мужчин-64(45,7%),

-по национальному признаку: якуты-63%, русские-15%, малочисленные народы-10%, другие-12%,

-по локализации патологического процесса: в печени-72(52%), в легких-53(38%), другие (селезенка, головной мозг, сердце)-15(10%).

За период 2010-2012гг по поводу эхинококкоза легких 9 больным(6,4%) была проведена эхинококкотомия.

Выводы: Таким образом, заболеваемость эхинококкозом находится на высоком уровне практически на всей территории Республики Саха (Якутия). В основном встречается у жителей районов-78,6%, в возрасте от 50 до 60 лет и старше, по полу - у женщин(54,3%), по национальному признаку – у якутов(63%). Чаще всего патологический процесс локализуется в печени(52%).

**ЭНДОСКОПИЧЕСКОЕ СТЕНТИРОВАНИЕ ПИЩЕВОДА
У НЕОПЕРАБЕЛЬНЫХ БОЛЬНЫХ**

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Цель исследования: изучить особенности стентирования пищевода у больных раком пищевода с использованием стентов различных модификаций.

Материалы и методы. За период с 2009 по настоящее время нами было выполнено эндоскопическое стентирование 6 больным по поводу рака пищевода. Возрастной интервал пациентов от 70 до 93 лет. Все имели 3-4 степень дисфагии после химио и лучевой терапии. Большинству пациентов были установлены нитиноловые стенты M.I. Tech (Корея), также использовались стенты фирмы Wilson Cook (США). В 1 случае установлен стент с антирефлюксным клапаном, показанием для её установки служил рак пищеводно-желудочного перехода. Перед стентированием больным проводится эндоскопическое и рентгенконтрастное исследование для определения характера и протяженности сужения, а также забирался биопсийный материал для определения гистологической структуры опухоли. Введение стента производится после премедикации (атропин, реланиум) под местной анестезией в положении больного на левом боку. После эзофагоскопии и введения струны, под эндоскопическим контролем устанавливается проксимальный край стента в сжатом состоянии, после чего он выталкивается и расправляется в просвет пищевода. Рентгенологический контроль с контрастным веществом (76% урографин) проводится в первые сутки после процедуры, для оценки проходимости пищевода и уровня стояния эндопротеза.

Результаты. У 5-х больных уже на следующие сутки после стентирования появлялась возможность приема жидкой и густой пищи, а через 3-5 суток явления дисфагии полностью исчезли. Осложнений при установке саморасширяющихся стентов не было. В раннем периоде после стентирования у 1-го больного появился болевой синдром. Среди поздних осложнений через 8 месяцев от момента установки стента у 1-го больного выявлен продолженный рост опухолевой ткани, который вызвал стеноз просвета пищевода над стентом. Данному больному проведено стентирование стент в стент.

Выводы. Таким образом, учитывая малую травматичность эндоскопического стентирования, эта манипуляция является методом выбора для паллиативного

лечения пациентов с неоперабельными формами рака. Применение методики эндопротезирования позволяет сократить время пребывания больных в стационаре. При этом одним из наиболее очевидных преимуществ и достоинств стентирования является сохранение возможности перорального питания, что существенно повышает качество жизни больных.

YOUNG SCIENTISTS

I PLACE

PLASMOCYTOID DENDRITIC CELLS THEIR ROLE IN CHC PATHOGENESIS IN ADULTS AND CHILDREN

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After description the plasmocytoid dendritic cells (PDC) in 1999 new page in the human immune response was opened.

Purpose: to establish PDC role in pathogenesis of CHC in children and adults.

Materials and methods: One hundred sixty one persons: 133 patients in the various phases of CHC (58 of children and 75 adults) are surveyed, 28 people (16 children and 12 adults) - healthy individuals. Determination of quantity of PDC in blood was carried out by a method of a flow cytometry with use of monoclonal antibodies to specific markers of PDC (CD303 and CD123). IFN determination (the producing function of PDC) was carried out by IFA ELISA method, with previous stimulation of ODN2216 and IL3.

Results: Production of IFN in PDC is significantly higher in patients with CHC, than in healthy individuals, and remains higher by all key parameters, defining a natural history of CHC, in adult patients, than in children. The number of PDC is higher in children, than in adults, however is significantly lower, than in healthy individuals. Natural inversely proportional correlation between degree of IFN

production and viral load is revealed. IFN level in PDC is high both in adults, and in children with low viral load (461,1±262,2 pg/ml in adults, 153,5±38,07 pg/ml in children), and low IFN-genesis corresponds to a high viral load (147,1±59,77pg/ml and 75,76±20,72 pg/ml, p<0,05). The correlation between IFN production in PDC and cytolysis is shown. The increase in IFN production in adults correlates with aminotransferases levels increase (132,8±42,72 pg/ml with normal levels of ALT, AST, 314,9±137,7 pg/ml with ALT, AST <UNL, p<0,05), but has a feedback in children (146,7±36,73 pg/ml and 86,19±23,64 pg/ml respectively, p<0,05). It is shown that number of PDC in adult patients closely correlates with a stage of liver fibrosis: it sharply decreases from 8,4±0,9 cells/ml in F0-1 to 3,9±0,9 cells/ml in F4 (METAVIR) (p<0,05), and IFN production increases in proportion to a stage of fibrosis (from 68,32±33,21 pg/ml in F0-1 to 291,3±195,9 pg/ml at F4, p<0,05).

Conclusion. The obtained data for the first time show close correlation between quantities of PDC with the key parameters defining a history of CHC. That testifies to an important role of these new immune cells in CHC pathogenesis in adults and children.

II PLACE

CLINICAL AND LABORATORY EVALUATION OF COURSE AND PROGNOSIS IN TOXIC HEPATITIS

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Goal: to evaluate clinical and laboratory features of toxic hepatitis and predict its outcome in cases, associated with ingestion of alcohol surrogates. Materials and methods. Retrospective analysis of clinical and laboratory data of 54 patients (men - 35, women - 19, average age 43 (29-49) years), admitted to the medical department of Chelyabinsk State Clinical Hospital № 9 for the period 2006 to 2007 with manifestation of toxic cholestatic hepatitis after ingestion of alcohol surrogates (alcohol for external use «Mozheveloviy»). Long-term results were estimated in 2012. Statistical processing has been done with Statistica-6, Medcalc Version 11.5.0.0. Re-sults. According to clinical data at the time of hospital admission in 100% of cases there were diagnosed intense jaundice, dyspepsia, asthenia syndrome and itching in 60% of cases, hepato-megaly with abdominal pain in the right upper quadrant in 33%, fever, hypotension, bradycardia in 12% of cases. In biochemical analysis there were detected hyperbilirubinemia (2 - 24 stand-ards) in 100% of cases predominantly by direct fraction, increased GGT (4.5 -80 standards), al-kaline phosphatase (1.5 -5 standards), hypercholesterolemia 2-3 standards in 80% of cases, in-creased AST (3-32 standarts), ALT (4-25 standards). During

the course of disease jaundice per-sisted for 6 to 12 months with a significant reduction in total and direct bilirubin fractions and no significant dynamics in GGT, alkaline phosphatase, and cholesterol. During the first month of disease 10 patients died (18%) as a result of liver failure, in the subsequent period 7 patients died (13%). According to the results of the logistic regression ($\chi^2 = 43,9, p < 0.001$), the factors associated with a fatal outcome were the white blood cell count in CBC (OR = 4.8, 95% CI 1,12-20,55 p = 0.03) and serum creatinine (OR = 1.1, 95% CI 0.99 = -1.22, p = 0.09). Predictive value of the model is 93.3%. White blood cell count in CBC above $9.7 \times 10^9 / L$ (specificity 100%, sensitivity - 71.3%, area under the ROC curve - 0.93, p < 0.001) and direct bilirubin above 109 micromol / L (sensitivity - 100%, specificity - 60.3%, area under the ROC curve - 0.72, p = 0.001) are significant factors in prediction of outcome in ROC-analysis.

Conclusions. Toxic hepatitis caused by ingestion of alcohol surrogates are associated with severe prognosis. For prediction of outcome of toxic hepatitis it is necessary to create special prognostic model.

III PLACE

RISK FOR DECOMPENSATION, HCC AND LIVER-RELATED DEATH AND THEIR PREDICTORS IN PATIENTS WITH CHRONIC HDV-INFECTION: RESULTS OF 10-YEAR FOLLOW-UP IN HEPATOLOGY DEPARTMENT

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Chronic delta hepatitis (CHD) is one of the most serious and rapidly-progressive diseases of the liver, carrying high risk for liver cirrhosis (LC) and hepatocellular carcinoma (HCC). HDV-infection, being the liver disease with the most serious prognosis is at the same time of the ones with least studied natural history and effective treatment options.

Aims: to assess the risk for liver decompensation, HCC and liver-related death and to identify their predictors in patients with chronic HDV-infection.

Materials and methods: HBsAg (+) patients with serum markers of hepatitis delta (anti-D and HDV RNA), treated in E.M. Tareyev Nephrology, Internal and Occupational Diseases Clinic from 2002 to 2011 were included in the study. Careful evaluation of anamnesis and physical signs of liver disease, laboratory parameters including AST,ALT, GGT, ALP, TP, bilirubin, cholinesterase, creatinine, BUN, prothrombin, immunoglobulins, AFP, ANA and crioglobulins were performed for every patient. Markers of viral hepatitis in serum were evaluated by ELISA and HBV, HCV and HDV replication by PCR. All patients have undergone abdominal US (contrast-enhanced CT or MRI when needed) and upper GI endoscopy when indicated. Assessment of liver fibrosis was made by means of liver biopsy and elastomerty (Fibroscan, Echosens, Paris, France) in 31 (30.4%) patients. LC was diagnosed using liver biopsy/elastometry and/or clinical and laboratory evaluation results. Statistical analyses were performed using SPSS v.17 software (IBM Corporation, New York, USA). Significance of differences were assessed by Mann-Whitney U-test for nonparametric data. In cases of parametric data, t - test was used instead. Chi-squre test was used to compare categorical data, a p value less than 0,05 was considered significant. P values between 0.05 and 0.15 were considered as tendency to significant difference. Prognostic factors were assessed using logistic regression analyses with backward elimination of insignificant variables. Cumulative probability of survival, risk for decompensation and HCC were calculated by the Kaplan-Meier method.

Results: 102 (20.6%) out of 495 HBsAg (+) patients, followed-up in the clinic during mentioned period, have revealed markers of HDV-infection (mean age 39 years, male 58%)

65 (63,7%) patients, first diagnosed with HDV-infection, had histological and/or clinical signs of LC. 39 (38%) of those had compensated and 26 (25,5%) – decompensated liver disease. 2 patients, first diagnosed with HDV, already had HCC.

Decompensation

42 patients (mean age 44.3 years, male 47.6%) with compensated

LC developed decompensation during follow-up. First episode of decompensation occurred after 45±33.1 months upon diagnosing LC on average. The most frequent decompensation episode was ascites (32 пациента, 76.2%), followed by jaundice (4 пациента, 9.5%), upper GI bleeding (3 пациента, 7.1%) and hepatic encephalopathy (3 пациента, 7.1%).

By logistic regression analyses, low serum albumin, high γ -globulins and high bilirubin levels were significantly associated with decompensation (table 1).

Table 1. Decompensation predictors

Predictors	β	Sig.	Exp(B)	95% CI для Exp (B)	
				Lower	Upper
Albumin	-0,451	,011*	0,637	0,450	0,902
γ -globulins	0,139	,069*	1,150	0,989	1,336
Bilirubin	0,071	,106**	1,074	0,985	1,171

*- significant difference, **-tendency for significant difference

Patients with normal/low level of albumin had 0%/15%, 5%/20% и 22%/50% risk for 1-year, 2-years and 5-years decompensation risk, respectively (figure 1).

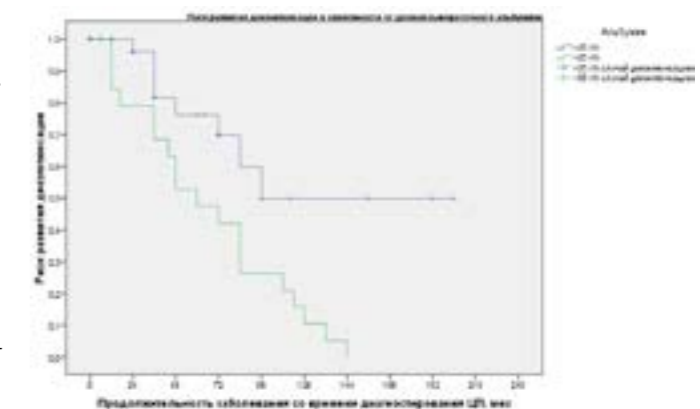


Figure 1. Decompensation risk depending on serum albumin level

HCC

8 (7.8%) patients developed HCC during follow-up (mean age 50.8 years, male 50%). Mean duration of the liver disease at diagnosing HCC was 337±113.7 months. Older age, high serum ALP and AFP were significant predictors of HCC (table 2).

Table 2. HCC predictors.

Predictors	β	Sig.	Exp(B)	95% CI для Exp (B)	
				Lower	Upper
Older age	0,082	,058**	1,085	0,997	1,181
Serum ALP	0,006	,070**	1,006	0,999	1,013
AFP	0,017	,180**	1,017	0,992	1,042

*- significant difference, **-tendency for significant difference

Survival

18 (17.8%) cases of liver-related death occurred during follow-up (mean age 44.1 years, male 72.2%): 9 (50%) patients of liver failure, 6 (33.3%) patients of HCC, 1 patient of upper GI bleeding, 1 patient – post liver transplantation and another patient of pneumonia.

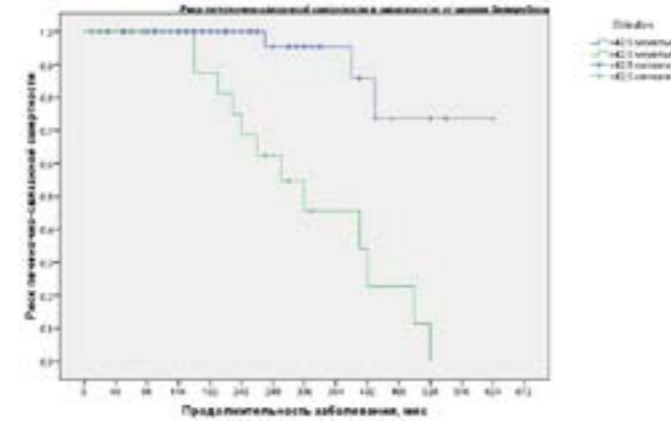
High serum bilirubin and low prothrombin were significant predictors of liver-related death (table 3, figure 2).

Table 3. Liver-related death predictors

Predictors	β	Sig.	Exp(B)	95% CI для Exp (B)	
				Lower	Upper
Bilirubin	0,062	,007*	1,064	1,018	1,114
Prothrombin	-0,138	,075**	0,871	0,749	1,014

*- significant difference, **-tendency for significant difference

Figure 2. Risk of liver-related death depending on level of serum bilirubin



Conclusions: 20.6% of patients with HBV had markers of HDV. Almost 2/3 of newly diagnosed HDV-infected patients already had LC. Low albumin, high γ -globulinemia and hyperbilirubinemia are significant predictors of decompensation. Ascites was the most frequently seen at first decompensation episode in HDV patients. Chronic delta patients with low albumin level had 50% decompensation risk at 5 years. Overall, 7.8% patients have developed HCC over the follow-up, older age, serum ALP and AFP being significant predictors. During follow-up, liver-related death occurred in 17.8% patients, mostly of liver failure and HCC. High serum bilirubin and low prothrombin level were significantly associated with mortality.

ALCOHOLIC LIVER DISEASE

CORRECTION OF NUTRITIONAL DISORDERS IN CASE OF ALCOHOLIC LIVER DISEASE

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Issues of nutritional support of patients with acute and chronic liver diseases are the subject of extensive discussion.

In the intensive care unit treatment was given to fifty-eight-years old patient with a diagnosis of alcoholic cirrhosis, active, C class under Child-Pugh, decompensation stage, complicated by portal hypertension, ascites, encephalopathy, hepatonephric syndrome. Before entering the intensive care unit he was administered dietary menu No. 15, vitamins, diuretics, prednisolone, methacin, Essentiale, Ursosan, Duphalac. The disease continued to progress. At intensive care unit the success in the patient's treatment was achieved by the correction which took place prior to malnutrition. At the beginning of treatment the parenteral, and then enteral nutrition in the form of artificial balanced high-caloric nutrient mixtures was used. The significant correlation was found between the replenishment of daily need for calories and decrease in the severity of alcoholic liver disease complications, such as encephalopathy, ascites, hepatorenal syndrome. Such relationship was confirmed also by improvement of laboratory parameters. When admitting the following symptoms were noted: complaints of weakness, fatigue, sleep disorders, memory loss, mood instability, pain in legs. Clinical and laboratory parameters: tense ascites, peripheral edema, oliguria, AST 1.65 mmol /l, ALT 0.72 mmol / l, total bilirubin 701 mmol / l, total protein 35 g / mol, acute renal failure of 3rd degree by RIFLE. In 2.5 weeks of treatment with the use of artificial nutrition counting 3,000 kcal/d the subjective state of the patient improved significantly, and listed laboratory values reached norm.

Thus, timely correction of nutritive disorders helps to improve the values of not only trophic status, but also the functional state of the liver in general.

THE IMMUNOLOGICAL STATUS IN PATIENTS WITH CHRONIC ALCOHOLIC AND ALCOHOLIC+ VIRAL HEPATITIS IN THE NORTH REGION

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Purpose: To estimate the immunological status of patients with chronic alcoholic and alcoholic+viral hepatitis in the North region.

Materials and methods: The analysis of immunological indicators carried out in groups of patients with chronic alcoholic hepatitis (CAH) – 56, alcoholic and viral chronic hepatitis (AVCH) - 72 and 30 patients of control group of donors.

Results: More profound changes in indicators both cellular, and humoral immune system are revealed in CAH. The tendency to reduction of absolute quantity of lymphocytes (P<0,001) was observed in CAH group. The quantity of all subpopulations of T-lymphocytes significantly changed in CAH vs. control group (P<0,001) except for the relative count of T-suppressors: their number significantly decreases only in comparison with group of donors (P<0,05). Indicators of humoral immunity were characterized by increase of JgA levels in patients with CAH (P<0,05) in comparison with control group and AVCH group.

The JgG serum levels in group of AVCH increased slightly (P< 0,05) in relation to control. Concentration CIC in serum of blood in CAH group increased considerably in comparison with control group (P<0,001) and was significantly higher, than similar indicators in group of ACVH. The tendency to decrease in total number of lymphocytes both with and without activity (P<0,05) is revealed in patients with ACVH. Reduction of quantity of T-lymphocytes and their subpopulations correlated with toxic effect of alcohol in injured with HBV liver cells.

Lack of T-helpers, possibly, correlates with marrow injury and other haematogenic organs with HBV, and also effect of alcohol and its metabolites on these organs.

Conclusions: Degree of f immunological abnormalities depends on activity of disease in CAH and AVCH.

DIFFERENT TREATMENT APPROACHES FOR ACUTE ALCOHOLIC HEPATITIS.

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Aim: to compare efficacy and safety of Budesonide and Prednisolone in treatment of acute alcoholic hepatitis (AAH).

Methods: 35 patients with AAH were randomised in 2 groups and enrolled in the prospective trial. Group 1: 15 patients (7 men, 8 women), average age 46,53±11,01. Median alcohol daily intake - 77 g., lower and upper quartiles - 55 and 96 g. Duration of alcohol intake - 13,41+8,55 years. Discriminant function (DF) average value was 65,22 (from 37,2 to 145,4). Group 2: 20 patients (16 men, 4 women), average age 46,5±11,89. Median alcohol daily intake - 70,55 g., lower and upper quartiles - 37 и 88 g. Duration of alcohol intake - 16,85+13,32 years. The average value of DF - 58,11 (from 32,1 to 121,7). Groups were comparable in key features. In group 1 Budesonide was prescribed 9 mg/daily per os. In group 2 – Prednisolone 40 mg/daily per os. Response criteria – Lille model. Statistical analyses were performed using SPSS 17.0 statistical package.

Results: There was no statistical significance in efficacy (p = 0,810) and short-term survival (p = 0,857). In group 2 adverse events were statistically more frequent than in group 1: 70% vs. 26,7% (p = 0,011). Hepatorenal syndrome occurred frequently in group 2 (p = 0,033).

Conclusions: There was no statistical significance in efficacy of Budesonide and Prednisolone in treatment of AAH. Adverse events as a whole and hepatorenal syndrome specifically occurred statistically more frequent on application of Prednisolone.

TOXIC INJURY OF LIVER AND OPTIMIZATION OF ITS PHARMACOTHERAPY

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Purpose of study: to optimize therapy of toxic hepatitis caused by alcohol substitute poisoning.

Materials and methods: retrospective analysis of 60 patient medical records was conducted. The biochemical parameters of liver, blood clotting system were examined, ultrasound of the abdominal cavity and liver autopsy in 5 patients were conducted.

Results: men (76.67%) aged 30 to 60 years prevailed. When admitting there were complaints on icterus (98.3%) and skin itch (51.7%). Objectively: in 90% - hepatomegaly, cholestasis, cytolytic syndrome, lower serum creatinine, latent anemia, in 25% - leukocytosis, increasing echogenicity and liver size (100%) and spleen size (7%), esophagus candidamycolysis (48,57%), erosive lesions of gastrointestinal tract (31.42%). The duration of hospitalization was significantly correlated with the level of total (r = 0,56) and direct bilirubin (r = 0,59) on admission. Detoxification and basic therapy was administered to all patients. In addition, 63.3% of patients were administered L-2-pyrrolidone-5-carboxylate (Metadoxyl) 10 ml/day (600 mg). In retrospect, the patients were divided into groups: I – metadoxyl was not administered, II group – it was administered in 4 weeks after admission, III group – from the moment of admission. Only in III group there was firm improvement. In II group the basic therapy did not give a positive effect, despite its strengthening. Only after adding metadoxyl the doubtful, but the positive trend appeared. Death was observed in 8.33% of cases.

Conclusions: Toxic hepatitis caused by alcohol substitute poisoning is characterized by intermitten course with devastating skin itch, intrahepatic cholestasis with fatty or balloon dystrophy of hepatocytes, infiltration of the portal tracts, and focal necrosis. Increase in the doses of prednisolone, Ursosan, number of sessions of plasmapheresis doesn't produce desired effect. Addition of L-2-pyrrolidone-5-carboxylate (metadoxyl) from the moment of admission increases the effectiveness of therapy.

FEATURES OF DISTURBANCES OF THE LIPID METABOLISM AND ADVANCE OF THE ENDOGENIC INTOXICATION SYNDROME AT PATIENTS WITH CHRONIC ALCOHOLIC HEPATITIS

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Complexity of a problem of chronic alcoholic hepatitis consists in its frequent combination to pathology of other organs, many-sided mechanisms of pathogenesis.

Research aim – to study features of disturbances of lipid metabolism at patients with the chronic alcoholic hepatitis (CAH) with different degree of severity of endogenic intoxication syndrome (SEI).

Material and methods: Under observation there were 94 patients with CAH, at the age of 31-57 years. At all the patients the complex assessment of indicators of function of liver, lipid metabolism (total cholesterol (TC), lipoproteins of high (HDL), low (LDL) and very low density (VLDL)), intensity of lipid peroxidation, activity of endogenic antioxidant system, severity of SEI was carried out. Depending on degree of SEI severity (indicators of middlemolecular peptides of blood serum (CM), albumin/gamma-globulin coefficient and the mean corpuscular volume of erythrocytes (MCV) all patients were divided by groups – the minimum 37 patients, moderate – 46 and severe degree – 11.

Results. At patients with exacerbation of CAH in process of intensifying activity of inflammation the intensification of processes of lipid peroxidation, decreasing of endogenic antioxidant protection activity was caused by change of physical and chemical properties of cell membranes. Essential factor of CAH progression is SEI that characterized by increasing of CM contents in blood, value of MCV, decreasing of albumin/gamma-globulin coefficient. Strong positive correlation between concentration of CM in blood and indicator of MCV (r = + 0,86, P <0,05) was established. At studying lipid metabolism, TC, HDL and LDL decreasing that correlated with degree of SEI was revealed.

Thus, uncontrollable intensifying of lipid peroxidation processes, dislipidemia at CAH patients are interdependent processes which promote increase of endogenic intoxication, i.e. disease progressive. Research of the specified above indicators is necessary for an assessment of the forecast of disease and development of treatment.

DYNAMICS OF CHOLESTASIS MARKERS IN PATIENTS WITH ALCOHOLIC CIRRHOSIS DURING USE OF S-ADENOSIL-L-METHIONINE.

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The purpose of our research was the assessment of dynamics of cholestatic syndrome in patients with liver alcoholic and mixed (alcoholic+viral) cirrhosis during use of S-adenosil- L - methionine in comparison with traditional IV detoxication infusions.

163 patients with LC complained with cholestatic syndrome were included in clinical research who were admitted in A.A.Vishnevsky Central Military Hospital in the period of 2007-2012 years. There were 32 (19,6%) women, 131 (80,4%) men. Average age of patients made 52,7±0,7 (24-78) years. The diagnosis of alcoholic cirrhosis is confirmed according to modern standards. Patients with LC Child-Pugh class B prevailed.

For an assessment of degree of cholestasis the total bilirubin (TB, cut-off is 3,4-25,0 μmol/l), alkaline phosphatase (AP) (cut-off is 40-150 U/l) and γ-glutamyl transferase (GGTP) (cut-off is 9-64 U/l) levels were measured.

The average level of TB was 156,7±81,7 μmol/l (58,9-816,9). An increased AP level, average 286,8±112,6 U/l (39-1193 U/l) occurred in 142 (87,1%) patients. Increased GGTP levels occurred in 156 (95,7%) patients - 247,4±65,6 U/l (43-918).

Distribution of patients to two groups was random. The first group of 177 (71,8%) patients received detoxication therapy (2-3 liters per day) in addition to IV S-adenemionine 1600-2400 mg/day followed by oral S-adenemionine reception in a similar dose for the long period, up to 3-6 months. The second group consisted of 46 (28,2%) patients receiving only detoxication therapy (2-3 l/day). Control laboratory tests was made on the 1-2nd and 10-12th days of treatment.

CLINICAL AND DIAGNOSTIC FACILITIES OF TRANSIENT LIVER AND SPLEEN ELASTOGRAPHY IN CIRRHOSIS PROGNOSIS

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Aims: Assessment clinical and diagnostic facilities of transient liver and spleen elastography (TLSE) in patients with alcoholic liver disease.

Materials and methods: 171 patients [95 (55,6%) men and 76 (44,4%) women aged from 19 till 55 years (p<0,05)], with alcoholic liver disease on the basis of Clinical hospital No. 1 in the period of November 2010 till December 2012. Among them: steatosis – 60 (35,1%), alcoholic hepatitis – 58 (33,9%), alcoholic cirrhosis – 53 (31%) patients (p<0,05). Ultrasonography with an assessment of a portal blood-groove was carried out. TLSE was performed with FibroScan (Echosens, France). In 97 (56,7%) patients liver biopsy with US control was made as a reference method. Elastographic indicators of a spleen (kPa) were estimated with the modified scale of METAVIR confirmed by morphological (spleen tissue) data.

Results: Coincidence of results of a pulse liver elastography and morphological data was observed in 93 (95,8%) patients. In additional spleen elastography (SE) it was established that in 103 (60,2%) patients with fibrosis stage F1-F2-F3 (liver elastography) the indicator of SE made L2-L4 (p<0,001). That testifies to an atrophy of lymphoid follicles, fibrosis of pulp and capsule sclerosis which are signs of development of portal hypertension.

Conclusions: Prevalence of elastographical indicators (kPa) of spleen over liver ones (kPa) may show a possible transition to cirrhosis in non-compliant patients. Use of a complex TLSE in follow-up period helps to correct treatment tactics.

Distribution of components of a cholestatic syndrome in groups depending on treatment option

Tests	1 st -2 nd days of treatment		10-12 th days of treatment	
	groups		groups	
	I	II	I	II
Total bilirubin (μmol/l)	159,3±68,7	144,5±73,4	79,8±38,2*	118,3±49,6
AP (U/l)	283,6±82,6	286,3±93,2	143,4±76,3*	203,3±62,7
GGTP (U/l)	248,3±63,3	242,8±65,6	128,7±45,5*	187,3±49,4

* statistically significant (p<0.05).

Conclusions. Significant positive dynamics of markers of cholestasis syndrome in patients getting S-adenemionin vs. group of comparison are showed. Patients with Child-Pugh class A have a better improvement of markers of cholestasis than patients with B class.

RESORT TREATMENT OF PATIENTS WITH ALCOHOLIC HEPATITIS AT EARLY STAGES OF THE DISEASE DEVELOPMENT

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The question of alcohol abuse prevention and the treatment of its consequences continue to be a relevant medical and social problem.

Research purpose. To develop and to substantiate scientifically the possibility and reasonability of spa treatment with the patients suffering from alcohol-induced liver injury.

Data and research methods. In Pyatigorsk Research Institute of resort studies there have been examined 470 patients suffering from alcoholic hepatopathies with early prenosological forms of the disease. Biochemical, electrophysiological and immunological indices have been studied. They described pathological process activity in the liver. Spa treatment was conducted against the background of clinical nutrition, exercise therapy (ET), application of average-mineralized drinking mineral waters, low-sulfide and radon baths of Pyatigorsk resort.

Results of the research. At the end of the spa treatment course with ¾ patients decreased the frequency of pain and dyspeptic syndromes, improved indices of functional liver condition. Therapeutic and rehabilitation value of the spa treatment was also confirmed by the results of long-term follow-up of the patients. The stability of the therapeutic effect remained till 7-12 months, aggravations decreased in 3.7 times (from 33 to 9), the number of days of temporary disability in 2.9 times for 1 patient (from 27.4 to 9.6).

Conclusion. Resort treatment with internal and external application of mineral waters in early terms of chronic alcoholism is an effective method of patients' rehabilitation.

CLINICAL DIAGNOSTICS OF ALCOHOLIC CIRRHOSIS

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One hundred sixty three patients with liver cirrhosis (LC) admitted in A.A.Vishnevsky Central Military Hospital in the period of 2007-2012 years were included in clinical research, among them: 32 (19,6%) women and 131 (80,4%) men. Average age was 52,7±0,7 (24-78) years. The diagnosis of cirrhosis was confirmed according to modern standards. Patients with LC Child-Pugh class B prevailed.

More than 27% of patients confirmed alcohol abuse in communication at the first visit. Poll of relatives and studying of previous medical histories were carried out also. Almost all patients admitted the fact of alcohol abuse further. Besides, practically all patients demonstrated common symptoms of alcoholic intoxication – Dupuitren's contracture, a gynecomastia in men, significant hepatomegaly, spider nevi, injury other target organs.

Incidence of diagnosing of cirrhosis signs

All patients had scleral icterus, 61 (37,7%) patients had icterus. Ascites occurred in 110 (67,5%) patients, esophageal and gastric varices- in 128 (78,1%) patients. Portal encephalopathy is diagnosed in 69 (42,1%) patients. Hepatomegaly was defined in 134 (82,5%) patients. Signs of coagulopathy were revealed in 149 (91,2%) patients.

Conclusion. Routine clinical methods of examination allow to define an alcoholic etiology of cirrhosis with high degree of reliability. Laboratory and instrumental techniques confirm a cirrhotic stage of CLD, specify its severity and complications.

OUTCOMES OF TOXIC HEPATITIS CAUSED BY SUBSTITUTES OF ALCOHOL

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Three thousands patients with toxic hepatitis due to substitutes of alcohol are registered in Chelyabinsk region in 2006-2007. 244 persons (8%) died of hepatic insufficiency in 6 months from the disease onset.

Research objective. To estimate long-term outcomes of toxic hepatitis due to substitutes of alcohol (alcohol for external use "Juniper") with definition of predictors of death.

Materials and methods. The retrospective analysis of clinical and laboratorial data and survival of 73 patients (men 49, women 24, middle age of 44 (32-49) years), admitted in hospitals in 2006-2007 is carried out. Statistical processing of a material is carried out with software package of Statistica-6, Medcalc with application of logistic regression for forecasting of a course of a disease, creation of ROC curves for identification diagnostic significant tests. The MELD and also R (a ratio of hepatocellular and/or cholestatic defeat) score are defined for prognosis estimation.

Results. All patients had severe toxic hepatitis with the expressed cholestatic syndrome resistant to therapy. 16 patients (20%) died within the first month of a disease due to hepatic insufficiency, for the subsequent period-13 patients (19%) died. The MELD index was informative in this group of patients, the R index indicated the mixed defeat and didn't influence the prognosis in 78% of cases. Own predictive model of survival of patients is developed: level of leukocytes in FBC (OS=4,8, 95% C.I. 1,12-20,55, p=0,03) and creatinine level (OR=1,1, 95% of DEE 0,99 =-1,22, p=0,09) - the prognostic value of model - 93,3%. Direct bilirubin level (AUROC 0,79, C.I. 0,58-0,83, p=0,001) and leukocytes counts (AUROC 0,93, C.I. 0,83-0,98, p<0,001) appeared to be significant for prognosis.

Conclusions. Our data showed that the most significant predictors of a lethal outcome were degree of the inflammatory response, high bilirubin levels and hepato-renal syndrome.

PSYCHOLOGICAL FINDINGS OF PATIENTS WITH FATTY LIVER DISEASE OF VARIOUS ETIOLOGIES

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Purpose. Comprehensive study of the psychological characteristics of patients with fatty liver disease alcoholic and non-alcoholic etiology.

Materials and methods. We examined 59 patients with alcoholic fatty liver disease etiology (AFLD), 60 patients with non-alcoholic fatty liver disease etiology (NAFLD), the control group consisted of 32 healthy volunteers of similar age and gender. Steatohepatitis diagnosis was confirmed clinically and morphologically. Psychological status was assessed using the The Small Minnesota Multiphasic Personality Inventory and Eysenck test. Each patient signed an "informed consent" to participate in the research. The differences between the parameters of comparison were considered statistically different at p ≤ 0,05.

Results. Psychological status of patients with fatty liver disease alcoholic and non-alcoholic etiology did not differ significantly between the groups, but differed from the control (p <0.05). In the control group, the results of the study were lower than in the groups with steatohepatitis on the following scale: the first "neurotic overcontrol or hypochondria," the fourth "impulsivity or psychopathy," the seventh "reactive anxiety or psychasthenia" the eighth "individualistic" the and nine "optimistic." Results for the test were as follows Eysenck – the level of neuroticism was the highest in patients with NAFLD (p <0.05 in comparison with the control and AFLD), with the level of extraversion was highest in patients with AFLD (p <0.05 in comparison with control and NAFLD).

Conclusions: We have defined psychological profile of patients surveyed groups – emotionally labile, prone to hypochondria, self-assured, with high levels of anxiety and neuroticism personality type. More accentuated test results psychological characteristics of patients with AFLD.

AUTOIMMUNE LIVER DISEASES

DIAGNOSTIC VALUE OF SYSTEMIC SYMPTOMS OF THE PRIMARY SCLEROSING CHOLANGITIS

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*Clinic for nephrology, internal and occupational diseases named after E.M. Tareev, State-financed Educational Post-Secondary Institution - I.M. Sechenov First Moscow State Medical University, Moscow city, Russian Federation***Introduction.** Primary sclerosing cholangitis (PSC) is a slowly progressive chronic liver disease characterized by non-suppurative destructive inflammation and fibrosis of the bile ducts, resulting in development of secondary biliary cirrhosis.**Purpose of the study.** Study the prevalence of autoimmune diseases in patients with PSC.**Materials and methods.** 93 patients with primary sclerosing cholangitis observed in Clinic for nephrology, internal and occupational diseases named after E.M. Tareev. In the group there were 47 men and 46 women, average age $32,6 \pm 11,1$ years old, average duration of the disease $1,9 \pm 2,8$ years. Study materials were archived data from case histories and medical treatment records, as well as medical records of prospectively traced patients.**Results.** Autoimmune diseases such as systemic symptoms were observed in 79.6% of patients. Wide range of systemic symptoms were noted in patients with PSC: ulcerative colitis, Crohn's disease, hemorrhagic vasculitis, autoimmune thyroiditis, Sjogren's syndrome, vitiligo, recurrent urticaria, scleritis, keratitis, conjunctivitis, sarcoidosis, nodular erythema, chronic glomerulonephritis, fibrosing alveolitis, psoriasis, type 1 diabetes, autoimmune hemolytic anemia. The most frequent were ulcerative colitis (49.5%) and Crohn's disease (17.2%). In 20.3% of patients with PSC more than autoimmune disease was registered: in 14% of patients - two autoimmune diseases, in 4.3% - 3, in 1.1% - 4, in 1.1% - 5 autoimmune diseases.**Conclusions:** 1) More than 79% cases of PSC were accompanied by extrahepatic manifestations. 2) One in five patients with PSC has 2 or more autoimmune diseases (in addition to PSC). 3) The most common extrahepatic manifestations of PSC in the Russian population of patients are intestinal, skin, and thyroid lesions.**TUMOR NECROSIS FACTOR-ALFA IN PATIENTS WITH AUTOIMMUNE LIVER DISEASES AND CHRONIC HEPATITIS C**Marchenko N.V.¹, Raikhelson K.L.¹, Karev V.E.², Smirnov D.R.³, Borisov A.A.³¹North-Western State Medical University named after I.I. Mechnikov, Saint-Petersburg, Russia²Scientific Research Institute of Children Infection Diseases FMBA of Russia, Saint-Petersburg, Russia³City Clinical Hospital # 31, Saint-Petersburg, Russia**Introduction:** Tumor necrosis factor-alpha (TNF α) is one of the proinflammatory cytokines and immunomodulator. The role of TNF α in development and maintenance of a chronic inflammation at autoimmune liver diseases (AILD) and chronic hepatitis C (HCV) is actively investigated. The aim of our study was to assess the serum TNF α level and expression of TNF α in liver tissue patients with AILD and HCV.**Materials and methods:** 33 patients included 11 cases of PBC, 10 cases of AIH and 10 HCV were examined. The serum TNF α level was studied by enzyme-linked immunoabsorbent assay (ELISA). The expression of TNF α and CD68+ cells were investigated by immunohistological examination in liver biopsies. The number of CD68+ macrophages and TNF α were counted in 15 HPF (x400). The expression of TNF α was quantified as a percent positive TNF α cells rather CD68+ as a whole. Activity scores were similar in all groups (METAVIR A2-A3).**Results:** In all group patients, the serum TNF α level was within the reference values. The average level expression of TNF α was $0,23 \pm 0,21$ (%) in PBC, $0,52 \pm 0,41$ (%) in AIH and $1,42 \pm 1,05$ (%) in HCV patients. The expression of TNF α was statistically significantly high in patients with HCV in comparison with AILD (23 AILD vs 10 HCV, $p < 0,02$, 12 AIH vs 10 HCV, $p < 0,03$, 11 PBC vs 10 HCV, $p < 0,006$). On the other hand, no statistically significant difference were encountered in the expression of TNF α within group AILD patients when compared AIH and PBC (11 PBC vs 12 AIH, $p < 0,06$).**Conclusions:** Our study did not demonstrate the increasing of serum TNF α level of AILD and HCV patients. We found the difference in expression of TNF α in liver tissue at patients with hepatitis of various etiologies (AILD and HCV).**HEPATOPROTECTIVE EFFECTS OF POLY(ADP-RIBOSE) POLYMERASE (PARP) INHIBITOR 4-HYDROXYQUINAZOLINE (4-HQN) ON EXPERIMENTAL CONCANAVALIN A INDUCED HEPATITIS**

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PARPs are a family of enzymes which synthesize poly(ADP-ribose) - PAR. PARP-1, the most abundant isoform, is activated by DNA breaks and catalyzes the post-translational modification of proteins. It attaches PAR to acceptor proteins, including histones, DNA repair proteins, transcription factors. Excessive activation of the enzyme has been shown to contribute to inflammation and tissue injury. PARP-1 is considered as a promising target for pharmacological intervention in the treatment of various disorders. The role of PARP-1 in autoimmune liver diseases and clinical perspectives of PARP inhibitors are still unclear. Here, we investigated the influence of PARP-1 inhibitor 4-HQN on the morpho-functional state of mouse liver in immune-mediated hepatitis induced by polyclonal T cell activator concanavalin A (ConA). It is widely used murine model for human T-cell dependent autoimmune liver disorders. Con A administration (25 mg/kg) resulted in an increase in liver malondialdehyde (MDA), a measure of lipid peroxidation, and serum alanine aminotransferase (ALT). Pretreatment with 4-HQN (50 mg/kg, 2h before ConA) significantly decreased MDA level and ALT activity by 1.3 and 2.2 times, respectively ($P < 0.01$). A histological study of liver was performed using a semiquantitative scoring system. It was shown, that PARP inhibition decreased the total score of vascular injury (sum of scores for microvessel enlargement, microvascular hyperemia, thrombosis, vessel wall damage and perivascular edema) from 13.1 ± 0.5 in Con A hepatitis to 9.0 ± 0.5 after treatment with 4-HQN, $P < 0.001$ (vehicle control 0.6 ± 0.3). Inhibition of PARP activity resulted in a marked improvement in the liver parenchyma. 4-HQN administration decreased the total score of parenchymal injury (calculated as a sum of scores for hepatocyte dystrophy and liver cell death, disorganization of hepatic plates, leukocyte infiltration into the parenchyma and morphological signs of Kupffer cells activation) from 15.6 ± 0.5 in ConA - induced hepatitis to 11.7 ± 0.3 after 4-HQN treatment, $P < 0.001$ (vehicle control 2.2 ± 0.4). These results suggest that PARP plays an important role in immune-mediated liver injury and PARP inhibitor 4-HQN exerts significant hepatoprotective, anti-inflammatory and antioxidant effects against Con A - induced T cell-mediated hepatitis in mice.**THE BONE MINERAL DENSITY IN PATIENTS WITH AUTOIMMUNE HEPATITIS, PRIMERY BILIARY CIRRHOSIS AND OVERLAP SYNDROM**

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*North-Western State Medical University named after I.I.Mechnikov, Saint-Petersburg, Russia***Introduction/Aims:** Osteopenia is one of the complications of autoimmune liver diseases (AILD), that accompanied by intrahepatic cholestasis syndrome. Probably, the malabsorption of vitamin D and calcium are played a major role in genesis of AILD, which arises due to lack of bile in the intestine. Promotes to the formation of osteoporosis are often administered therapy of corticosteroids to these patients. The aim of this study was to determine bone mineral density (BMD) in patients with AILD, such as primary biliary cirrhosis (PBC), autoimmune hepatitis (AIH) and overlap syndrome (AIH/PBC).**Materials and methods:** Dual-energy X-ray absorptiometry (DXA) was performed on L1-L4 lumbar spine at 13 female (5 - AIH, 4 - PBC, 4- AIH/PBC). The median age was $56,5 \pm 7,9$ years. The median duration of disease was $4,7 \pm 2,8$ years. In accordance with the recommendations of WHO T-score was assessed, that based on a comparison of the obtained values of BMD with the reference data. All patients received the basic therapy (AIH - glucocorticosteroids, PBC - UDCA), calcium and vitamin D supplementation. Results: The average value of T-score was $(-1,62) \pm 0,16$ in AIH, $(-3,18) \pm 1,36$ in PBC and $(-1,08) \pm 1,28$ in AIH/PBC. The frequency of osteoporosis (T-score < -2.5) was significantly higher in PBC (75%) in comparison with AIH (20%) and AIH/PBC (0%) ($p < 0,05$, $p < 0,04$, respectively). Statistically significant difference was not found between patients with AIH and AIH/PBC.**Conclusions/Discussions:** Even the short-duration of PBC leads to the development osteoporosis which probably caused by more expressed cholestasis. In our study glucocorticoid therapy AIH is less contributed to the development of osteoporosis.**VIRAL HEPATITIS**

CHRONIC GLOMERULONEPHRITIS (CGN) THE MIXED TYPE IN PATIENT WITH CHRONIC HEPATITIS B (CHB)
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A 30 y.o. patient addressed in infectious diseases department at 06.02.2012 with fatigue, epigastral discomfort. The sudden onset was in November, 2011, oedema of shins and feet, arterial hypertension 160/100 mm Hg, headache, nausea occurred. A nephrotic syndrome was diagnosed: proteinuria 4,4 g/d, the total protein 50,4 g/l, increased serum creatinine 116,3 $\mu\text{mol/l}$. 25.11.2012 patient was admitted in nephrological department. Diagnosis: CGN, mixed type, anasarka, bilateral hydrothorax, ascites, respiratory insufficiency. Positive HBsAg and splenomegaly are revealed. Steroids, antihypertensive drugs, anticoagulants and antiagregants with good response were administrated. During steroid therapy ALT and AST levels increased (up to 109 U/l and 46 U/l respectively), high viral load (HBV DNA 10^8 IU/ml), positive HBeAg, advanced liver fibrosis (F3 METAVIR). HBeAg-positive CHB (moderate activity, high viral load) was diagnosed and HBV-associated CGN mixed type with intact kidneys function as well. Entecavir 0.5 mg/d was added to therapy. At the 30th week of therapy HBV DNA was undetectable, at the 42nd week - HBeAg seroconversion. Consolidation of antiviral treatment within 12 - 24 months is planned.

Conclusions:

1. Carrying out therapy of HBV-associated CGN, without purpose of antiviral treatment is accompanied by risk of latent HBV-infection activation due to prolonged immunosuppression.

2. Antiviral agents with high activity (entecavir) are recommended for treating patients with HBV-associated kidney injury.

HEART RATE VARIABILITY AS A PREDICTOR OF ASSESSING THE SEVERITY OF A PATIENT WITH LIVER CIRRHOSIS
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Purpose. Evaluate the relationship of heart rate variability in patients with varying degrees of severity of cirrhosis of viral etiology.

Materials and methods. We examined 103 patients with cirrhosis of viral etiology. The patients were divided into three groups according to severity of the disease - in classes A, B, C on Child-Pugh. Group A - 36 (34.9%) patients, in group B - 34 (33%), patients in group C - 33 (32.1%) patients. To assess the status of autonomic nervous system to use the program «CORVEG». Each patient signed an "informed consent" to participate in the research. The differences between the parameters of comparison were considered statistically different at $p \leq 0,05$.

Results. Calculated indicators of the activity of different parts of the autonomic nervous system. As a method of prediction and classification class A, B and C were used classification trees - a method to predict the observations or objects belonging to a particular class of a categorical dependent variable, depending on the respective values of one or more independent predictor variables. The first branching performed on resting heart rate ≤ 87.813 , the higher the heart rate, the more sympathetic influence in the group. Further branching - in terms of "Autocorrelations" alone to "Very low frequency" at get up "Variation range" at get up, "Dispersion" at get up, "Excesses" at rest and at get up, and then on the "minute volume of blood circulation" and terms of "Moda" at get up. The resulting classification tree allows a correct prediction of reference to a particular group of patients with liver cirrhosis (classes A, B, C on Child-Pugh) in terms of the mathematical analysis of heart rate at 73%.

Conclusions. Severe autonomic dysfunction determines the number of symptoms that worsen cirrhosis and its prognosis. The severity of cirrhosis (classes Child-Pugh) are statistically significantly associated with heart rate variability.

NEW OPPORTUNITIES IN ADDRESSING SOME OF THE SIDE EFFECTS OF ANTIVIRAL THERAPY OF PATIENTS WITH CHRONIC HEPATITIS C
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The aim of the research: to study the therapeutic efficiency of the remaxol in correcting undesirable effects of antiviral therapy (AVT). Study materials: were observed in patients with CHC at the age of 21-57 years who have not received antiviral treatment. Patients were divided into 2 groups: 30 patients (group 1) received OEM remaxol and symptomatic treatment and 30 patients receiving OEM and symptomatic funds (2 group). In all of the surveyed there were no changes on the part of blood, kidneys, thyroid gland, there were the normal levels of creatinine plasma and tireotropinog hormone. Remaxol administered intravenously kapelno in a daily dose of 400 ml within 5 - 7 days. Efficacy of the drug was assessed by the degree of severity of clinical manifestations of the undesirable effects of the HTP. Results: in the 91,6% of patients within a week after the beginning of the HTP appeared fever to 39C, chills, 95% of patients make complaints to fatigue, weakness, 63.3% of patients in (1 group of 17 people. 21 - in the 2 group) noted nausea, lack of appetite. These symptoms regarded as a manifestation of side-effects OEM (flu like, asthenic and dyspeptic syndromes). After therapy remaxol in group 1 manifestations of influenza-like syndrome significantly decreased and did not require the appointment of fever-reducing drugs in 66.6% of and at the same level observed in only 23.4% of patients, while in group 2 patients with previous complaints remained in 93,3% ($p < 0.05$). Asthenia, in group 1 has been perpetuated by 50%, in group 2 - in 93 % of the surveyed ($p < 0.05$). Dyspeptic syndrome in patients of the 1 group was celebrated in 23.3%, which is fairly less than in group 2 patients (66,6%). Conclusions: the inclusion of remaxol in the composition of complex therapy of patients with CHC, located on antiviral therapy helps to reduce clinical signs of side effects of HTP (dyspeptic, asthenic, influenza-like) ($p < 0.05$).

PECULIARITIES OF HEMOSTASIS SYSTEM IN PATIENTS WITH CHRONIC HEPATITIS AND LIVER CIRRHOSIS OF DIFFERENT ETIOLOGY
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Purpose - to detect disorders in hemostasis system in patients with chronic hepatitis C (CHC), alcoholic hepatitis (AH) and hepatitis of combined etiology (CHC+AH) and liver cirrhosis (LC).

Materials and methods: 134 patients were examined, among which men - 63.7% prevailed, average age - $41,4 \pm 5,7$ years. By etiology: 25 patients with CHC, 18 - AH, and 39 patients with CHC+AG). Liver cirrhosis (LC) at decompensation stage was detected in 52 patients, among with in 8 (15.4%) patients with the outcome of CHC, in 12 (23%) - against the background of AH and in 32 (61.5%) - CHC + AH. Death was in 3 patients: 1 man aged 52 years - LC in the outcome of AH and two women - LC in the outcome of CHC+AH. The clinical picture in all patients regardless of etiology was characterized by severe weakness, subfebrile T0, presence of secondary hepatic signs, loss of appetite, icterus, hepatosplenomegaly. Ascites was detected in 38 of 52 patients with LC (73%), at that in the majority of patients - in the outcome of HCC + AH - in 27 (52%). The longest period of bed days was recorded in patients with CHC + AH - $34,0 \pm 2,1$, which was significantly higher than in case of AH - $18,7 \pm 1,3$ ($p < 0.01$).

Results. It was found that in all patients AT was significantly lower than in healthy individuals almost twice. In patients with CHC+AH the amplitude of AT was even less by 3 times compared with normal values. AE and NO levels were determined also significantly below normal in all patients, regardless of etiology. The lowest rates of hemostasis were in patients with LC in the outcome of hepatitis of combined etiology at decompensation stage. Levels of PTI in patients with CH of any etiology was within normal limits. In case of LC regardless of the etiology the IPT was below normal - $60,0 \pm 2,4\%$. Its minimum values were observed in patients with LC in the outcome of AH - $55,0 \pm 4,7\%$. EF level was 2 times higher than normal value in all patients with CHC regardless of AVT, but did not differ significantly between the groups.

THE CORRELATION BETWEEN CLINICAL MANIFESTATIONS IN PATIENTS WITH CHRONIC HEPATITIS B (CHB)
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The Pearson correlation analysis by the program «Statgraphics Plus for Window» was carried out for discreet symptoms and signs in cohort of 131 patients with chronic hepatitis B (CHB) registered at time of their hospitalization due to the attack of CHB.

It has been shown that levels of total bilirubin has direct link with alkaline phosphatase ($r = 0,5$, $p = 0,00001$), value of thynol test ($r = 0,4$, $p = 0,0006$), diameter of a portal vein ($r = 0,3$, $p = 0,04$), grade of icterus ($r = 0,3$, $p = 0,00001$). Value of alanine aminotransferase (ALT) has direct link with gamma glutamine transferase (GGT, $r = 0,4$, $p = 0,002$), and prothrombin index (PTI) the direct link with the total protein level in blood serum ($r = 0,4$, $p = 0,002$) and heterogeneous liver on ultrasonography (USG, $r = 0,4$, $p = 0,00001$).

Direct correlation is also established between data of USG: diameters of portal and splenic veins ($r = 0,8$, $p = 0,003$), size of the right liver lobe and longitudinal size of a spleen ($r = 0,5$, $p = 0,02$), longitudinal size of a spleen and diameter of a splenic vein ($r = 0,7$, $p = 0,003$).

Dynamics of total bilirubin levels (ratio of levels at the time of hospitalization and release) have a direct and strong correlation with ALT dynamics ($r = 0,5$ at $p = 0,02$) and thymol test ($r = 0,9$ at $p = 0,0001$), but have a feedback with PTI dynamics ($r = - 0,8$ at $p = 0,0008$).

Results of these researches demonstrated a number of correlations between various clinical manifestations of CHB. That allowed to obtain new data on pathogenetic features of a CHB, interrelation of dynamics of change of separate symptoms and signs during pathogenetic therapy.

THE LABORATORY AND MORPHOLOGICAL CHARACTERISTICS OF CYTOKINE-INDUCED THYREOPATHY IN CHRONIC HEPATITIS C (CHC)
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Introduction. The aim of antiviral therapy in chronic hepatitis C (CHC) is permanent full remission. Hence, in some cases therapy may be complicated by development of the thyroid negative phenomena due to environmental factors affecting thyroid gland (TG). That reduces compliance and efficiency of therapy.

Purposes. Studying laboratory thyroid tests and morphological changes in TG and development cytokine-induced thyreopathy (CITP) in patients with CHC during antiviral therapy.

Materials and methods. 294 patients with CHC (RNA pos.) was given standard antiviral therapy for 24 or 48 weeks depending on HCV genotype. Inhabitants of the Kiev region (Kiev and suburb - 76,7%, other regions of Ukraine - 23,3%), of them 178 men and 116 women, prevailed. Average age was $36,01 \pm 1,26$ years, an alanine aminotransferase (ALT) levels was $100,03 \pm 9,37$ U/l, HCV RNA - $5,9 \pm 4,4 \times 10^6$ IU/ml, genotype 1 occurs in 57,48% cases. Patients with initial autoimmune thyroiditis, with Graves'S disease, after thyroidektomiya were excluded. Antiviral therapy included in the majority of cases (61,22%): pegylated interferon (α -2a or α -2b) with ribavirine in standard dosing.

Results. In 255 patients (86,73%) there was no thyroid dysfunction during antiviral therapy. Evident CITP occurred in 39 of 294 patients (13,27%), with prevalence of female patients (33) i.e. by 8 times more in women comparing with men. In 82,5% of patients CITP manifested in the first 20 weeks of therapy (early CITP). In 74,36% (29) cases thyroid complications proceeded on autoimmune type with progressing increase of antytheroid antibodies - antibodies to thyreoglobuline (antiTTG) and/ or antibodies to thyreoperoxidase (antiTPO), in 97,44% (38) thyroid dysfunction was registered. In 16 patients of reproductive age (41,03%) CITP had two-phase current - the 1st phase of hypofunction in 1-2 months followed by the 2nd phase of a hypothyroidism which proceeded 2-5 times more, like postnatal autoimmune theroiditis. In 22 (56,41%) patients monophasic CITP occurred - only hypothyroidism (7 patients) or a hypothyroidism (15 patients). Thyroid tests in hyperfunction levels were: thyreostimulating hormone (TSH) - $0,02 \pm 0,01$ $\mu\text{IU/ml}$ (N 0,4 - 4,0), free thyroxine (FT4) - $3,62 \pm 1,21$ ng/dl (N 0,65-2,3), antiTTG- $338,53 \pm 155,53$ IU/ml (N ≤ 100), antiTPO - $406,86 \pm 325,55$ IU/ml (N ≤ 50). In the middle of hypofunction the laboratory picture changed ($M \pm m$): TTG- $48,09 \pm 10,12$ $\mu\text{IU/ml}$, FT4 - $0,46 \pm 0,11$ ng/dl,

LIVER STEATOSIS IN PATIENTS WITH METABOLIC SYNDROME AND CHRONIC HEPATITIS C (GENOTYPE 1)
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Purpose. To determine incidence of identification of fatty liver in patients with the chronic hepatitis C (CHC), genotype 1, and metabolic syndrome (MS). **Materials and methods.** Two hundred ninety patients with excluded non-metabolic reasons of liver steatosis are included in research. The MS was stated by criteria of IDF 2005. Needle liver biopsy was performed in all patients. Hepatocytes steatosis was stated if $\geq 5\%$ liver cells had fatty dystrophy. The diagnosis of CHC is confirmed with standard virological, biochemical and histological methods, all included patients were infected with the 1st genotype HCV. Surveyed are divided into 3 groups: group 1 - 73 patients with CHC (genotype 1) and MS, group 2 - 118 patients with CHC (genotype 1) without MS, group 3 - 99 patients with MS without CHC. **Results.** Fatty liver was revealed in 44 (60,3%), in 11 (9,3%), and in 77 (77,8%) patients of groups 1, 2 and 3 respectively. **Conclusions.** Incidence of liver steatosis is significantly higher in patients with MS both in the presence of CHC, and without a HCV infection in comparison with patients with CHC (genotype 1) and normal weight. It confirms lack of influence of the 1st genotype of HCV on development of fatty liver. It is possible to consider MS as a factor influencing development of liver steatosis that worsens both a natural history of CHC, and response to antiviral therapy.

ATTG-of $878,72 \pm 336,73$ IU\ml, ATTPO - $317,63 \pm 141,08$ IU\ml. Antibodies to a TSH receptor raised only in TG hyperfunction up to $27,73 \pm 17,18$ IU\l, and at hypofunction didn't exceed reference levels - $1,05 \pm 0,52$ IU/l (positive if $> 1,5$).

The autoimmune thyroiditis-like changes in TG fine needle biopsy in 11 patients with CITP during antiviral therapy are found in 8 persons: a diffuse infiltration of lymphocytes and plasma cells with formation of lymphoid follicles with the light germinative centers, - destruction and atrophy of thyroid follicles owing to a productive inflammation and formation of connective tissue, - the high grade metaplasia with oxyphil cells. In 3 patients the morphological findings reminded chronic nonspecific thyroiditis with the microscopic changes: - a diffuse or focal lymphoid infiltration of TG tissue with formation of lymphoid follicles, with seldom high functioning active centers, - replacement of a functioning parenchyma with the connective tissue, - the general dystrophic and degenerative changes or oxyphil metaplasia due to an inflammation in follicular epithelium.

Results. 1) The CITP occurred in 13,27% of patients (male:female ratio of 8:1) during standard antiviral therapy of CHC. 2) Early two-phase CITP with an autoimmune component at women of reproductive age were most common and reminded postnatal thyroiditis. At men and at women in the period of a menopause exclusively monophasic thyreopathy was observed. 3) 11 patients demonstrated morphological changes in TG typical for autoimmune thyroiditis (in 8 cases) and for chronic nonspecific thyroiditis (in 3 cases). 4) Antibodies to a TSH receptor levels increased in hyperthyroidism and remained or dropped to normal level in case of hypothyroidism

LIVER FIBROSIS IN PATIENTS WITH METABOLIC SYNDROME AND CHRONIC HEPATITIS C (GENOTYPE 1)

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Purpose. To define distinctions fibrosis degree in patients with chronic hepatitis C (CHC) and HCV genotype 1 and metabolic syndrome (MS) in comparison with patients without MS / without CHC.

Materials and methods. Two hundred eighty nine patients who were divided into 3 groups. The main group included 73 patients with CHC (genotype 1) and MS corresponding to criteria of IDF 2005. The group of comparison 1 was made by 117 patients with CHC (genotype 1) without MS, with normal weight. The group of comparison 2 (99 patients) was presented by patients with MS and without HCV infection. Patients with the six-months history of HCV infection confirmed with standard tests. Other chronic diseases of the liver (except NAFLD) were excluded. Existence of at least one of the following criteria patients with MS was the basis liver biopsy: diffuse changes of liver in ultrasonography, dyslipidemia, increases ALT, AST levels. The needle liver biopsy is executed to all patients. Assessment of liver fibrosis was carried out with Ishak scale (1-6 points). Depending on results liver fibrosis was conditionally divided on mild(1-2 points), moderate (3-4 points) and advanced (5-6 points).

Results. In the main group (CHC, genotype 1 and MS) mild fibrosis is revealed in 61 patients (83,6%), moderate – in 6 (8,2%), advanced – also in 6 patients (8,2%). In group of comparison 1 (CHC without MS) 109, 4 and 4 patients (93%, 3%, 3%) had the according indicators respectively. In group of comparison 1 (MS without HGS) – 97 patients had mild fibrosis (93%), 4 patients – moderate fibrosis (3%) and 4 (3%) – advanced fibrosis.

Conclusion. More expressed liver fibrosis is much more common in patients with CHC and 1 genotype and with MS in comparison with patients only with CHC (genotype 1) or only with MS. This fact can form the basis for the recommendation of treatment of MS to improve a natural history of CHC and to increase the efficiency of antiviral therapy.

FREQUENCY OF OCCULT HEPATITIS B VIRUS INFECTION IN BRONCHIAL ASTHMA

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Introduction: Immune disorders in bronchial asthma contribute to development of occult hepatitis B virus infection.

Aim: Detect the frequency of association of occult hepatitis B virus infection with bronchial asthma.

Material and methods: Examined 129 sick persons with mixed forms of bronchial asthma without anamnestic data about the acute hepatitis B virus infection they had. The diagnosis is documented based on clinical and laboratory-equipment data.

Outcomes: Among the examined sick persons with bronchial asthma the frequency of hepatitis B virus infection was observed in 56,6% (73 patients). Among 50 patients with bronchial asthma with negative HBsAg the presence of positive antibodies to Cor Ag are detected in 92% (46 patients), in general among women - 66% (33 patients), aged 40-59 – 76% (38 patients). It should be noted that, in sick persons with occult hepatitis B virus infection prevailed the heavy form of heavy form of bronchial asthma in 69,5% (32 patients), in the presence of hepatomegaly in 65,2% (30 patients), despite the normal activity of transaminase – 84,8% (39 patients).

Conclusions: It is established high frequency of association of occult hepatitis B virus infection with bronchial asthma and its influence upon the severity of this pathology of lungs.

SERUM MARKERS OF HERPES SIMPLEX TYPE 1 (HSV-1) IN PATIENTS WITH CHRONIC HEPATITIS AND LIVER CIRRHOSIS.

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Ubiquity of prevalence of HSV is well-known. Nearly 100% of human population are HSV IgG positive. Quite accurate tendencies to increase of a marker of this infection – HSV IgM – in patients with chronic diffuse liver diseases (CDLD). HSV reactivation and replication may occur in individuals with various forms of immune deficiency. This infection should be excluded in patients with hepatitis of uncertain etiology. HSV can take part in pathogenesis of a number of CDLD.

Purposes. define prevalence of HSV antibodies in patients with chronic hepatitis (CH) and liver cirrhosis (LC) [HSV IgM and HSV IgG].

Materials and methods. levels of HSV IgM and HSV IgG were measured in 50 healthy donors and 89 patients with CH and LC, using the IFA method.

Results. Prevalence of HSV IgM and HSV IgG in donors were 45,24 and 100%, respectively, whereas in the general group of patients with CDLD 67,42 and 100%, respectively. Thus, prevalence of HSV IgG was the same - 100% - both in patients with CDLD, and in healthy individuals. At the same time, it was tended to the bigger prevalence of HSV IgM in patients of group CDLD (p>0,05). 32,5% (n=40) of patients with CH were high positive for HSV IgM and 17,5% were with moderate increased levels of antibodies (total 50% of seropositive). Other 50% of patients left were seronegative. Among patients with LC (n=49) 59,2% were seropositive with a high levels of antibodies, 22,0% demonstrated moderate levels, and 18% were seronegative for HSV IgM (p<0,05 in comparison with healthy donors).

Conclusions. Nearly 100% of healthy donors and patients with CDLD are seropositive for HSV IgG. That fact reflects universal prevalence of HSV infection. The prevalence of positivity both HSV IgM and HSV IgG in patients with CH practically doesn't differ from healthy donors whereas the majority of patients with LC had a reliable increase of HSV IgM levels. High levels of HSV IgM indicate on possible active HSV replication at considerable part of patients with LC. That statement can be the evidence of participation of HSV in pathogenesis of LC and also to be manifestation of immune deficiency in this group of patients.

SERUM MARKERS OF EPSTEIN-BARR VIRUS (EBV) IN CHRONIC HEPATITIS (CH) AND LIVER CIRRHOSIS (LC)

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The chronic Epstein-Barr virus infection (EBV) is characterized by the chronic or recidive mononucleose-like symptoms, such as a fever, hepatosplenomegaly, hepatitis and lymphadenopathy. The given infection should be excluded in patients with a hepatitis of unclear aethiology, and also in persons with immune deficiency.

The Aim and the Tasks. To assess the prevalence of IgM and IgG anti-EBV-antibodies among patients with CH and the LC (EBV-IgM and EBV-IgG).

RESULTS. The prevalence of EBV-IgM and EBV-IgG in controls was accordingly 7.5 and 9.8 %, whereas in the general group of patients with Chronic Diffuse Liver Disease the prevalence was of 31.03% and 32.58 % correspondingly. It more than 3 times exceeded the donors` level (p<0.05). In the group of CH patients (n=40) EBV-IgM seronegativity was registered in 85 % of patients. There were 12.5 % of patients with moderate antibodies level, and 2,5 % had very high level of antibodies. Among LC patients (n=49) 53.06% were EBV-IgM seronegative, and 46.97 % were seropositive. 28.57 %of them had very high level of antibodies, and 18.37 % had moderate level. The prevalence of EBV-IgG antibodies in CH was 20 %, including 12.5 % with very high level of antibodies and 7.5 % with moderate level. In LC 57.14 % of patients were EBV-IgG seronegative, 30.61 % had high EBV-IgG level and 12.24 % - moderate.

CONCLUSIONS. Almost one third of patients with Chronic Diffuse Liver Disease were EBV-IgM and EBV-IgG seropositive , that significantly difered them from the control group (donors). In CH the EBV-markers positivity varies between 15 to 20 %, whereas almost half of LC patients had high levels of EBV-IgM and EBV-IgG. EBV-IgM is considered to be the marker of active EBV replication in the significant part of LC patients. The results obtained specify the participation of the EBV in the pathogenesis of the liver diseases, particularly in the interference between hepatotropic viruses, and the modification of CH and LC clinical features.

SERUM MARKERS OF CYTOMEGALOVIRUS (CMV) IN CHRONIC HEPATITIS (CH) AND LIVER CIRRHOSIS (LC)

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The Ubiquitariness of CMV is well-known. Practically 100 % of human population are CMV-IgG positive. At the same time the reactivation of a virus and its replication can take place in persons with various forms of immune deficiency. The CMV infection should be excluded at patients with a hepatitis of not clear ethylogy. CMV can take part in the pathogenesis of some chronic liver diseases.

The Aim and the Tasks. To assess the prevalence of IgM and IgG anti-CMV-antibodies of IgM and IgG classes among patients with CH and the LC (CMV-IgM and CMV-IgG positive).

MATERIAL AND METHODS. In 50 healthy donors and 89 CH and LC patients the levels of antibodies to CMV-IgM and CMV-IgG were determined by ELISA method.

RESULTS. The prevalence of CMV-IgM and CMV-IgG in controls was accordingly 47,62 % and 95,24 %, whereas in the general group of patients with Chronic Diffuse Liver Disease (CDLD) the prevalence was of 70,8 % and 100 % correspondingly. Thus, the prevalence of CMV- IgG was identical both at patients, and at healthy persons and made practically 100 %. At the same time, there was a tendency to greater frequency of CMV-IgM in patients of the general CDLD group (p> 0,05). Patients with CH (n=40) were CMV- IgM seropositive in 47.5 % of persons, with very high level of antibodies, and 52,5 % were seronegative. Among LC patients (n=49) 79,6 % were CMV -IgM seropositive, and 20,1 % - were seronegative (p <0.05 in comparison with donors). 69,4 % of them had high level of antibodies, and 10,2 % had moderate level.

CONCLUSIONS. Practically 100 % of donors and patients with CH and LC are CMV-IgG seropositive, that reflects universal distribution CMV among people all over the world. In CH patients the positivity both of CMV -IgM, and CMV -IgG did not differed from the donor`one, as well as the majority of LC patients had elevated CMV-IgM level of antibodies, but not of the CMV -IgG. Higher levels of IgM in LC patients probably specifies the active replication of CMV in the significant part of patients. It can be the sign of CMV participation in the pathogenesis of LC, and also may reflect the presence of severe immune deficiency in this group of patients.

HEPATITIS C: CURRENT PROBLEMS OF DIAGNOSTICS, TREATMENT AND PREVENTION OF INFECTION.

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Among viral hepatitis which are transmitted by the parenteral way hepatitis C is the most significant problem for the public health. First of all, this is due to the global spread of the infection, high levels of morbidity, the ability to form chronic infection, leading to cirrhosis, to primary liver cancer. An addition, hepatitis C virus is able to infect and cause pathological changes in different kind of human organs. At the same time, there is still no vaccine against hepatitis C, and the medicines currently used, still little effective, expensive and not to be harmless to the patients. Thus, development and improvement of new methods of diagnostics of an infection necessary for monitoring, treatment and prevention of hepatitis C is highly actual for health care.

There were infectious highly productive for cell cultures HCV strains which have been isolated from human blood serum samples of HCV infected patients as a result of an in vitro studies. A collection of different subtypes HCV strains that are suitable for developing diagnostic and prophylactic drugs was formed. For the first time, in vitro and in vivo the conditions were created for preclinical study of medical and preventive drugs. Received results of study suggest real possibility for the creation of cultural inactivated vaccine against hepatitis C.

AN EFFECTIVENESS OF THE COMBINED TREATMENT IN PATIENTS WITH CHRONIC HEPATITIS C COMBINED WITH DIABETES MELLITUS TYPE II

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Objective: to investigate an effectiveness of the combined treatment of chronic hepatitis C (CHC) in patients with diabetes mellitus type 2 (DM 2).

Materials and methods. 58 patients with chronic hepatitis C and with diabetes mellitus type 2 were included into investigation. The viral etiology of the CHC had been proven by detection of HCV antibodies in plasma with ELISA method and PCR detection of RNA HCV viral load in real time. All patients had HCV genotype 1 and a viral load 4x10⁵ – 6x10⁵ MO/ml as well as type 2 diabetes mellitus mild to moderate stage of compensation. Patients were divided into two groups: group 1 (n = 32) - patients who had received only antiviral therapy (AVT) in standard dose and group 2 (n = 26) + AVT and maintenance therapy. The maintenance therapy included Heptral by the following scheme: 800 mg for 10 days IV, then at the same dose PO for a month on the 1st, 4th, 8th, 12th months of antiviral therapy course and continuous intake of Ursfolk 15 mg / kg daily. Duration of treatment was 48 weeks, regardless of viral load or received viral response. Clinical symptoms, biochemical parameters and viral load were assessed at baseline and at 1, 4, 12, 24 and 48 weeks of therapy. The type and dose of hypoglycemic medications remained unchanged throughout the whole treatment period.

The study's results. Rapid viral response was obtained in 9.4% of patients of group 1 and 11.5% in group 2. Early viral response occurred in 15.6% and 23.0% respectively. In group 1 side effects of AVT had 100% of patients and 5 patients (15.6%) discontinued treatment (1 patient had depression, 2 of them had anemia, and another two had diabetic decompensation). In the second group, the side effects were observed in 61.5% respectively, but medical corrections were not required. No any significant depression in patients in group 2 were observed. Steady viral response was obtained in 31.25% and 38.5% of patients respectively.

Conclusions. A comprehensive approach to the treatment which include Heptral and Ursfolk in patients with chronic hepatitis C and type 2 diabetes improves the efficiency of antiviral therapy and reduces the occurrence of it's side effects.

IMPACT OF HBEAG SEROCONVERSION ON THE COURSE OF CHRONIC HEPATITIS B

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The aim of our research was to characterize the course of chronic hepatitis B (CHB) after HBeAg-AbHBe seroconversion.

Materials and methods. 115 patients with HBeAg-negative CHB were examined, 100 (87,0%) of them at the hepatitis stage, and 15 (13,0%) at the liver cirrhosis stage. Diagnosis was based on clinical and laboratory data, as well as histological methods (in 62 patients), serological markers of HBV (HBsAg, HBeAg, AbHBe, AbHBcorIgM, IgG) and PCR detection of HBV DNA in the blood in all patients and in the liver tissue in 62 (53,%) patients.

Results. Viremia disappeared in 47 (40,9%) CHB patients after HBeAg-seroconversion, while viral genome localization in the liver tissue persisted in all 62 patients who received a liver biopsy, and all 115 patients showed clinical and laboratory signs of necroinflammation.

CHB activity was weak in the majority of patients, 52 (45,2%), whereas moderate CHB activity was detected in 15 (13,0%) patients, high CHB activity in 33 (28,7%), and liver cirrhosis of high activity in 15 (13, 0%).

Patients with viremia displayed a higher activity of the process. They had higher levels of ALT (98,7±12,3 U/l vs 83,8±17,6 U/l (p> 0,05)), alkaline phosphatase (178,9±20,1 U/l vs 146,5±19,2 U/l (p<0,05)), γ-globulins (22,8±2,3% vs 20,5±3,2% (p>0,05)), and histologic activity index (8,8±0,7 vs 8,1±0,6 (p>0,05)), however, sclerosis index was higher in patients without viremia (2,1±0,65 vs 1,9±0,5 (p>0,05)). Patients without viremia were 9,6±5,8 years older (p<0,05), and had a 7,5±6,3 years (p<0,05) longer history of infection compared to those with viremia.

Conclusions. Despite the fact that viremia disappeared in 40,7% of patients with chronic hepatitis B after HBeAg-seroconversion, necroinflammation in the liver and tissue localization of the virus persisted, and liver cirrhosis developed in 13,0% of patients after 20 years of disease.

TELIVUDINE IN THE TREATMENT OF CHRONIC HEPATITIS B

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The aim of the study was to examine the effectiveness of Telbivudine in treatment of patients with chronic hepatitis B (CHB). The efficacy of the drug was studied in 26 patients with chronic HBV-infection: with CHB - 25, with liver cirrhosis - 1, average age - 40 years, males - 18, females - 8. The complex of clinical laboratory and imaging studies was used for diagnosis. Patients were selected for the antiviral treatment with fibrosis of grade 2 or more (according Metavir scale), and viral load more than 2000 IU / ml. Two groups of patients were identified after the response to antiviral therapy: I-st - with undetectable HBV DNA after third month of treatment (8) and II-nd - with a decrease in viral load> 1log10 in the end of the third month (18). In the I-st group men were 6, while women - 2, the average age - 34,37 ± 3,01 years, initial viral load - 13,258 ± 4475 IU / ml. II-group consisted of 18 patients, men - 12, women - 6, the average age - 36,4 ± 3,17 years, the initial viremia - 179,814,179 ± 85,402,141 IU / ml. By the end of the third month in the I-st group was noted the disappearance of the hepatitis B virus, which preserved in the following months. In the II-nd group by the end of the third month viral load decreased to 18,099 ± 9523 IU / mL (p <0.05), by the end of the 6th month - up to 308 ± 150 IU / ml, which was significantly lower than baseline data and from 3-d month monitoring (p <0.05, p <0.05). In this group of patients was detected a significant decrease in ALT from 153,26 ± 28,8 to 46,55 ± 4,09 U / L (p <0.001), and AST from 79,0 ± 14,6 to 35,7 ± 3,2 U / l (p <0.05). Patients continue treatment, perform their routine clinical monitoring. None of the patients had side effects, and in the course of therapy there were no relapses. Telbivudine, from our point of view, could be more widely used in the treatment of patients with CHB.

PREVALENCE OF AUTOANTIBODIES IN PATIENTS WITH VIRAL HEPATITIS (VH).

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Puprposes: analysis of prevalence of an antinuclear factor/antibodies (ANF=ANA), anti-mitochondrial antibodies (AMA), anti-smooth muscle antibodies (SMA), antibodies to parietal gastric cells (PGC Ab), antibodies to microsomes of liver and kidneys type 1 (LKM-1 Ab) in patients with chronic virus hepatitis (CH) B and C.

Materials and methods: 98 patients with CHC and 25 patients with CHB were included in (5 from them were infected with B+D viruses), who don't receive antiviral therapy (interferon +/- nucleos(t)ide analogues) at the moment of measurement of levels of autoantibodies. Patients with mixed-hepatitis (CHB+CHC), HIV infection were excluded. Levels of autoantibodies were measured by a method an indirect immunofluorescence test: ANA on the cellular Hep-2 line with definition of 6 types of a luminescence, AMA, SMA, PGC Ab and LKM-1Ab - on a threefold substratum. Diagnostic considered a level ≥1:160 for ANA, ≥1:20 for AMA, SMA, PGC Ab and LKM-1 Ab.

Results: Any of specified autoantibodies or their combination was revealed in 36% (35/98) patients with CHC and in 32% (8/25) patients with CHB (χ²=0,678). Increased ANA levels were most common: 25,5% and 24% of patients with CHC and CHB, respectively (χ²=0,877), in levels 1:160-1:320 (only ANA level 1:1280 with homogeneous type of a nuclear luminescence in combination with SMA level 1:640 was found in 1 patient with CHB). In most cases ANA with fine granular or cytoplasmic types of a nuclear luminescence were detected, one patient with CHC demonstrated a big granular type of luminescence and one – homogeneous type of a luminescence of ANA. AMA were revealed at 1% of patients with CHC and at 4% of patients with CHB (χ²=0,293) in levels up to 1:320. Increased SMA levels occurred only in combination with ANA - in 7,1% of patients with CHC and in 12% of patients with CHB (χ²=0,428), PGC AB - 1% patients with CHC and also didn't appear in patients with CHB (F-test=1,0), LKM-1 Ab- in 8,2% of patients with CHC and also appear in patients with CHB (F-test=0,315).

Conclusions: Autoantibodies are a common finding in patints with chronic hepatitis. ANA is most often of them.

THE CHOLESTEROL METABOLISM MALFUNCTION AGAINST THE BACKGROUND OF BILIARY INSUFFICIENCY OF THE CHRONIC HEPATITIS B PATIENTS

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The purpose: to study the cholesterol metabolism malfunction of the chronic hepatitis B patients in an integration stage (HBV) with biliary insufficiency.

Materials and methods: 32 sick men with HBV are examined, the diagnosis has been confirmed by means of IFA and PCR analyses. The average age was 35±6.5. The disease duration has not exceeded 5 years from the moment of hepatitis diagnosing. Biliary insufficiency diagnosing was made by the chromatic duodenal sounding method. Also analysis of biochemical indicators of blood with obligatory research of hepatic tests, lipid a spectrum and bilious acids was made for all patients.

Results: patients suffered from HBV mulfunction of biochemical structure in gallbladders and hepatic portions of bile have been revealed, namely cholic acids concentration was authentically lowered, and as consequence the holato-cholesteric factor was lowered. During calculation of total flow rate of components authentic decrease flow rate of cholic acids was also revealed. The decrease of total flow rate of cholic acids (biliary insufficiency) was revealed at 24 patients (in 75 % of cases). During studying of indicators of lipid exchange that patients with diagnosed biliary insufficiency had, the increase of cholesterol level of 17 patients (70,8 % of cases) in a biochemical blood test revealed.

Conclusions: Thus, chronic biliary insufficiency is revealed at 75 % of patients with HBV, and 70,8% of patients had hypercholesterolemia diagnosed, that testified to high risk of atherosclerotic disease development at the given patients category.

The participation form – thesis only.

EPIDEMIOLOGICAL AND CLINICAL INTERPRETATION OF THE RESULTS OF SCREENING FOR MARKERS OF HEPATITIS B AND C IN PATIENTS WITH NEUROSURGICAL PATHOLOGY

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The study was performed at the Scientific Research Institute for neurosurgery named after academician N.N. Burdenko under the Russian Academy of Medical Sciences. All patients admitted to the surgical treatment, were tested for HBsAg and HCVAb on the day of hospitalization. In 2012, 6700 patients were tested for markers of parenteral viral hepatitis, 332 patients with the presence of these markers in the blood were tested for the activity of alanine aminotransferase (ALT). Blood tests for HBsAg and HCVAb were performed using ARCHITECT and AxSYM (Abbott Diagnostics, USA) systems. In order to identify hepatitis C core antigen «HCV Ag ARCHITECT system» (Abbott Diagnostics, USA) test was used. Positive results for HBsAg were confirmed by automated neutralization test in these systems. Confirmation of positive results for HCVAb was performed by immunoblotting (Inno-Lia, Innogenetics, Belgium). The rate of detection HBsAg among patients was 1,2% ± 0,1. In terms of dynamics by years the decrease in such level is noted, so in 2009 the level of infecting the patients with hepatitis B virus was 1.8%, in 2010 - 1.5%. The rate of detection of antibodies to hepatitis C virus in the same group was 3,7% ± 0,2 p <0.0001. Undoubtedly, mass vaccination against hepatitis B of the Russian population has significant effect on the frequency of HBsAg detection. Half (50.2%) of those with the presence of antibodies to hepatitis C virus had antigen against such virus, indicating active viral replication and suggesting the presence of high epidemiological risk when performing surgery in these patients. When studying the ALT activity the significant differences among patients with HBsAg and HCVAb were detected. In patients with HBsAg the speed of hyperenzymemia was 7,4% ± 2,9, in persons with HCVAb - 23,5% ± 2,7, p = 0.011. It is necessary to note that the occurrence of hyperenzymemia among the persons with the presence of both antibodies and antigens against hepatitis C virus was reliably higher than in those patients in whose blood only antibodies to hepatitis C virus were detected and antigen was not determined (respectively 42,8% ± 4,4 and 4,0% ± 1,6 p <0.0001).

Given these data, it can be assumed that the increase of ALT activity in these patients is associated with infecting with the hepatitis C virus and is a sign of a chronic HC-viral infection, proceeding with virus replication.

CHRONIC HEPATITIS C (CHC) AND HELICOBACTER PYLORI.

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Purposes: studying a gastroduodenal zone (GDZ) in patients with chronic hepatitis C (CHC), comparison of the functional liver and gastric and duodenum mucosa tests.

Materials and methods: 69 patients with CHC were included with standard clinical and laboratory examination. Levels of antiphospholipid antibodies (APA) were determined in blood serum. Malonic dialdehyde (MDA) and superoxide dismutase (SOD) were determined in blood serum and in gastric mucosa (GM). Existence and H. pylori bacterization degree in GM were investigated. Gastroduodenoscopy with morphological studying of biopsy samples was also performed. Patients with CHC were divided into 2 groups: group A (17 patients with minimal H. pylori bacterization), and group B (69 patients with the maximal H. pylori bacterization).

Results: chronic gastritis and duodenitis were diagnosed in 72% (36) and in 65% (37) of patients in B group, respectively, while in A group: 28 % (14) and 35% (13), respectively. Activity of ALT 1,6±0,3 mmol/h/l and AST 0,6±0,2 mmol/h/l in group B were lower, than in group B: 2,2±0,3 mmol/h/l and 0,85±0,17 mmol/h/l, respectively (p<0,01). Increased IgA (3,0±0,26 g/l), increased IgM (2,0±017 g/l), APA (21,8±0,65) in serum were revealed in group A. MDA levels were increased both in serum and GM (7,1±0,35 nmol/ml, 26,55±0,8 nmol /g.t.) .

Results in group A: IgA (2,0±0,3 g/l), Ig-M (1,7±0,15r.n), APA (19,8±0,6), MDA in serum 6,67±0,09 nmol/l, and in GM (20,8±0,4 nmol / g.t.) . The activity of SOD 2,5±0,11 u/g.t. was decreased in GM group B, increased in blood serum i(2,2±1,0 nmol/ml) in group B, while comparing with group A: 3,1±0,2 U / g.t./min and 47,8±0,8 nmol/l, respectively.

Conclusions: A high association between CHC and incidence of GDZ pathology is revealed. Reliable correlation between degree of H. pylori bacterization and incidence and severity of GDZ pathology and liver function abnormalities.

DIRECT METHODS OF NONINVASIVE DIAGNOSING OF LIVER FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS C (CHC).

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Purposes: analysis of comparative data in direct methods of noninvasive liver fibrosis diagnosing in patients with chronic hepatitis C (CHC) and different stages of fibrosis.

Materials and methods: 205 patients of age 18-60 years with CHC in a replicative phase were included. All patients were divided into 5 groups according to liver fibrosis stage, established by morphological method and staging with METAVIR scale: (1) F0 – 17, (2) F1 – 96, (3) F2 – 26, (4) F3 – 22 and (5) F4 – 44 patients. The control group was made by 24 healthy individuals. Direct methods of noninvasive liver fibrosis diagnosing were presented with transient liver elastography (TEG) and measuring levels of the hyaluronic acid (HA) in blood serum. Statistical data processing was performed with methods of nonparametric statistics (SPSS 17.0), reliability of distinctions of tests and data was thus estimated upon transition from each fibrosis stage to the subsequent, and also in comparison with control.

Results: The results received during TEG in patients with CHC without liver fibrosis (stage F0), have no significant differences from data in control group, but increase while moving to F1 stage. Range of values increased at a stage of significant fibrosis (F2), but distinctions with the previous stage (F1) had no reliable. Increase of range of values according to TEG was noted at a stage advanced fibrosis (F3) and was characterized by reliable distinctions with stage F2. The maximum values of liver tissue density were registered in patients with liver cirrhosis (F4), thus distinctions with stage F3 also were statistically significant.

Results of definition of HA levels in patients with fibrosis F0-F3 showed a tendency to gradual increase. And these deviations had no significant character in comparison with level in control group. At the same time development of cirrhosis was associated with reliable increase in HA blood levels, that allows to differentiate cirrhosis with any other stage of fibrosis with probability about 95% in patients with CHC in case HA>100 mg/gl.

Conclusion: TEG allows to register quite accurately transition from one stage of liver fibrosis to another in patients with CHC, thus most precisely the border between stages is defined at the grades levels of F0/F1, F2/F3, F3/F4. Levels of serum HA doesn't allow to distinguish stages of liver fibrosis, except cirrhosis (stage F4).

E-SELECTIN IN CHRONIC LIVER DISEASES

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The aim of study is to assess plasma levels of E-selectin in chronic liver diseases.

Material and methods. 198 patients (125 men, 73 women) at age from 23 years to 59 years (27 men, 17 women) were examined: 28 patients with chronic viral hepatitis (CVH) B, 93 patients with CVH C, 62 patients with viral liver cirrhosis (LC), and 15 patients with alcoholic LC. 7 patients with alcoholic liver cirrhosis additionally had signs of acute alcoholic hepatitis. The control group included 40 healthy volunteers at age from 22 years to 55 years. Blood concentration of E-selectin was carried out by means of ELISA.

Results. E-selectin plasma levels were increased in chronic liver diseases with most prominent values in group of patients with liver cirrhosis. Type and genetic and phenotypic features of viruses did not influence on adhesion molecule content in blood. However plasma concentration of mediator rose in cases of high viremia of HBV и HCV. In patients with alcoholic liver cirrhosis values of E-selectin in blood were higher than in viral liver cirrhosis especially in cases of combination with acute alcoholic hepatitis. Relationship of E-selectin with expressiveness of cytolytic and inflammatory syndromes in chronic liver diseases was detected. Severe cases of liver cirrhosis (classes B and C according Child-Pugh, decompensated portal hypertension and hypersplenism) were characterized by higher parameters of E-selectin in blood than the compensated variants of disease.

Conclusion. Elevation of E-selectin levels in blood is observed in chronic liver pathology especially in cases of severe variants of disease. Those results testify to the pathogenetic importance of disorders of intercellular interactions in progressing of chronic liver disease.

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SOME MECHANISMS OF APOPTOSIS AT PATIENTS WITH VIRUS HEPATITIS**Ivanova M.R., Shakova H.H.***Kabardino-Balkarian state university, Nalchik, Russia*

36 patients with viral hepatitis B and 59 patients with chronic viral hepatitis C who underwent treatment were examined in infectious hospital of Nalchik. The following data were obtained when genotyping viruses of hepatitis with parenteral mechanisms of conducting in studied groups of patients: 43% of patients with the HCV-infection had 1b a genotype, 56% 3a and 1% with a genotype 2. Genotype A of hepatitis B virus had a rather high specific weight (47%), the second in frequency was a genotype D (39%). By results of the conducted researches increased concentration of TNF- α in blood serum in all patients with viral hepatitises B and C was recorded. Higher rates were detected in patients with chronic viral hepatitis C. On the other hand, in the course of RNA TNF- α on lymphocytes of peripheral blood in group of donors matrix research this indicator was not detected, and begins expressed only in patients. Besides, increase of concentration of a FAS soluble receptor in patients' blood serum, more expressed in patients with chronic viral hepatitis B. On the other hand, the increase in an expression of CD95 on lymphocytes of peripheral blood takes place in patients. Matrix RNA of CD95 on lymphocytes of peripheral blood in control group is defined, but in groups of patients with chronic viral hepatitis B and C shows more expressed increase of an expression of mRNA. Unlike the above mentioned indicators of TRAIL serum concentration authentically decreases in groups of patients, in comparison with control group. On the other hand, DR5 expression on lymphocytes of peripheral blood in group of patients raises. Though in control group of donors mRNA TRAIL in lymphocytes of peripheral blood isn't defined, mRNA TRAIL expression begins at patients with chronic viral hepatitis. Thus, it is possible to speak about crucial importance of proteins of hepatitis B and C viruses in activation TNF- α induced apoptosis in lymphocytes of peripheral blood. On the other hand – increase of serum concentration of a soluble receptor of FAS and TNF- α indicates possibility of viruses hepatitis B and C antigens to change a receptor phenotype of peripheral blood lymphocytes.

PECULIARITIES OF INTERFERON FORMATION IN NEWBORN CHILDREN OF MOTHERS WITH DIFFERENT FORMS OF HCV-INFECTION**Kisteneva L.B., Cheshyk S.G., Parshina O.V., Guseva T.S., Malinovskaya V.V., Malyshev N.A., Mandjiev G.D.***Federal State Institution "Scientific Research Institute for Virology named after D.I. Ivanovskiy" under the Ministry of Health of Russian Federation, Moscow, Russia*

IFA method was used to examine levels of α -IFN production in infants of RNA HCV-positive and RNA HCV-negative mothers. It was found that the content of α -IFN in the blood plasma and the level of spontaneous production of interferon in children of HCV-infected mothers are higher than conventional norms, regardless of the variant of HCV-infection. Induced production of α -IFN in children of HCV-infected mothers corresponds to the norm, although the average value of the parameter is below the average level in children of apparently healthy mothers (control group). A detailed analysis revealed that in 36.0% children of RNA HCV-positive mothers the induced production of α -IFN was below normal level, and in 48.0% - higher than the normal level. Among infants of RNA HCV-negative mothers the induced production of α -IFN was below normal in 43.5% of cases, and higher than normal levels in 30.4% of children.

The content of γ -IFN in the plasma of children of all HCV-infected mothers did not differ from the conventional norms, and its level of spontaneous production in both forms of infection was significantly higher than rate in children of the control group. It was demonstrated that the induced production of γ -IFN exceeded normal levels in 44.0% of infants of RNA HCV-positive mothers and 58.7% of infants of RNA HCV-negative mothers. Mean values of induced production of γ -IFN in infants of RNA HCV-positive and RNA HCV-negative mothers exceeded the conventional norm by 3.2 and 2.0 respectively.

γ -IFN-inducible protein (IP-10) was studied by IFA method as a criterion for evaluation of regulatory action of γ -IFN. It was detected that the levels of IP-10 in the blood plasma of children of HCV-infected mothers was significantly lower than in infants of the control group. Spontaneous production of IP-10 doesn't vary in the main groups of children and the comparison group, and the average level of PHA-stimulated production of IP-10 is 2 times lower in children of RNA HCV-negative mothers.

In the course of correlation analysis the relationship between parameters of PHA-induced production of IP-10 and induced production of γ -IFN was not found ($r=0,0106$).

From the analysis of the effectiveness of the antiviral treatment, depending on the availability of IR retired eight patients with HCV-1 and 2 patients with HCV-2/3 at the failure of the study protocol. Thus, in the analysis of the effectiveness of the antiviral treatment, depending on the presence of insulin resistance included all 196 patients - 112 patients with HCV-1 and 84 with HCV-2/3.

Among patients with HCV-1 without IR, SVR rate was 46% ($n = 23/50$) of patients, and in patients with HCV-1 with IR SVR rate was 44% ($n = 16/37$) of patients, ($p = 0,44$). Among patients with HCV-2/3 without IR, SVR achieved 100% ($n = 40/40$) of patients without IR, and in patients with IR, SVR reached 91% ($n = 19/21$) patients, ($p = 0,016$).

Conclusions:

Insulin resistance is characteristic of a half of the patients with CHC. Influence of insulin resistance ($HOMA-IR \geq 2$) on the efficacy of antiviral therapy of chronic hepatitis C with PegIFN α -2b and ribavirin is dependent on the HCV genotype. The frequency of sustained virological response in patients with genotype 1 HCV with and without insulin resistance was not significantly different: 44% vs 46%. Patients with 2/3 genotype HCV were significantly different: 91% vs 100%.

TEFFICACY OF ANTIVIRAL TREATMENT OF CHRONIC HEPATITIS C WITH PEG-IFNA-2B AND RIBAVIRIN IN COMBINATION WITH METFORMIN IN PATIENTS WITH INSULIN RESISTANCE ,DEPENDING ON HCV GENOTYPE**Khafisova O.O., Mazurchik N.V., Ogurtsov P.P.***The centre of Liver Researches at Medicine faculty of "People's Friendship University of Russia", Moscow, Russia.*

Aim: evaluate the cure rate of patients with chronic hepatitis C in combination with insulin resistance to standard therapy (PegIFN α -2b + ribavirin) and metformin, depending on the genotype of HCV.

Materials and methods: research work is based on a study 106 patients with CHC and IR In this prospective study included all patients older than 18 years with chronic hepatitis C, first held antiviral treatment with PegIFN α -2b and ribavirin in the centre of Liver Researches at Medicine faculty of PFUR in 2007–2011. Follow-up was from 1 to 4 years.

The main criterion for inclusion in this study was the presence of chronic HCV-infection (detection of antibodies to HCV and HCV RNA in serum) caused by 1 or 2/3 genotype of HCV.

Insulin resistance (IR) was studied, using the method of Homeostasis Model Assessment. HOMA-index (HOMA-IR) calculated on the basis of indicators of insulin and glucose in the blood serum of one portion: $HOMA-IR = \text{fasting insulin (MkME / ml)} \times \text{fasting glucose (mmol / L)} / 22.5$. Criterion for the presence of IR was considered important $HOMA-IR \geq 2$.

For statistically data used Microsoft Excel and Statistica 6.0 for Windows. All patients were treated with a standard combination therapy with PegIFN α -2b at a dose of 1.5 mg / kg / week and ribavirin at a dose of 15 mg / kg / day.

48 out of 106 patients with IR were given also metformin, 20 mg / kg / day.

Results: among patients with chronic hepatitis C and IR were 48 people on metformin, among them - 25 patients with HCV-1 and 23 patients with HCV-2/3. They were assigned to metformin, as a preparation for the correction of IR in a dose of 20 mg / kg / day. Metformin was administered either in conjunction with the antiviral treatment, or for 3-6 months before the antiviral treatment continue throughout the course of therapy. Patients of the second (control) group did not receive metformin ($n = 58$), of which there were 37 patients with HCV-1 and 21 patients with HCV-2/3. Patients

ANTIVIRAL THERAPY WITH PEG-IFN-A2B AND RIBAVIRIN IN COMBINATION WITH METFORMIN EFFICACY IN PATIENTS WITH CHRONIC HEPATITIS C AND INSULIN RESISTANCE, DEPENDING ON THE LEVEL OF IR (HOMA-IR 2-4 AND HOMA-IR ≥ 4) AND BMI**Khafisova O.O., Mazurchik N.V., Ogurtsov P.P.***The centre of Liver Researches at Medicine faculty of "People's Friendship University of Russia", Moscow, Russia.*

Aim: evaluate the cure rate of patients with chronic hepatitis C in combination with insulin resistance to standard therapy (PegIFN α -2b + ribavirin) and metformin, depending on the IR- level and BMI.

Materials and Methods: research work is based on a study 106 patients with CHC and IR In this prospective study included all patients older than 18 years with chronic hepatitis C, first held antiviral treatment with PegIFN α -2b and ribavirin in the centre of Liver Researches at Medicine faculty of PFUR in 2007–2011. Follow-up was from 1 to 4 years.

The main criterion for inclusion in this study was the presence of chronic HCV-infection (detection of antibodies to HCV and HCV RNA in serum) caused by 1 or 2/3 genotype of HCV.

Insulin resistance (IR) was studied, using the method of Homeostasis Model Assessment. HOMA-index (HOMA-IR) calculated on the basis of indicators of insulin and glucose in the blood serum of one portion: $HOMA-IR = \text{fasting insulin (MkME / ml)} \times \text{fasting glucose (mmol / L)} / 22.5$. Criterion for the presence of IR was considered important $HOMA-IR \geq 2$.

For statistically data used Microsoft Excel and Statistica 6.0 for Windows. All patients were treated with a standard combination therapy with PegIFN α -2b at a dose of 1.5 mg / kg / week and ribavirin at a dose of 15 mg / kg / day. 48 out of 106 patients with IR were given also metformin, 20 mg / kg / day.

Results: Patients were divided into groups depending on the level of insulin resistance (HOMA-index values). Patients with HOMA-index 2 - 4 ($n = 62$), metformin+ ($n = 26$) & metformin- ($n = 36$) and patients with $HOMA-IR \geq 4$ ($n = 44$), metformin+ ($n = 22$) & metformin- ($n = 22$). Thus, with HOMA-index of 2 to 4, the SVR rate among patients receiving metformin was 84% ($n = 22/26$), and are not receiving metformin, achieved SVR 69% ($n = 25/36$), $p = 0,009$. In patients with $HOMA-IR \geq 4$, metformin+ SVR rate was 81% ($n = 18/22$), whereas patients with $HOMA-IR \geq 4$, not receiving metformin, achieved SVR, only 45% ($n = 10/22$), $p = 0.0001$. Patients in both groups were divided

receiving and not receiving metformin did not differ significantly by gender and age, the average viral load and distribution of genotypes 1 and 2/3 patients HCV. In the group of HCV-1 patients received metformin, the share achieved SVR was 68% ($n = 17/25$), whereas in the group of patients not treated with metformin with HCV-1, the number reached SVR was only 44% ($n = 16 / 37$), $p = 0,005$.

Thus, correction of insulin resistance with metformin in patients with the most refractory to antiviral therapy in genotype 1 HCV led to the growth of its productivity by 1.5 times. In the group of patients treated with metformin, with HCV-2/3, the proportion reached SVR rate was 100% ($n = 23/23$), whereas in the group of patients not treated with metformin with HCV-2/3, the number reached SVR was only 91 % ($n = 19/21$), $p = 0,016$.

Among the adverse events in the metformin were: single diarrhea (14%, $n = 7/48$). Significant decrease in glucose levels in patients with insulin resistance, metformin, have been reported - the average level of glucose to start taking metformin $5,54 \pm 0,1$, after the completion of therapy - $5,14 \pm 0,12$, $p = 0,07$. No patient was noted clinical episodes of hypoglycemia. Average HOMA-IR before the HTP in patients receiving metformin was - $4,09 \pm 0,43$, and after its completion - $1,94 \pm 0,12$, $p = 0,0001$. Average body weight in the group of patients treated with metformin, was $77,4 \pm 16,7$ kg, after antiviral treatment- $71,5 \pm 14,8$ kg, $p = 0,3$. Thus, metformin is not only effective, but also safe for use in patients with chronic hepatitis C, who get antiviral treatment, as product reduces IR.

Conclusions:

CHC patients with insulin resistance adding metformin, 20 mg / kg / day as the third component of antiviral therapy is safe and improves its efficiency: with genotype 1 HCV - from 44% to 68%, with 2 and 3 - from 91% to 100%.

PREVALENCE OF INSULIN RESISTANCE IN PATIENTS WITH CHRONIC HEPATITIS C IN THE RUSSIAN POPULATION AND ITS IMPACT ON THE EFFICACY OF THE TREATMENT OF CHRONIC HEPATITIS C WITH PEG-IFNA-2B PLUS RIBAVIRIN, DEPENDING ON HCV GENOTYPE**Khafisova O.O., Mazurchik N.V., Ogurtsov P.P.***The centre of Liver Researches at Medicine faculty of "People's Friendship University of Russia", Moscow, Russia.*

Aim: to study the prevalence of insulin resistance in patients with CHC in Russian population, and its influence on the formation of sustained virological response (recovery) with standard antiviral therapy of CHC combination PegIFN α -2b and ribavirin, depending on HCV genotype.

Materials and Methods: research work is based on a study of 211 patients with CHC. In this prospective study included all patients older than 18 years with chronic hepatitis C, first held antiviral treatment with PegIFN α -2b and ribavirin in the centre of Liver Researches at Medicine faculty of PFUR in 2007–2011. Follow-up was from 1 to 4 years.

The main criterion for inclusion in this study was the presence of chronic HCV-infection (detection of antibodies to HCV and HCV RNA in serum) caused by 1 or 2/3 genotype of HCV.

Insulin resistance (IR) was studied, using the method of Homeostasis Model Assessment. HOMA-index (HOMA-IR) calculated on the basis of indicators of insulin and glucose in the blood serum of one portion: $HOMA-IR = \text{fasting insulin (MkME / ml)} \times \text{fasting glucose (mmol / L)} / 22.5$. Criterion for the presence of IR was considered important $HOMA-IR \geq 2$.

For statistically data used Microsoft Excel and Statistica 6.0 for Windows. All patients were treated with a standard combination therapy with PegIFN α -2b at a dose of 1.5 mg / kg / week and ribavirin at a dose of 15 mg / kg / day.

Results: HOMA-IR level was ≥ 2 in 106 patients (51%).

Of the 211 patients, seven people included in the study, to assess the effectiveness of the antiviral therapy was not possible, due to patient refusal of further treatment and observation, or loss of contact.

Among patients with genotype 1 virus, SVR was 52% ($n = 61/118$), with 2/3 genotype - 93% ($n = 80/86$).

ANTIVIRAL THERAPY FOR CHRONIC VIRAL HEPATITIS B
BY ENTECAVIR

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The last decade has given the opportunity of a new strategy of treatment of patients with chronic viral hepatitis and to reduce the incidence of this infection. The nucleoside analog Entecavir has a high genetic barrier to the development of resistance, so he pertains to the drugs of first line therapy. Objective: to evaluate the results of antiviral therapy by Entecavir in patients with chronic viral hepatitis B.

Materials and methods. Were analyzed outpatient cards of patients with chronic viral hepatitis B, receiving antiviral treatment Entecavir (0.5 mg/day daily) based on polyclinics Chita citi. Total for 2009-2011 years 48-week course of therapy received 18 patients. The diagnosis of chronic viral hepatitis B confirmed serologically – by serologic method of Immune-enzyme analysis, molecular-genetic methods of PCR in 100 %. The men in the group observations made 38,9 % (7), women - 61,1 % (11). The average age was 40.7±of 2.54 years. The high level of viremia (> 800000ME/ml) before starting antiviral therapy is registered in 8 (44,4 %) patients. Increase in transaminaz in 2-3 norms were observed in 3 (16,6 %) patients.

Results. Early virological response was observed at 47.3 % of cases (HBV DNA has not been determined in blood serum after 12 weeks from the beginning of treatment). At the moment the end of the therapy of hepatitis B virus DNA was not defined in 8 patients (44.4 %). Three patients (16.6 %) there was a decrease in viral load at 2 log of the initial value, the rest of the data has been thrown out. After the treatment in 100 % of cases registered in normalization of transaminases. Adverse events were observed in 3 patients (16.6 %) in the form of a dyspeptic manifestations (nausea, loss of appetite). In 83.4 % of cases the drug was well tolerated.

Conclusions. Results of treatment of chronic viral hepatitis B Entecavir confirm its effectiveness. The lack of serious adverse events therapy the drug.

COMPARATIVE ANALYSIS OF SERUM PHOSPHOLIPID LEVELS IN
PATIENTS WITH CHRONIC HEPATITIS AND CIRRHOSIS ASSOCIATED
WITH HEPATITIS C VIRUS

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The purpose of the study was to study the characteristics of the phospholipid changes of blood serum from patients with chronic hepatitis C (CHC) and liver cirrhosis (LC) associated with the hepatitis C virus.

The study involved 25 patients with chronic hepatitis C (group I) and 22 patients with CA (group II).

Research methods. To determine the phospholipid fractions used the thin layer chromatography method. Were investigated blood serum concentration of lysophosphatidylcholine (LPC), phosphatidylcholine (PC), sphingomyelin (SM), phosphatidylethanolamine (PE). The results were compared with the spectrum of 20 healthy persons. To estimate the difference used Student's t test.

The results of the study. Were determinate violation of phospholipids (PL) synthesis in patients in both groups, which is manifested by increased of LPC and PE fractions. Thus, the LPC fraction in groups I and II was increased to (11,03 ± 0,85)% and up to (12,40 ± 0,86)%, (p <0.05), respectively, the PE level was raised to (17,61 ± 1,19)%, (p <0.05) - in the first group and up to (23,76 ± 1,90)% - in II (p <0.001). Opposite changes marked by the SM and PC: the level of SM was decreased significantly (p> 0.05), and the level of PC to (55,02 ± 1,82)%, (p <0.05) - in the first group and to (46,50 ± 2,00)%, (p <0.001) - in patients' group II. There was a significant difference in reducing the SM and PC: changes in these parameters was more pronounced in group II patients, indicating the depth of the destruction of the membrane matrix of hepatocytes.

Conclusions. Were determinate violation of PL synthesis in patients in both groups and redistribution of individual fractions - reduction of SM and PC and elevated levels of LPC. Nature of the change of the PL spectrum depended on the severity of the pathological process in the liver.

PRODUCTS OF LIPIDS PEROXIDATION LEVELS IN RED BLOOD CELLS
IN PATIENTS WITH CHRONIC HEPATITIS C AND NORMAL ALANINE
AMINOTRANSFERASE LEVELS.

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Aims: to establish levels of products of lipids peroxidation (LP) in red blood cells (RBC) in patients with chronic hepatitis C and normal alanine aminotransferase (ALT) levels.

Materials and methods: Twenty eight patients with CHC (HCV RNA positive) with the ALT serum levels from 12 to 38 U/l were observed. Diene conjugates (DC), trienketones, Schiff's bases levels after their extraction from membranes of RBC by a mix chloroform/isopropanolol were measured, and also the oxidation index (OI). Measurements carried out with four lengths of waves: 220, 232, 278, 440 nanometers.

Results: Levels of products LP (relative units) in RBC in patients with CHC with normal ALT levels are presented in the table.

	healthy	ALT norm
Oxidation index	0,51±0,06	0,83±0,128*
Diene conjugates	0,46±0,07	0,64±0,03*
Trienketones	0,35±0,9	0,42±0,07
Shiff's bases	0,15±0,05	0,17±0,05

* <0.05 (in comparison with healthy individuals)

Conclusions: The oxidation index is significantly higher (in comparison with normal counts) in patients with chronic hepatitis C and normal serum ALT levels. That indicates on increase of oxygen residuals amounts and their damaging action on hepatocytes.

THE COMPARATION BETWEEN HEPATOCYTES CYTOLYSIS AND
INFLAMMATORY ACTIVITY IN LIVER TISSUE IN PATIENTS WITH
RECURRENT CHRONIC HEPATITIS.

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Aims: to estimate interrelation between alanine aminotransferase (ALT) levels and degree of inflammatory activity in a liver at patients with chronic hepatitis B (CHB) and chronic hepatitis C (CHC) recurrence.

Materials and methods: Sixty seven morphological samples (needle biopsy) of liver (CHB – 35, CHC - 32) were analyzed and compared with ALT serum levels.

Results: Coefficients of correlations (R) of various morphological features with ALT serum levels are presented in the table.

Parameters	R	p
Periportal necrosis	0,50	0,001
Intralobular necrosis	0,54	0,001
Portal tracts inflammatory infiltration	0,28	0,05
Lobules inflammatory infiltration	0,39	0,05
Follicles ib portal tracts	0,77	0,09
Adipose degeneration of hepatocytes	0,52	0,60
Councilman bodies	0,53	0,90
Bile ducts destruction	0,41	0,20
Sinusoid cells hyperplasia	0,67	0,08
Portal and periportal fibrosis	0,52	0,02

Conclusions: Weak correlation between ALT levels and hepatocyte necrosis is revealed in patients with recurrence of chronic virus hepatitis (R=0,50, R=0,54, p=0,001) that testifies role of ALT levels in valuation of morphological activity of hepatitis.

CONCENTRATION OF P-SELECTIN IN BLOOD
IN CHRONIC LIVER DISEASES

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The aim of study is to assess plasma levels of P-selectin in chronic viral hepatitis (CVH) and liver cirrhosis (LC).

Material and methods. 198 patients at age from 23 years to 59 years were examined (125 men, 73 women): 28 patients with CVH B, 93 patients with CVH C, 62 patients with viral LC, and 15 patients with alcoholic LC. 7 patients with alcoholic liver cirrhosis additionally had signs of acute alcoholic hepatitis. Patients with liver cirrhosis were divided into classes A (39 patients), B (28 patients) and C (10 patients) depending on Child-Pugh criteria. The control group included 54 healthy volunteers at age from 22 years to 55 years. Blood concentration of P-selectin was carried out by means of ELISA.

Results. P-selectin plasma levels were increased in chronic liver diseases with most prominent values in cases of liver cirrhosis. Type of virus and viral load of HBV и HCV did not influence on content of mediator in blood. Patients with chronic viral hepatitis C with 1 genotype and patients with HBeAg-positive variant of HBV-infection had higher parameters of P-selectin in blood. In patients with alcoholic liver cirrhosis values of P-selectin in blood were higher than in viral liver cirrhosis especially in cases of combination with acute alcoholic hepatitis. Increase of adhesion molecule concentration in plasma with expressiveness of cytolytic syndrome in liver cirrhosis was detected. Correlation of P-selectin with activity of aspartate aminotransferase in patients with liver cirrhosis was positive. Prognostic severe cases of liver cirrhosis were characterized by higher parameters of P-selectin in blood than the compensated variants of disease.

Conclusion. Elevation of P-selectin levels in blood is observed in chronic liver pathology especially in cases of severe variants of disease. Those results testify to the pathogenetic importance of platelet activation in progressing of chronic liver disease.

The work was performed as part of the grant of President of Russian Federation № MD-934.2012.7.

COMPARATIVE DESCRIPTION OF HEPATIC FIBROSIS
IN CHILDREN AND ADULTS ACCORDING TO FLEXOGRAPHY
AND PUNCTURE BIOPSY DATA

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“The gold standard” of hepatic fibrosis evaluation is biopsy the findings of which are based on the examination of a small site of hepatic tissue and do not always correspond to the real condition of the liver in general. Nowadays the assessment of fibrosis intensity by means of Fibroscan apparatus when the indicators of hepatic tissue density are estimated in 10 or more points that covers the area of up to 4-6cm3 at one measurement is being used more often.

Purpose: To compare the frequency of fibrosis formation in children and adults according to the indicators of flexography (FGI) and puncture biopsy (PBI) in the cases of various liver disorders.

Materials and Methods: 1323 adult patients and 269 children were included in the research. 2192 FGI (among them 404 with children including neonatal hepatitis (NH) - 68, chronic hepatitis (CH) B - 89, CH B+D - 7, CH C - 153, autoimmune hepatitis (AIH) - 69, Wilson-Konovalov's syndrome (WKS) - 18) and 124 PBI (89 with adults and 35 with children) were performed. Fibroscan apparatus FGI and PBI data with the assessment of fibrosis stage by METAVIR criteria were used. The results of flexography given in kilopascals (kPa) were compared with histologic study of fibrosis by biopsy in the same patients.

Results: The research demonstrated that the features of fibrosis in the cases of different liver disorders (of viral, bacterial, and metabolic aetiology) among adult patients were registered in 50,5%: FI – 18,1%, FII - 16,7%, FIII - 16,1%, FIV – 9,6%. The direct relation of the age with the duration of the disease was marked as well. So in the group of patients of 35,5±0.2 years old the stage FIII-IV was registered in 8,7% cases, and in the group of 60,5±0,3 years old - in 28,1% (p <0.01).

Hepatic fibrosis was diagnosed in 31,2% cases among children: FI – 12,9%, FII – 5,4%, FIII - 6,6%, FIV – 6,3%. In 68,8% of the children the fibrosis was not revealed. The direct relation of hepatic fibrosis with the age of the child, the terms of contamination, and the duration of the disease was impossible to identify, but a clear dependence on the etiological agent was established. So fibrosis of III-IV stages (F III-IV) was revealed

EFFICIENCY OF GEPAFOR® IN TREATMENT HEPATITIS A.

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Aims: to study efficiency and safety of the preparation Gepafor® in patients with drug-induced hepatitis during tuberculosis chemotherapy.

Materials and methods. Sixty patients with tuberculosis are included in randomized research with drug-induced liver injury due to specific chemotherapy, aged from 18 till 60 years. Patients from the main group (30) against standard chemotherapy were treated with Gepafor® containing extract of a thistle (Silybum marianum) and sorbed bifido-and a lactobacilli, the group of comparison received Silimar®. Single, daily and course doses of extract of a thistle in both groups were identical. All patients before treatment had the disturbed microflora balance of the gut with clinical manifestations.

Results. In Gepafor® group, the average ALT and AST levels after 2 weeks of treatment authentically (p<0,05) decreased (from 95±2,13 to 43,1±8,7 U/l to 90,1±19,6 to 44,1±7,8 U/l respectively), thus treatment of tuberculosis wasn't cancelled. In group of Silimar®, decrease in these indicators didn't occur (65,5±14,7 and 64 ±29,3, 57,9±15,6 and 65±28,8 U/l respectively), 47% of patients stopped chemotherapy due to deterioration of ALT and AST levels. In Gepafor® group clinical manifestations of dysbacteriosis of the gut disappeared in 60% of patients, and decreased in 40%. In patients treated with Si-limar®, there was no effective influence on the microflora of the gut and clinical manifestations of dysbacteriosis. There were no side effects in Gepafora® and Silimara® groups.

Conclusions. Gepafor® is effective in drug-induced hepatitis and dysbacteriosis of the gut, promotes disappearance of the phenomena of drug-induced against with safe adequate chemotherapy dosing.

more often among the children with neonatal and autoimmune hepatitis (32,6% and 47,4% correspondingly), but in the cases of viral hepatitis B and C this stage of fibrosis was not established.

The identity of the results of these two methods - FGI and PBI composed 75,8% (94 for 124 patients). The difference in the indicators among children was registered 2,6 times less often than among adult population (11,4% and 29,2% correspondingly). The error range did not exceed one stage, and only in 5,6% of the cases (7 patients) the fixed deviations composed two stages. F0-1 indicators of FGI were lower, and F3-4 ones above PB data. The greatest divergence of fibrosis indicators according to PBI and FGI were noted at the absence of fibrosis (F0) or its minimum manifestations (F1). The divergence percent at F0-1 among children composed 25,0% whereas it reached 38,5-40,0% among adults. In the cases of expressed fibrosis progress F3-4 the frequency of discrepancy was considerably lower - 4,8% and 18,6% correspondingly.

Conclusions: Flexography is an informative method of hepatic fibrosis diagnostics for both children and adult population in the cases of chronic hepatitis and other liver disorders. The accuracy of fibrosis stage identification is greatly influenced by such factors as cholestasis, ascites, overweight in adults, constitutional features of thorax in children, and the experience of the researcher as well.

FIBROSIS OF THE LIVER AT CHC (ACCORDING TO THE INDIRECT ELASTOMETRY) DEPENDING ON THE PERFORMANCE OF ALT

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Quantitative determination of ALT is one of the most commonly prescribed of clinical-diagnostic research in chronic hepatitis C (CHC), because it is the most significant and specific. Is there a correlation between the intensity of cytolysis and the severity of liver disease in patients with CHC? Can testify moderately (ALT10N) expressed cytolysis of the advanced stage of the CHC? Objective: to Examine the performance of ALT at different degrees of severity of liver fibrosis in patients with CHC. The research methodology: we examined 30 patients aged 19-68 years (-22 husband. man, wives.-8) with chronic hepatitis C (CHC). ALT determined based on the enzymatic colorimetric method in accordance with the recommendations of the International Federation of Clinical Chemistry IFCC. Diagnosis verification by ELISA, PCR. Assessment of liver fibrosis was carried out with the help of indirect elastometry on the Fibroskan with the definition of the stage of fibrosis on a scale METAVIR. In 14 patients (47%) ALT was within normal limits, although in 8 of them found an increase in the elasticity of the liver from F1 to F4 on the system METAVIR. The patients were divided into 5 groups depending on the detected violations of the liver density: F0 - in 10 patients, F1 - in 5 patients, F2 - in 8 patients, F3 - in 3 and F4 - 3 patients. The average value of ALT in group 1 (F0) was 40,6 U/L, while in 60% of patients of the 1 group ALT was the norm. Indicators of ALT in group 2 (F1) amounted to 66,1 U/L and 40% were in norm. In 3 group (F2) ALT moderately raised (4N) (17,1 U/L) in 60% of patients of this group. In the 4th group (F3) indicators ALT increased up to 2 N (95,1U/L) in 63% of patients. In 67% of patients 5th (F4) the group changes in the indicators ALT is not revealed, the remaining they made 47,7 U/L. Conclusions: 1) In the CHC in 57% of patients with normal levels of ALT elasticity of the liver broken from F1 to F4 by METAVIR, 2) Less than the total of deviations from the norm in terms of ALT at the degree of fibrosis stage F0 and F4, 3) Indicators of ALT in patients with CHC do not reflect the severity of fibrosis changes of the liver.

DIELECTROPHORESIS OF ERYTHROCYTES, ELLIPSOMETRY IN DIAGNOSTICS OF THE ACTIVITY OF CHRONIC VIRAL HEPATITIS

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Task of study: To evaluate the potentials of optical methods for the study of the erythrocytes (Er), and sera in patients with chronic viral hepatitis (CVH) with varying degrees of virology, bio-chemical activity for use in diagnostics. Er parameters were studied using dielectrophoresis, serum indicators - by ellipsometry. In total 43 men (37.6 4.8 years) with chronic viral hepatitis (HBV, HCV, HBV + HCV, fibrosis F1-2) of different virological, biochemical activity were studied, and 20 people - a control group with no signs of liver damage. It was found that in case of CVH the strain amplitude, membrane capacitance, polarizability at all frequencies, the dipole moment of Er, the refractive index of thin films is significantly lower and the generalized parameters of viscosity, hardness, conductivity, index of aggregation, destruction of Er, thickness of thin films from the serum are higher than in the control group (p <0,0001-0,05). With increasing viral activity, the dipole moment, speed of Er movement towards electrodes, membrane capacitance and polarizability decreases in firm rise of cells' tendency to aggregation and degradation. (P <0.001-0.05). In case of CVH the gradation of thin films of sera in terms of evenness depended on the severity of the lipid metabolism disorder ($r = 0.67$, $p < 0.03$), the refractive index was determined by the degree of cytolytic activity of enzymes (ALT, AST) and cholestasis (GGT, ALP) ($r = 0.59$, $p < 0.02$), which affects the change in the parameters of Er. Using the methods of dielectrophoresis of Er and ellipsometry of thin films of the serum enables to obtain additional information about on the disorder of rheology in patients with chronic viral hepatitis of different activity.

ALTEVIR EFFECTIVITY IN HCV THERAPY (GENOTYPE 1)

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The final aim of antiviral therapy of HCV is virus eradication, which can be charged by early and persistent viral response.

Materials and methods: We treated 28 patients with HCV 1b genotype, men – 20, women – 8, age 18-36 years. Median of HCV is 6 years. Activity of liver inflammation was low – 17, intermediate – 11, HCV viral load was 105-106 copies per ml. The diagnosis has been conformed by liver toxicity analysis and HCV IgM, HCV IgG and RNA PCR.

The therapy plan was: altevir 3mln ED once a day – 28 days, then 3mln ED – 3 times a week during 48 weeks plus ribavirini 15 mg/kg her day 48 weeks.

During treatment period we controlled liver toxicity on 2nd-4th-24th-36 and 48 week.

Results: On treatment week 2: ALT – N – 78,6%, decreasing ALT activity up 2-3 times 14,3%, no ALT – change – 7,1%. On treatment week 4, 12,24 - ALT – N in 92,9% patients. On treatment week 4 patients had viral false (liver toxicity G1). Treatment week 4 patients had viral load decreased up to 102-103 cop/ml, other patients HCV PCR was negative. Treatment week 12, 24 HCV PCR – negative in 27 patients, others was up to 103 copies. On treatment week 36, 4 patients had viral false, PCR-HCV was 105 cop/ml with ALT elevation, they were excluded. 3 patients were excluded jn TW 24, because of AE.

Results: Antiviral therapy with interferon α 2b (Altevir) showed EVR in 83,2%, PVR – 60,7% patients.

ANTIVIRAL EFFECTS OF FOSFOGLIV-FORTE

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Aims: to reveal additional indications for use a drug "Fosfogliv-Forte" in patients with liver and bile ducts pathology.

Material and methods: 84 outpatients (64 women, 20 men) aged from 25 to 63 years followe up for 3-18 months were observed with cytolysis syndrome (ALT and AST \leq 2,5 N), in the absence of markers of hepatitis A, B or C. In blood count there were low ESR, lymphocytosis and monocytosis. Treatment with gepatoprotectors (essential phospholipids, ursodeoxycholic acid, ademetonine etc.) has a very short-term and not full effect or were inefficient.

Results and discussion: additional research by gastroenterologist autoimmune and alcoholic liver injury were excluded, but CMV, EBV and herpes virus antibodies class IgG were revealed in different combinations. "Fosfogliv-Forte" 3 capsule per day during meals was appointed for 5 weeks. Positive dynamics occurred: cytolysis syndrome regressed and in 63 patients (75%) full remission is reached. The tendency to normalization of lymphocytes counts is noted.

Conclusions:

1. in the presence of mild cytolysis for an exception of its reasons it is recommended to reveal antibodies to EBV, CMV and herpes virus.

2. Fosfogliv-forte combinis properties of a gepatoprotector and an antiviral drug is rather effective in treatment of combined (viral and metabolic) liver diseases.

RESULTS OF CURRENT ANTIVIRAL THERAPY OF CHRONIC HEPATITIS B

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Due to the number of antiviral drugs the rational choice of therapy of the first line at HBeAg-negative patients with chronic hepatitis B (CHB) can be difficult. Currently two various therapeutic strategies may be used: duration limited therapy with pegylated interferon-alpha or long-term therapy with nucleosides analogs (NA).

Purpose. To study efficiency of treatment patients with CHB with new NA – telbivudine ("Sebivo").

Materials and methods. Eighteen patients with HBe-negative CHB (10 men and 8 women) aged from 25 till 60 years were observed, one patient – with CHB-cirrhosis (Child-Pugh class B). In 7 (38,9 %) patients high viral load (1,0x10⁷⁻⁹ IU/ml) was registered. Patients received telbivudine 600 mg daily for 1 year. Treatment was continued for 2 years in 4 patients. Dynamical fibroelastography (FEG) was performed for every patient, and liver biopsy was made in 6 patients. Liver fibrosis (F1-2) revealed in 17 patients, low or moderate inflammatory activity, index<10 points by Knodell score. The follow-up period after the end of treatment was 6-12 months.

Results. The biochemical response was received in 3 months in 12 patients (66,7%), and HBV DNA was undetectable in 6 patients (33,3%) in 3 months and in 15 (83,3%) after 24 weeks of antiviral therapy. In a year of therapy the virologic response was observed in 16 (88,9%) patients. Degree of reduction of fibrosis (FGE) was observed in 10 (55,6%) patients HBV recurrence (HBV DNA decreased >1log¹⁰ IU/ml in comparison with the lowest level during therapy) was registered in 2 (11,1%) patients.

Conclusions. Thus, modern NA telbivudine provides a effective suppression of up to undetectable HBV DNA in the majority of CHB patients (88,9%) after 48 weeks of therapy and promotes fibrosis regression that testifies to high drug efficiency.

REAMBERIN'S APPLICATION IN COMPLEX THERAPY OF ACUTE AND CHRONIC HEPATITIS B

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Our researches showed that virus hepatitis B is accompanied by change of functional activity of erythrocytes, violation of an oxygen exchange and hypoxemia development. It served as motivation for inclusion in complex therapy of sick SVG and HVG Reamberini (possesses anti-hypoxemic and antioxidant action, reduces production of free radicals and restores an energy potential of caged).

Solution Reamberini 5 % applied solution a method intravenous infusions on 400,0 ml in a day, 3-5 introductions to 14 patients with sharp and 16 – with the chronic course of virus hepatitis B. The control group was made by patients who didn't receive реамберин.

Dynamic supervision and repeated researches of biochemical indicators revealed the following. At 10 of 14 patients with acute virus hepatitis B decreased bilirubin indicators with (115±8,9 micromol/l) to (29,4±2,8 micromol/l), ALAT with (4,2±0,9 micromol/hour/l) to (1,9±0,7 micromol/hour/l), in control group these indicators remained at former level: bilirubin – (124,6±10,7 micromol/l), decreased to (87,3±8,7 micromol/l). ALAT – (4,2±0,9 micromol/hour/l) decreased to (4,0±0,9 micromol/hour/l). At 13 of 16 the patients with HVGB are revealed a similar situation. Indicators of bilirubin decreased with (75,3±6,4 micromol/l) to (18,4±2,4 micromol/l), ALAT with (3,6±0,7 micromol/hour/l) to (1,4±0,6 micromol/hour/l), and in control group bilirubin indicators with (81,3±7,3 micromol/l) decreased to (65,8±4,9 micromol/l), activity of ALAT remained at former level: at sick HVGB made (3,5±0,4 micromol/hour/l), in control group – (3,6±0,4 micromol/hour/l).

Thus, as a result of complex treatment with application Reamberini at patients with virus hepatitis B positive dynamics is received at the sharp course of a disease at 71,4%, at chronic at 81,2% of patients that allows to recommend to include this preparation in the scheme of treatment of patients both with sharp, and with the chronic course of a disease.

PROGNOSTIC POSSIBILITIES OF IFN A AND Г FOR THE HCV - TREATMENT EFFICIENCY IN HIV-PATIENTS

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Aim: to research interaction specifics between IFN α and γ and to determine their prognostic role in HIV - patients during HCV – treatment.

Methods: our study included 40 co-infected patients (HIV/HCV). All patients were treated with PEG-interferon-alfa-2a and ribavirin for 48 weeks. According to treatment outcome they were divided on 2 groups: 1 group – 22 patients achieved EVR, ETR and SVR, in 2 group – 18 patients, HCV – treatment wasn't effective. Control group consists of 10 healthy donors.

Results: IFN γ level was higher in both groups in compare with control group. At the time of EVR increasing of IFN α level was observed in both groups I compare with initial levels (Pm-u \leq 0,05). At week 12 in 2 group IFN γ level was decreased significantly in compare with initial levels (12,90 and 4,20 pg/ml, respectively, Pm-u \leq 0,05). During treatment (week 48) in 2 group showed significant decreasing of IFN α level, almost at 11 times in compare with week 12 (400 and 36pg/ml, respectively, Pm-u \leq 0,05), and at the same time - IFN γ increasing up to 14,70pg/ml (Pm-u \leq 0,05). But in 1 group we observed moderate decreasing of IFN α level (from 691,0pg/ml at week 12 to 376,70pg/ml at week 48, Pm-u \leq 0,05) and IFN γ level decreasing (from 10,95 до 7,30 pg/ml, Pm-u>0,05, at weeks 12 and 48 respectively).

Conclusion: therefore, IFN α and IFN γ as cytokines have synergetic interactions and regulate each other according to feedback principle. Because of this, initial levels of IFN α and IFN γ , and also their "each other dependent" changes play important role in for HCV – treatment prognosis.

THYROID FUNCTIONAL CHANGES IN PATIENTS WITH CHRONIC HEPATITIS B AND C

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Study objective was to estimate thyroid functional state in patients with chronic hepatitis B (HBV) and C (HCV). Two groups of patients were followed up. First group consisted of 40 patients with HCV (45% males of average age 35, 9 \pm 1,5), second group consisted of 40 patients with HBV (52,5% males of average age 43,2 \pm 1,7). The diagnosis was confirmed by detecting HbsAg, HbeAg, IgM anti-HBc, anti-HCV (core, NS 2-5), HCV RNA and HBV DNA in patients. Serum thyroid hormones including thyroid stimulating hormone, T3 and T4, together with antibodies to thyroglobulin and thyroid peroxidase were measured, thyroid ultrasound was performed for all patients with further referral to the endocrinologist with serum tests and ulytrasound results.

Average thyroid hormones amount in serum was within normal ranges in patients with HCV and HBV, particularly thyroid stimulating hormone was 2,23 \pm 0.18 and 1,68 \pm 0.15 μ IU/ml, T3 – 2,89 \pm 0.54 and 2,23 \pm 0.09 nmol/l, total thyroxine – 112,0 \pm 8,91 and 109,47 \pm 4,22 nmol/l, free thyroxine – 18,70 \pm 0.61 and 17,82 \pm 0.59 correspondingly. Antibodies to thyroglobulin and thyroid peroxidase were not detected. According to thyroid ultrasound diffuse non-homogeneous changes were revealed in 62,5% patients from the 1st group and in 30% patients from the 2nd group, with nodules in 17,5% and 12,5% correspondingly, thyroid cysts were identified in 7,5% patients in both groups, signs of Hashimoto's thyroiditis presented only in patients with CHC (12,5%). Endocrinologist concluded Hashimoto's thyroiditis and hypothyroidism in 22,5% patients and euthyroidism in 62,5% patients from the 1st group, hypothyroidism was identified in 12,5%, hyperthyroidism in 2,5%, euthyroidism in 85% of patients from the 2nd group.

Consequently, patients with chronic hepatitis B and C had thyroid function changes that were prevalent in HCV patients.

RESULTS OF ANTIVIRAL THERAPY OF CHRONIC HEPATITIS WITH PEGINTERFERON ALPHA-2A (PEGASIS) IN PATIENTS TREATED BY PROGRAM HEMODIALYSIS

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Purpose: to evaluate the results of antiviral therapy (AVT) of chronic viral hepatitis C (CHC) with pegylated interferon alpha-2-a (Pegasis) in patients with end-stage renal disease (ESRD) treated by program hemodialysis (PGD).

Materials and methods: In the period from 2008 to 2010 11 patients with ESRD were treated by PGD, including 5 men and 6 women. The average age of the patients was 47 ± 8,8 years. Average duration of treatment by PGD was 12,36 ± 3,07 years. The reasons for the formation of ESRD in 10 patients was chronic diffuse glomerulonephritis with the outcome of nephrosclerosis, in 1 patient - hereditary nephritis (Alport syndrome). Treatment was carried out by means of Pegasis drug at a dose of 135 mcg per week. Efficacy was assessed by the definition of RNA HCV at 4th treatment week (rapid virologic response - RVR), at 12th week (early virologic response - EVR), at 24th and 48th weeks of treatment (current virologic response - CVR), at 24th week of observation after the end of treatment (sustained virological response - SVR).

Results. The average duration of chronic hepatitis C was 8,18 ± 2,22 years. Average level of HCV RNA before the AVT was 2.41 × 106 ± 2,85 x 106 IU/ml. All the patients underwent liver biopsy. The average value of IGA (by Knodell) was 5,5 ± 1,35 points, the stage of fibrosis 1-2. Full course of AVT (48 weeks) was conducted in 6 patients. For two of them the treatment completed on 24th and 46th weeks due to adverse phenomena. Three patients discontinued treatment on their own on 8th, 12th and 16th weeks of AVT. RVR was achieved in 87.5% of cases, EVR – in 80%. CVR was obtained in 9 of 11 patients (81.8%), at that in 4 patients – in case of early completion of AVT. SVR was preserved in 7 patients, accounting for 63.6%. Three of these treated patients completed therapy before 48 weeks.

Conclusions. Good results of AVT in the form of monotherapy by pelygated interferon alpha 2-a (Pegasis) in patients with ESRD treated by PGD were obtained. SVR was achieved in 63.6% of cases.

ON THE METABOLISM OF CYANOCOBALAMIN IN PATIENTS WITH CHRONIC HEPATITIS C.

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Krasnodar Hepatological Center conducted a research of 50 antiviral therapy HCV-patients by peginterferon and ribavirin in 2008-2010 and collected the following results: 1) macrocytic hemopoiesis was indentified in 22% native patients and apart from that in 36% patients during antiviral therapy, 2) in native patients macrocytic hemopoiesis was identified 11 times more often than anaemia, while in patients receiving antiviral therapy – 5 times more often, 3) an evident associative link was established not only between macrocytic hemopoiesis and pancreatitis (Q=0,7), but also between macrocytic hemopoiesis and thyroid pathology (Q=0,5). Macrocytic hemopoiesis is classified into megaloblastic (associated with a deficit of cyanocobalamin) and nonmegaloblastic (with hepatitis, hypothyroidism, alkololizm, splenectomy, etc.). But sometimes both types may be interrelated: 1) during destruction of hepatocytes B12 level may increase in blood (up to 30-40 times) with simultaneous decrease in hepar, 2) in 40% patients hypothyroidism associates with B12 deficit while thyroidectomy considerably decreases absorption of cyanocobalamin, 3) some drugs against pancreatitis interfere with parietal cells secretion and disrupt the synthesis of internal factor Castla, thus impeding absorption of B12, similar violations in HCV-infection may be of autoimmune etiology. Clinical symptoms of B12 deficiency and HCV-infection are similar: steatosis of liver, peripheral parasthesia, cognitive disorders, depression, cerebrovascular and heart diseases, osteoporosis, immunosuppression. B12 deficiency may not only contribute to the progression of HCV-infection (B12 inhibits translation of viral RNA), but also act as a negative predictor of response to antiviral therapy. The problem of B12 deficiency in HCV-patients gains its urgency taking into consideration the reviewed literary sources and the frequency of macrocytic hemopoiesis in treated patients.

SAFETY AND EFFICIENCY OF TELBIVUDINE IN HBEAG-NEGATIVE PATIENTS WITH CHRONIC HEPATITIS B

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Aim: To evaluate safety and efficiency of telbivudine (Sebivo) in HBeAg-negative patients with chronic hepatitis B (CHB).

Materials and methods. The study was conducted according to the definition of "observational studies» («non-interventional trials»).

Patients with CHB were collected from December 2007 to December 2008. 20 patients aged 18-69 were included in the study. CHB patients were received telbivudine orally at a dose 600 mg, 1 per day regardless of meal for 52 weeks. Estimation of safety, tolerability, detection of the clinical and laboratory parameters was performed at 4, 12, 24, 36 and 52 weeks.

Results. Before treatment, the median level of HBV DNA was 5,5 log10 copies/ml, activity of alanine aminotransferase (ALT) - 78 IU/ml. Complete virological response was achieved in 18/20 patients with chronic hepatitis B at the end of treatment, 2 patients didn’t finish treatment due to personal reasons. The HBsAg clearance was achieved in neither case. ALT level was normalized in all HBeAg-negative patients with chronic hepatitis B at 24 weeks and also didn’t exceed reference values after 52 weeks. The mild adverse events (malaise, dyspepsia) were estimated in a few cases and were not result in therapy stopping or hospitalization. Telbivudine was well tolerated and its safety was estimated. Patients’ adherence to treatment for all the visits and at the end of treatment was assessed as good.

Conclusions. Conducted prospective, observational study was demonstrated safety and tolerability of telbivudine (Sebivo) in HBeAg-negative patients with CHB. Serious adverse events were not registered. The efficiency of telbivudine was evaluated as high. This fact allows recommending the use of the drug for a challenging and long-term treatment of HBeAg-negative with CHB. The monitoring of patients is continuing.

INFLUENCE OF ANGIOTENSIN CONVERTING ENZYME I/D GENE POLYMORPHISM ON THE RATE OF PROGRESSION OF CHRONIC HEPATITIS C

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Fibrogenesis in the liver is a key process in the course of chronic hepatitis C (CHC). Several recent studies have shown that the renin - angiotensin system (RAS) played an important role in liver fibrosis, and the levels of angiotensin converting enzyme (ACE) (its major enzyme) were increased in patients with chronic hepatitis. I/D polymorphism of the ACE gene influence on the activity of ACE, and it is characterized by the presence (insertion (I)) or absence (deletion (D)) 287-basic - pair DNA sequence within the ACE gene. Taking into consideration these data, we can assume, that I/D polymorphism of the ACE gene influence on the pattern of fibrosis progression in CHC.

The aim of our study was to determine the relationship between I/D polymorphism of the ACE gene and the rate of disease progression in CHC.

Materials and methods. We studied 97 patients with CHC, who had genotype 1 virus, and 92 healthy controls. General examination, percutaneous needle biopsy of the liver with the assessment by METAVIR score, determination of I/D polymorphism of the ACE gene by PCR method, using amplifier “Tertsik”, were conducted in all patients with CHC. Patients were distributed into 2 groups according to the rate of CHC progression. The 1st group consisted of patients with slow disease progression and fibrosis stage F0-F2, the 2nd one – of persons with fibrosis F3-F4 (duration of infection in both groups were up to 10 years).

Results. We found that DD genotype was 1.7 times more likely for patients with CHC than for healthy individuals (65.98% vs. 39.13%). Whereby D allele was 1.4 times more common in patients of the 1st group (85.59% vs. 61.84%) (protective) and I allele is 2.7 times greater in patients of the 2nd group (38.16% vs. 14.41%) (profibrogenic). The presence of D allele (95.65%, p=0.0028) and DD genotype (91,3%, p=0.0006) were characteristic of women of the 1st group, and I allele (42,86%, p=0.0028), DI genotype (42,86%, p=0.0103) and II genotype (21.43%, p=0.0141) – of women of the 2nd group (differences didn’t achieve confidence level in men). In most patients in case of the slow progression of CHC the degree of necroinflammatory activity in the liver tissue was A1 (66.1%), and in case of the rapid progression - A2 (50 %), D allele was typical of people with A1 (94.87% and 71.88%), and I allele in patients with A3 (75% and 83.33%) during the slow and rapid progression of CHC.

Conclusion. DD genotype of ACE gene is dominant in patients with CHC, and D allele has a protective role in the progression of chronic hepatitis C, especially in women.

CHARACTERISTIC OF SEVERITY OF LIVER FIBROSIS AND DEGREE OF ACTIVITY OF CHRONIC VIRAL HEPATITIS B, C IN PATIENTS WITH HIV INFECTION

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The epidemic of HIV infection and chronic viral hepatitis is steadily spreading, especially among those of working age. Progression of hepatitis with the development of fibrosis and cirrhosis of the liver depends on a complex of factors, including prevailing state of the immune system. It is known that immunodeficiency in case of HIV infection is characterized by progressive decline in performance of CD-4 lymphocytes, and viral hepatitis is an immunologically mediated disease.

Purpose of study: To assess severity of liver fibrosis and degree of activity of chornic viral hepatitis B, C in patients with HIV infection, who passed and didn’t pass ART.

Materials of study: 86 patients with established diagnosis of chronic viral hepatitis B (CBH), chronic viral hepatitis C (CCH), mixed-Hepatitis (B + C) in combination with HIV infection at the age of 21 years to 50 years, passing treatment in Municipal State Clinical Infectious Hospital in hepatic department. All patients were infected by the parenteral way in the course of I.V. intake of psychoactive substances, and the experience of infection with viral hepatitis and HIV infection was the same and was 6-8 years. The majority of patients - 52% were in IV-B stage of HIV infection, 26% in IV-A, 22% patients at stage III (by VI. Pokrovskiy classification). Among 86 patients 49% (n = 42) received ART (I group) and 51% (n = 44) did not receive ART (II group). None of the studied patients received antiviral therapy of hepatitis. Complex biochemical and clinical tests of blood were conducted and the cell-mediated immunity (CD-4 and CD-8 cells) parameters were also assessed. To assess the degree of liver fibrosis the patients passed liver elastometry by means of apparatus FibroScan. In the course of statistical processing of material the methods of variation statistics and assessment of reliability of differences of indicators (Student t-test χ^2) were used.

Results of study: in patients receiving ART the level of CD-4 lymphocytes was 396 ± 41.5, and in patients not treated from HIV infection - 220 ± 61,2 (p <0,05). The patients in group I the minimum and mild degree of activity of chronic viral hepatitis was in 67.1% of cases, in 32.9% there was moderate-severe and severe degree. In group II of patients CBH of moderately severe and severe degree of activity was observed in 61.3% of cases. It is known that in the context of chronic hepatitis the hepatotoxicity of antiretroviral drugs occur more frequently than in patients without viral hepatitis. In

PROBLEMS OF MULTIVIRAL INFECTION IN CHRONIC HEPATITIS

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Several hepatotropic viruses of parenteral infection were discovered in the last decades of the XX century. Only hepatitis B, C, D viruses can lead to chronic liver disease in terms of evidence-based medicine. It is considered that this hypothesis is confirmed by multiple studies. However, epidemiological control and official registration of morbidity are related only with HBV and HCV. On the other hand HDV-infection, developing only in presence of HBsAg (the main marker of hepatitis B) is not registered at the present. This situation can be explained by the possibility of HDV-infection control using hepatitis B vaccination of children and people from risk groups. The quietness of the most gastroenterologists in respect of HGV and TTV viruses is based on lack significant progression of liver disease and specific treatment of their mono-infections. We established using molecular-biological and immunomorphological studies that lack of parenteral hepatotropic viruses monitoring led to a rapid growth of combined and multiviral chronic hepatitis and liver damage by a single virus was very rare in the last five years. These data complicate diagnostic, therapeutic and prognostic problems, because hepatotropic viruses not only dint in the immune system, but also lead to the depletion of all affected organ or organism resources. The amount of latent HBV-infection cases continues to increase despite the improvement of diagnostic test systems sensitivity. These and other problems of multiviral infection in chronic hepatitis and possible solutions will be presented in a report on the example of clinical cases after diagnostic study.

six patients receiving ART one had to differentiate worsening of viral hepatitis with increased activity of the process with hepatotoxic effect of antiretroviral drugs of II-IV degree. Later, at the background of detoxification therapy and administration of hepatoprotectors the clinical and laboratory manifestations of hepatitis were stopped without changing ART scheme. According to elastometry of liver in patients without ART the fibrosis degree was more pronounced: fibrosis at stage F3-F4 was detected in 28 patients (63.6%), while in patients with ART - in 17 (40.5%) (p <0,05). F1-F2 fibrosis was observed in 36.4% (16 persons) who did not receive ART and in 59.5% (25 persons) passing ART - drugs.

Conclusion: Thus, in patients with co-infection (HIV + viral hepatitis) at the background of treatment with antiretroviral drugs and, as a consequence, increase in level CD-4 lymphocytes there is less severe degree of activity of hepatitis and less pronounced degree of liver fibrosis.

SERUM LEVELS OF TRANSFORMING GROWTH FACTOR 1B AND TISSUE INHIBITOR OF METALOPROTEASE-1 IN PATIENTS WITH CHRONIC HEPATITIS C.

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Purpose. To study clinical significance of serum levels of transforming growth factor 1b (TGF-1b) and tissue inhibitor of metaloprotease-1 (TIMP-1) in patients with chronic hepatitis C (CHC).

Materials and methods: Sixty three patients with CHC aged from 19 to 57 years [middle age 35,6±10,5, men 41 (36,6±9,9 years), women 22 (37,2±11,3 years)] are observed. The diagnosis is established on the basis of clinical, biochemical, IFA and PCR methods. Stage of liver fibrosis defined with fibroelastometry (FE) by “Fibroscan” device (Echosens, France). The control group was made by 35 healthy individuals aged from 19 till 46 years (average age 32,5±10,6). Serum TGF-1b and TIMP-1 levels were measured in IFA with use of commercial kits (R@D, the USA).

Results: When studying fibrosis stage it is established that F0 (Metavir) is revealed in 22 (34,9%) patients, F1 – in 15 (23,8%), F2 – in 9 (14,4%), F3 - in 7 (11,1%) and F4 – in 10 (15,8%). There was reliable (p<0,001) TGF-1b and TIMP-1 levels increase in patients with CHC in comparison with control group. A positive reliable (p<0,01) correlation between TGF-1b and TIMP-1 serum levels, on the one hand, and activity of cytolytic enzymes, on another (r=0,57, r=0,63, respectively) is revealed. Positive reliable correlation dependence between the TGF-1b level and TIMP-1 and a fibrosis stage according to a FE (r=0,76 is established, to p<0,01, r=0,69, p<0,01, respectively).

Conclusions: Transforming growth factor-1b and tissue inhibitor of me-taloprotease-1 participate in immune pathogenesis in chronic hepatitis C and, with fibroelastometry, may be used as the noninvasive tests defining expressiveness of fibrous changes in a liver.

INFLUENCE OF PEGYLATED INTERFERON ALFA-2A (PEG-IFN-A2A) AND RIBAVIRIN (RVN) ON THE SERUM TRANSFORMING GROWTH FACTOR-1B AND TISSUE INHIBITOR OF METALOPROTEINASE-1 IN PATIENTS WITH CHRONIC HEPATITIS C (CHC)

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Purpose: to study influence Peg-IFN- α2a on TGF-1b and TIMP-1 levels in blood serum in patients with CHC.

Material and methods: Sixty three patients with CHC aged from 19 to 57 years [(middle age 35,6±10,5), men 41, women 22] are surveyed. The diagnosis is established on the basis of clinical, biochemical and IFA methods. HCV RNA was detected with PCR real-time method. Stage of liver fibrosis was defined by fibroelastometry with the "Fibroscan" device (Echosens, France). The control group was made by 35 healthy individuals aged from 19 till 46 years. All patients received standard antiviral therapy for 24 or 48 weeks depending on HCV genotype.

Results: In 42 (66,7%) patients with CHC it is established 1b genotype, in 21 (33,3%) patients - 3a genotype. High virus load (> 800 000 IU/ml) is revealed in 27 (39,7%) patients. It is established reliable (p<0,001) TGF-1b level and TIMP-1 increase in blood serum in comparison with control group. SVR was reached in 16 (76,1%) patients with 3a genotype and in 23 (54,7%) patients with 1b genotype. In patients with high viral load and genotype 3a the TGF-1b and TIMP-1 levels were authentically (p<0,05) increased in comparison with those in patients with a genotype 1b and low virus load. In patients reached SVR levels of TGF-1b and TIMP-1 are reliable (p<0,01) decreased in comparison with their pretreatment levels.

Conclusions: Achievement of the sustained virological response with use of peg-IFN-α2a and ribavirin in patients with CHC is associated with considerable decrease in the TGF-1b and TIMP-1 serum levels.

BASIC REGULARITIES IN PATHOMORPHOGENESIS OF CHRONIC HEPATITIS C (HCV-INFECTION)

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Objectives: To reveal basic regularities characterizing the pathomorphogenesis of chronic hepatitis C (HCV-infection).

Methods: 112 cases of chronic HCV-monoinfection were studied in search of correlations between HCV genotypes, replication markers, levels of viremia, the number of infected hepatocytes, and the degree of liver damage. Paraffin, semithin and ultrathin sections were used in morphological analysis of liver tissue samples obtained by needle biopsy.

Results: Genotyping of HCV showed that 53% of patients were infected with genotype 1b, 30% – with genotype 2 and 14% with genotype 3a virus. Patients with genotype 1b in most cases displayed mild (70%) or minimal (10%) activity of infectious process. High levels of viremia (106 – 108 RNA copies per 1 ml of blood plasma) were mostly associated with minimal changes in liver structure. The lack of direct relationship between virus replication and the degree of liver damage was further confirmed by statistical analysis – the presence of HCV RNA in blood or liver tissue samples (PCR findings) and the number of infected hepatocytes (assessed by NS3Ag expression) did not correlate with the activity of infectious process evaluated by examination of liver biopsy specimens and biochemical tests. Using semithin sections we have marked out the phenomenon of fine-vesicular subcytolemmal lipid infiltration and ascribed it to HCV replication phase.

Conclusions: HCV replication and the number of infected hepatocytes do not per se contribute significantly to the liver injury in chronic hepatitis C. There is substantial evidence suggesting that lipid droplets play an important role in reproduction of HCV particles either by providing a factor required for their infectivity or by incorporating them into a lipid transport system to export virus outside the cell.

MULTIFREQUENCY BIO-IMPEDANSOMETRY OF LIVER BIOPSY SAMPLES IN CHRONIC VIRAL HEPATITIS

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Purpose. Assessment of informational content of a low-invasive impedansometry liver biopsy samples in diagnostic algorithm in patients with chronic viral hepatitis (CVH).

Materials and methods. Seventy six patients with CVH B and C are surveyed (29 women (38%) and 47 men (62%), the average age - 37±2). All clinical examination, US in B- and CDC-mode, liver elastography were carried out. Carried out Liver biopsy under US-control with simultaneous measurement of a multifrequency bio-impedance (in vivo) and biopsy samples (in vitro) with the subsequent assessment of coefficient of liver impedance dispersion.

Results. There were high viral load in 67% of patients with CVH with ALT>ULN, 61% of them had load >400000 IU/ml in CHC and 39% had HBV DNA > 2000 IU/ml. Thirty four percent of patients had the minimal histological activity in liver, 21% -high activity and 55%-moderate activity. High impedance at all set frequencies are registered in 73% of patients, in the range 0,5-3,2kOm depending on the frequency of alternating-current. The impedance of liver significantly correlated (r>0,62) with activity of hepatitis. The coefficient of dispersion depended on severity of liver injury and was higher at absence of fibrosis according to morphology.

Conclusions. The divergence of clinical and laboratory indicators and morphological changes in liver are observed in patients with CVH. Bio-impedansometry of liver biopsy samples in the standardized conditions allows to improve an assessment of histologic changes in liver after routine biopsy.

SPONTANEOUS BACTERIAL PERITONITIS: ANALYSIS OF THE OCCURRENCE, CLINICAL AND MORPHOLOGICAL PARALLELS

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Objective: To conduct clinical and morphological analysis section of cases of patients with cirrhosis (the analysis for 2012 (Tomsk), specifying the frequency of spontaneous bacterial peritonitis (SBP), assess the timeliness of diagnosis. Materials and methods: Our study population consisted of 42 patients with cirrhosis, of which 21 cases with SBP. It is a retrospective analysis of 42 cases autopsy diagnosis of cirrhosis of the liver. 57.1% of cases of SBP were women, mean age 38,5 ± 6,8 y. 42.9% male with a mean age 49,5 ± 11,5 y. All the patients were subjected to the same tests for viral antigens and (or) alcohol abuse. Results and conclusion: It was found that out of the total number of autopsies (1158) the incidence of cirrhosis as the underlying disease was 0.27%.The causes of cirrhosis were as follows: viral infection (HBV, HCV) plus alcohol abuse (85.7%), alcohol abuse (7.1%) and 7.1% unspecified. 50% of cirrhotic transformation is accompanied by the development of SBP. In 57.1% of cases of SBP were women, mean age 38,5 ± 6,8 years, and 42.9% male with a mean age 49,5 ± 11,5 years. The causes of SBP were as follows: in 14.2% combined with a fatal GI hemorrhage and for 28.5%, with episodes of minor bleeding. SBP was associated in 66.6% with E. coli (50% - ESBL-producing), 14.2% were isolated E.coli and S.aureus, at 14.2% -other microorganisms. Development of abdominal sepsis were identified in 10 of 21 patients (47.6%) with an outbreak blood dissemination dropping into the lungs, pericardium, etc. 70% of the cause of sepsis was the combined effect of E.coli and S.aureus. Conclusion of sepsis in life was only in 10% cases, which demonstrates the complexity of the diagnosis and the necessary caution.

ASSOCIATION BETWEEN THE PROTEASE-ANTIPROTEASE SYSTEM AND MORPHOLOGICAL CHANGES IN THE LIVER IN CHRONIC HCV-INFECTION

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Objective: to establish the nature of the association between the protease-antiprotease system and alternative, necroinflammatory, sclerotic changes in the liver in chronic viral hepatitis C with alcohol disease and opium addiction. Materials and methods: 350 patients with chronic hepatitis C, including 200 people with isolated HCV-infection in 99 patients with chronic hepatitis C combination with alcohol disease, and in 51 with opium addiction. Studied the biochemical indicators of exchange of collagen and elastin in the blood serum. The plasma activity was measured collagenase, elastase, α1-proteinase inhibitor, α2-macroglobulin, and hydroxyproline content of the fractions. Histological activity index (A) and fibrotic score (F) was calculated on a scale METAVIR. Results: It was found that fibrosis in isolated HCV-infection is associated with a sharp increase elastase activity and lower concentrations α2-macroglobulin and fibronectin. Thus, at the level of elastase at F I was 92.1 nmol / min.L (Q1 = 90,2; Q3 = 96,2), whereas F II-III - 140,5 nmol / min.L (Q1 = 102, 5; Q3 = 151,0, p = 0.01). When unexpressed fibrosis level α2-makroglobulin was 3.6 IU / mL (Q1 = 1,3; Q3 = 4,3), whereas in the F II-III - 2,6 IU / mL (Q1 = 1,2; Q3 = 3,1, p = 0.01). At F I level fibronectin equald 180,5 mg / ml (Q1 = 151,1; Q3 = 191), whereas patients with severe sclerosis of 125.1 mg / ml (Q1 = 120,1; Q3 = 131,5, p = 0.008). We found a similar pattern in the group of HCV-infection with alcoholism. In the porto-portal and porto-central fibrosis in HCV-infection with alcohol dependence were found negative correlations between degeneration, necrosis and the degree of increase collagenase activity. Thus, a large hydropic (r = -0,58, p = 0,001) and fat (r = -0,49, p = 0,02) degeneration of hepatocytes determined less collagenase activity. In addition, the inverse correlation was detected between the occurrence of piecemeal (r = -0,61, p = 0,0001), intralobular necrosis (r = -0,44, p = 0,006) and the degree increase collagenase activity in HCV-infection with alcoholism .

POST-THERAPY MONITORING OF HEPATITIS C VIRUS MARKERS IN PATIENTS WITH CHRONIC HEPATITIS C

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Efficiency of antiviral therapy (AVT) with pegIFN and ribavirin of chronic hepatitis C is about 50-70% depending on genetic factors of hepatitis C virus (HCV) and a patient. Within 1-2 years after the AVT nearly 15-20% of patients display relapse. The aim of the study was to analyze post-therapy revealing of HCV markers.

Blood samples of 50 patients with sustained virological response (SVR) were analyzed within 3-7 years after the therapy end. HCV RNA was detected by real-time OT-PCR, using commercial assay «RealBest HCV RNA» with sensitivity 15 ME/ml ("Vector-Best", Russia). Antibodies to different HCV antigens were detected by ELISE method in commercial assays "RecombiBest anti-HCV-IgM" and "RecombiBest anti-HCV-spectrum" ("Vector-best", Russia).

HCV RNA was detected in 44% patients with SVR. More often HCV RNA was revealed within 2-4 years after the end of the therapy. Nearly 25% of patients displayed HCV genome within the time interval. The viral load in samples of these patients was low 25-50 ME/ml. These patients often showed appearance of anti-HCV IgM and its stable detection. The others patients, who were without HCV RNA within all period of monitoring, showed decline of antibodies to individual HCV proteins, especially to NS-antigenes.

In summary we will notice, that long (till 7 years) absence of HCV RNA in blood of patients after the AVT is associated with decrease in titers of antibodies to individual HCV antigens. HCV RNA appearance often occurs within 2-4 years after the treatment end.

HEPATITIS C VIRUS MARKERS IN DIFFERENT AGED PATIENTS GROUPS

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About 3% of population, including all aged groups, are infected by hepatitis C virus (HCV) in Russian Federation. The aim of the study was to analyze HCV markers in different aged patients groups: from 2 to 14 years (the 1st), from 18 to 29 years (the 2nd) and from 30 to 55 years (the 3d group).

Blood samples from 60 patients, who were included into these three groups on 20 people in each other, were analyzed. HCV RNA was revealed by OT-PCR with sensitivity of 50 ME/ml. Antibodies to HCV were determined by immunoenzyme method in commercial assays "RecombiBest anti-HCV-IgM" and "RecombiBest anti-HCV-spectrum" ("Vector-Best", Russia). The statically significance of differences between groups was estimated by Student’s t test.

Duration of the infection was identical (2-7 years) in all groups. Men prevailed (60%) in all groups. HCV genome was revealed in all adult patients and in 80% of the infected children. HCV subtype 1b dominated in all groups. However in the first two groups viral subtype 3a was 40% that is in 2 times more than in the third group. Frequency of anti-HCV IgM detection and its titers were almost identical in all groups. Anti-core IgG was found in statistically significance lower titers in children (p<0,01). Similarly immunoglobulines G to NS antigens (NS3, NS4ab, NS5a) were revealed in lower titers in children group than in two adult groups (p <0,01).

In summary we will note, that children with chronic hepatitis C showed serological markers of HCV in lower titers, than adult patients. HCV subtype 3a detection was higher in children and young adult patients, than in persons older 30 year.

CLINICAL PRESENTATION IN CHRONIC VIRAL HEPATITIS (CVH) OF MIXED ETIOLOGY

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Complex clinical and laboratorial examination of 120 patients (64 women and 56 men) was conducted, 30 patients have HCV, 30 - HBV infection and 60 mixed hepatitis: B+C, B+D, B+D+C. The analysis of history showed lack of an acute hepatitis manifestation in the majority of patients (78,4±6,3%). When studying a current of CVH in patients with mono- and mixed infection a great difference of signs is revealed. The undulating course of a disease is most common with appearing of new signs and worsening preexisting signs at the time of CVH attack.

Predominating signs are: astenovegetative signs (94,6±1,5%), changes of liver and spleen size (93,8±1,8%) and cholestatic symptoms (55,4±9,1%). The last ones preceded with higher rates of increased GGTP and AP levels in mixed CHV in comparison with mono-infection. Increased levels of cholestatic markers were associated with more expressed cytolytic (rS=0.8) and dysproteinemic (rS=0,5) syndromes, and also to hemorrhagic manifestations (rS=0,5) that is correlated with more expressed fibrous changes in a liver (rS=0,7). Astenovegetative manifestations and a splenomegaly occurred more often in presence of cholestasis (χ2=0,7, v = 1 art. of freedom, p <, 0,05). Extrahepatic pathology was registered in a third of 86 patients with a typical clinical presentation CVH (28 patients - 32,5±2,2%) and was presented: polymorphic itching exantema, eritema nodosa, urticaria, "flying" artralgiias and mialgiias, signs of pancreatopathy, hematologic abnormalities, endocrinopathy etc. Prevalence of extrahepatic pathology authentically occurred in monohepatitis, than in the combined forms (20,6±5,2% and 6,6±3,2%, p<0,05). In two patients with the mixed hepatitis B+D+C combinations of extra hepatic manifestations are revealed:crioglobulinic nephritis, Sjogren syndrome, autoimmune thyroiditis and chronic pancreatitis.

ANALYSIS OF THE EFFICIENCY OF ANTIVIRAL THERAPY IN PATIENTS WITH CHRONIC VIRAL HEPATITIS «C»

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Comprehensive evaluation of the efficiency, safety and tolerability of combination therapy with ribavirin, pegylated interferon and fast-release interferon (Roferon A) in patients with chronic viral hepatitis C was carried out. The study included 69 patients with chronic viral hepatitis C, among which women -64.8% and 35.2% men, aged 18 to 60 years.

The criterion of the effectiveness of treatment was disappearance of replicative markers in the blood of patients, and therefore the virological parameters of AVT effectiveness were taken into account: rapid virologic response (RVR), early virological response (EVR), the immediate virological response (IVR).

Results of conducted study enable to make the following conclusions:

- In 92.8% of cases, the development of side effects in terms of combined intake of pegylated interferon, ribavirin and Roferon in patients with chronic viral hepatitis C do not require discontinuation of treatment.
- The most frequent and significant side effects are neutropenia 80% and thrombocytopenia 92%
- Combined antiviral therapy with pegylated interferon and ribavirin is more effective in case of chronic viral hepatitis C with genotype 3 and 2 (88.8%) than 1 (40%).
- Combined antiviral therapy in patients with chronic viral hepatitis C with pegylated interferon and ribavirin is more effective (RVR was achieved in 74.0% of patients treated with pegylated interferon and ribavirin) compared to therapy with Roferon and ribavirin (SVR was achieved in 43.2%).

NEW ASPECTS OF THE IMMUNE RESPONSE DURING IFN THERAPY IN ADULTS AND CHILDREN WITH CHRONIC HEPATITIS C (CHC).

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Recently introduced plasmacytoid dendritic cells (PDC) play a key role in IFN production, especially in CHC. Influence of IFN therapy on PDC condition isn't studied.

Purpose: to show influence of IFN therapy on quantity and functional condition of PDC in CHC in adults and children.

Materials and methods: One hundred sixty one person - 133 patients in various phases of CHC (58 children and 75 adults), 28 healthy individuals (16 children and 12 adults) are surveyed. Determination of quantity of PDC in blood was carried out by a method of a flow cytometry with use of monoclonal antibodies to specific markers of PDC (CD303 and CD123). IFN determination (the producing function of PDC) was carried out by IFA ELISA method, with previous stimulation of ODN2216 and IL3.

In norm IFN levels in PDC are below detection level.

Results: According to the obtained data IFN-therapy significantly stimulates IFN production in PDC. Production of IFN is significantly higher in patients receiving therapy (adults: 1887±330,9 pg/ml, N=19, children 492,6±228,8 pg/ml, N=11), than in naïve patients (453,6±254,2 pg/ml, N=34 and 134,4±27,17 pg/ml, N=34 respectively), both adults and children (p<0,05). However IFN production is significantly lower in children, than in adults, both before antiviral therapy and during therapy. IFN production in PDC significantly decreases after the end of therapy, and remains significantly higher than normal (adults: 111,2±47,2pg/ml, N=28, children: 49,8±23,9 pg/ml, N=14, p<0,05). The absolute quantity PDC sharply decreases during treatment and significantly depends on the response to antiviral therapy. At the favorable answer decrease in absolute quantity of cells is observed (adults 9,2±0,9/ml before therapy and 3,7±0,5/ml after therapy, children - 15,4±1,2/ml and 7,1±1,15/ml, p<0,05 respectively). In the absence of virological response the quantitative parameters of PDC significantly don't change (7,2±0,9/ml in 11,6±1,6/ml, p<0,05). IFN production is lower, than in naïve patients.

Conclusion: IFN therapy significantly influences the PDC parameters. It's significantly shown that response to the antiviral IFN therapy significantly correlates with changes of quantity and functional activity of PDC.

ADHESION OF LYMPHOCYTES WITH PLATELETS AT PATIENTS WITH CHRONIC VIRUS HEPATITIS C

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Many aspects of the immune answer at hepatitis C remain obscure though it is actual as in theoretical aspect for understanding of changes in immunity, and on the practical level for the forecast of a course of disease. The purpose of the real work was studying of indicators of adhesion of lymphocytes with platelets at patients with chronic virus hepatitis C.

Materials and methods. 32 persons with HCV were surveyed. Women there were 31,3 % (10), men – 68,7 % (22), middle age made 37,68 ± 1,99 years. Disease duration till 5 years is revealed at 59,1 %, over 5 years – at 40,9 %. The first degree of biochemical activity of process was defined at 59,1 % of the sick HCV, the second – at 40,9 %. Definition of an indicator of adhesion of lymphocytes with platelets (LTA) carried out on a method offered by Y.A. Vitkovsky et al. (1999). Indicator of LTA expressed number of units of lymphocytes with platelets on 100 cages (norm – 13-15 %). Degree of adhesion (LTI) defined as number of blood plates, adgezirovanny on a surface of one lymphocyte (norm – 3,0 ± 0,3).

Results. It is established that at patients with chronic virus hepatitis About an indicator of LTA it was lowered – 10,0 ± 1,32 %. At the same time with this the average of the platelets which have come into contact to lymphocytes was reduced also: 2,46 ± 0,29. Thus at the persons who have fallen ill with HCV is less than 5 years ago, LTA made 10,23 ± 1,81 %, LTI – 2,35 ± 0,24, at the patients who have caught more than 5 years ago – 9,67 ± 2,01 % and 2,58 ± 0,61 respectively. At patients with the first degree of biochemical activity of process the indicator of LTA was the most minimum – 8,62 ± 2,48 %, degree of LTA made 2,48 ± 0,40. Adhesion of lymphocytes with platelets at patients with the second degree of activity of HCV made 12,0 ± 1,68 %, LTI – 2,39 ± 0,39.

Conclusions. Thus, at chronic virus hepatitis C adhesion of lymphocytes with platelets is reduced, i.e. there is a dysfunction of T-lymphocytes which is shown in reduction of their ability to adhesion of platelets. Thus decrease is more expressed at persons with the bigger duration of a disease.

Hepatitis C in Russian Federation

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2613 acute cases of hepatitis C accompanied generally by jaundice were registered in Russia in 2011 or 1.83 per 100 000 of general population. This index was worse as 21.1 0/0000 in 2000. One icteric acute hepatitis C case corresponds to 8 cases without jaundice which were basically out of registration. 57 028 chronic hepatitis C cases were diagnosed first time in 2011 or 39.92 0/0000. HCV provides 74.45% cases among all chronic hepatitis in Russia, whilst in Moscow it is 80.9%. The remarkable chronic hepatitis C incidence increase is identified. Also we found seroprevalence increase which reached 300 – 500% in some regions as well as number of infected pregnant. Half of patients are younger than 40 years, mainly 20-39 years old. 0.7% of cases are registered in children up to 14 years. The iatrogenic (2.7% in 2010) and IV drug addiction (21%) HCV transmission routes role has been decreased during several years. Natural routes of transmission are not active: 3.5% infection cases in newborns due to perinatal transmission, and 14 -16% cases in HIV co-infected patients. The delivery way and breast feeding do not influence on HCV transmission rate in infected woman in childbirth. Family transmission was found in 0.7 – 1.0% partners of chronically HCV infected females. HBV markers were found in 22% chronic hepatitis C cases. HBV vaccination is indicated in chronic hepatitis C patients without evidence of anamnestic HBV-infection. No vaccination adverse events rate increase or complications of chronic liver disease were identified in those patients. HCV markers are found in 83% of HIV infected patients during primary visit.

EFFECTIVENESS OF ANTI-VIRUS THERAPY OF PATIENT WITH CHRONIC HEPATITIS C (CHC) IN SPITE OF THE ABSENCE TRADITIONALLY REGISTERED PREDICTORS SVR

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It's well-known that there are a lot of difficulties in reaching sustained virological response (SVR) in the process of standard antiviral therapy (AVT) of patients with CHC 1b genotype and virus load of more than 2 mln.cop/ml. Even at the stage of fibroses (F) 1-2, if there is no RVR and EVR, duration of the course of treatment is from 48 to 72 weeks. Such virus kinetics with RVR and long period of averimie and sticking to this treatment during AVT are widely recognised and are considered to be necessary predictors of SVR.

That's why the case report of the patient with CHC 1b genotype forming SVR is very interesting. It should be mentioned that it was the case of patient with high baseline virus load without RVR and EVR and the period of averimie in the process of AVT was about 8 weeks.

Patient K.male, 32y. aHCV have been registered for 3 years, no clear risk factor can be identified. No excessive use of alcohol has been practiced. BMI =25,4. Asymptomatic state, no specific complaints. Biopsy of liver: HAL- 8 points, F-2 (metavir). HbsAg, aHBcor, aHIV- negativ, HCV RNA-4,6x107 cop/ml, 1b genotype, ALT-165E/l. Initially a standard course of AVT was planned peginterferon alfa2a180mg+ ribavirin 1200mg 48 weeks.

During this treatment AVT the following results were registered: during the 4th week HCV RNA-5,2 x 105, in 12 week 2x 103 cop/ml. After 16 weeks- HCV RNA has been negativ.

Because of the symptoms of skin disease (dermatitus) which developed during the course of the medication the patient gave up the treatment after 24 weeks. HCV RNA(-), ALT became normal, modification of antiviral medicines' doses wasn't present. When the patient's analyses were taken in 24 weeks, 1 and 2 years HCV RNA was not registered in blood samples, ALT remained within normal limits.

It can be supposed that in our case of the patient with a slow type of virologic response when the planned course of AVT must be 72 weeks, the formation of SVR was mainly influenced by the patients individual features (genetic ones, those connected with the system IL 28 B) or may be some other acquired features, some predictors of response to AVT which hasn't yet been investigated.

ASSESSMENT OF POSTVACCINAL HBV IMMUNITY IN MOSCOW

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The numerous researches in Russia and in the world (F.B.Hollinger et al. 1982, Alter et al M. 1990 P. van Damme et al. 1993, T.P. Grosheyde and P. van Damme, 1996, V.F.Uchaykin et al. 2001, I.V.Shakhgildyan et al. 2004, M.I.Mikhaylov et al. 2003, V. M. Romanenko, 2011, etc.) showed that vaccinal prevention of hepatitis B (HB) is the main and most effective method to decrease an incidence of HB. Introduction of vaccination against hepatitis B in a national calendar of preventive vaccination of the Russian Federation (1997), implementation of programs since 2008 of mass immunization within the national Health project had an essential impact on activity of epidemic process of HB in Moscow.

The research objective consisted in an assessment of epidemiological and immunological efficiency of mass immunization against hepatitis B in Moscow population. Data of official statistics (p. 1,2 of federal statistical supervision "Data on infectious and parasitic diseases") in 1999 – 2011 are used. Immunological efficiency was defined by chemoluminescence reaction on the automatic analyzer "Architect" with use of commercial test system (Abbott) in D.I.Ivanovsky Scientific research institute of virology of Russian Academy of Medical Science Concentration of antibodies of 10 IU/l was accepted as the protective level.

Implementation of big programs of specific prevention of hepatitis B in Moscow (51,6% of the population of the city, children till 17 years – more than 95%, adults of 18-55 y.o. – 65% are vaccinated at the time of 01.01.2012) led to considerable decrease in incidence of acute HB (from 65,1‰ in 1998 to 3,4‰ in 2011), level of HBV carriage in population (from 98,1‰ in 1998 to 25,1‰ in 2011), indicators of mortality from acute HBV (from 0,12‰ in 2003 to 0,04‰ in 2011). Significant decrease of acute HB incidence among all age and social groups of the population, especially in age group of 15-19 y.o. (1998 – 359,0‰, 2011-1,0‰) and 20-29 y.o. (1998 – 245,0‰, 2011 - 8,2‰) is noted. In the last 3 years (2009-2011) intensity of epidemic process of chronic hepatitis B (CHB) decreased and currently is 9,8 - 10,3 per 100.000 of population.

ANALYSIS OF HEMATOLOGICAL TOXICITY CASES FREQUENCY IN PATIENTS WITH CO-INFECTION HIV + CHRONIC VIRAL HEPATITIS C WHO HAD RECEIVED COMBINED ANTIVIRAL THERAPY

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Goal of investigation. Retrospective analysis of patients with chronic viral hepatitis C laboratory data had received antiviral therapy in 2010-2012 y.

Materials and methods. Continuous retrospective analysis of cases history of patients with co-infection HIV + chronic HCV received combined antiviral therapy in infectious department of Smolensk Clinical hospital №1 in 2010-2012 had been made.

Results and discussion. 41 patients' cases histories were analyzed. 36 patients (87.8%) had undesirable hematological actions: 16 of them (44.4%) showed anemia, 11 (30.5%) had neutropenia and thrombocytopenia was found in 9 patients (25.1%).

At the 12ve week of antiviral treatment signs of hematological toxicity were revealed in 24 patients, at the 24th week in 7 patients in addition and all 36 patients presented these signs by the 48th week. At the 12ve week of antiviral therapy laboratory signs of anemia were revealed in 11 patients, 4 of them had drop in hemoglobin level lower than 100mg/l what demanded reduction of Ribavirin dose, neutropenia was in 7 patients, thrombocytopenia in 6 patients. At the 24th week of treatment anemia was found in 14 patients, 5 persons had level of hemoglobin less than 100mg/l with reduction of Ribavirin dose. Decrease of neutrophils level at the 12ve week was found in 7 patients, at the 24-th week neutropenia was revealed in 9 patients, 4 of them needed reduction of pegilated interferon dose by the 48th week, 11 patients had neutropenia, 5 of them received reduced dose of pegilated interferon.

Resume. Progress of side hematological actions in patients with co-infection HIV + Chronic viral hepatitis C is present from 12ve week of antiviral therapy, especially anemia and neutropenia which are results of antiviral drugs dose reduction in 27%.

CLINICAL AND MORPHOLOGICAL CHARACTERISTICS OF CHRONIC HEPATITIS B AND C IN COMBINATION WITH LIVER HEMOSIDEROSIS

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Liver hemosiderosis (LHS) - hemosiderin deposits in the cytoplasm of hepatocytes and Kupffer's cells – is a morphological marker of anemia of inflammation (anemia of chronic illness) Purpose of study is clinical and morphological characteristics of chronic hepatitis B and C (CH-B and C) in combination with LHS.

133 cases of CHB (69) and CHC (64) were studied. Etiology of disease was confirmed by serum ELISA test and PCR. Complex examination of patients included liver function tests, study of metabolism and common stock of iron. All the patients passed biopsy of liver to clarify the activity and stage of disease. Presence of LHS was determined on sections stained for iron by Pehrls' method. Study group included 56 cases (CH-B - 27, CH-C- 29) in conjunction with the LHS, the comparison group - 77 cases (CH -B - 42, CH -C - 35) without this feature.

In patients of the main group the functional iron pool was reduced (Hb 131,4 ± 1,9 g / l, serum iron 19,2 ± 0,2 mmol / l, transferrin saturation with iron 26,3 ± 0,7%) in comparison with comparison group (Hb 142,1 ± 1,4 g / l, serum iron 22,8 ± 0,3 mmol / l, transferrin saturation with iron 33,2 ± 0,9%). The following peculiarity of CH combined with LHS were determined: 1) moderate and severe chronic hepatitis in the main group was more frequent than in the comparison group: 54,9 ± 4,5% and 37,8 ± 3,5%, respectively (p < 0,05), and 2) the occurrence of moderate and severe liver fibrosis in the presence of LHS was 64,8 ± 4,3%, and in its absence - 47,3 ± 3,6% (p <0,05), and 3) the first symptoms of the disease the patients of main group noted 3,8 ± 0,6 years prior to the last hospitalization, and patients of comparison group - 2,1 ± 0,2 years (p <0,05).

Thus, KHS is an important diagnostic and prognostic morphological marker of CH-B and C. It is confirmed by evident association of phenomenon with a decrease in functional iron pool, longer course of the disease, increased degree of liver fibrosis and inflammation activity.

INFLUENCE OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) ON EFFICIENCY OF ANTIVIRAL THERAPY IN PATIENTS WITH CHRONIC HEPATITIS C (CHC) AND HIV.

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Purpose: to study influence of HAART on the frequency of steady virologic reply (SVR) in patients with CHC treated with IFN-alpha 2a and.

Materials and methods. One hundred thirty nine residents of the Leningrad region are included in research, with 48- or 72-weeks course antiviral therapy ≥ 6 months ago. Groups are allocated: 1-not receiving HAART (n=74), 2- with HAART (n=65). Groups were comparable on age (median (25/75%) is 30(27/32) in the 1st group and 31(28/34) in the 2nd group respectively, p=0,158), sex (men of 58,1% in the 1st, 58,5% in the 2nd group, p=0,966), viral load (median (25/75 %) – 1430000 (376875/5 mln) IU/ml in the 1st, 1910000 (448000/5 mln) – in the 2nd group, p=0,724), to Quetelet's index (23(20/25) and 22 (21/24), p=0,791). The parenteral way of infection was dominating in both groups.

Groups differed on presumable duration of CHC (10,5(7/12) years in the 1st, 12 (10/14) years in the 2nd group, p=0,029), liver fibrosis degree (3 and 4 stages (Metavir) were dominating in the 2nd group, p = 0,029), HIV viral load in blood plasma (3935(1190/17765) copies/ml in the 1st, 150(50/810) copies/ml in the 2nd group, p<0,001). At statistical data processing used criterion χ2 Pearson and Mann-Whitney's U-test (since at least one of compared selections differed from normal distribution).

Results: SVR was reached in 67,6% of patients from the 1st group and in 69,2% of patients of the 2nd group, p=0,833. Genotype 1 SVR - 60% in the 1st group and 57,6% in the 2nd group, p=0,845. Genotype 3a SVR – 80,6% in the 1st group and 88% in the 2nd group, p=0,440. 24 persons (17%) didn't finish 48 week course of antiviral therapy for various reasons, in 5 of them SVR is reached (are included in 1 group), in 19 – wasn't reached (are included in the 2nd group). Correlations between achievement of SVR and HAART weren't revealed (p 2x of criterion of Spearman 0,835). Among 5 persons of interrupted antiviral therapy, but reached SVR 3 had genotype 3a, 2 – genotype 1.

Conclusions: Antiviral therapy of CHC is effective in HIV-positive patients. HAART has no essential impact on efficiency of therapy of CHC.

REASONS OF WITHDRAWAL OF ANTIVIRAL THERAPY OF CHRONIC HEPATITIS C (CHC) IN HIV-INFECTED PATIENTS.

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One of considerable problems in treatment of CHC in HIV-infected patients is the early termination of therapy up to 25% and more.

Purpose: to analyze the reasons of withdrawal of antiviral therapy in HIV-positive patients and correlation with HAART.

Materials and methods: One hundred thirty nine residents of the Leningrad region received ribavirin and pegylated INF alpha 2a were included in research. Seventy four patients received also HAART, 65 didn't receive it. The detailed characteristic of selections – see abstract T.A.Stasishkis et al. "Influence of HAART on efficiency of antiviral therapy in HIV-infected patients with hepatitis C (CHC).

Results: Twenty-four (17%) patients didn't finish the appointed course of antiviral therapy, 5 of them reached SVR, and 19 – didn't reach.

Among patients reached SVR termination term and the reason were: week 12/use of IV drugs (IVD)– 1 person received HAART, week 24/change of a residence – 1 person, week 28/bilateral pneumonia – 1 person received HAART, week 32/ expressed weakness – 1 person, week 32/ long business trip – 1 person. Other 18 patients: week 4 / IVD use in 1 person and alcohol abuse - in 2 persons (one of them received HAART), week 12 / change of a residence - 2 persons, week 24 / no response in 4 persons (3 received HAART), expressed weakness - in 2 persons (one received HAART), IVD use in 3 persons (one of them received HAAART), change of a residence - 1 person, week 28 / IVD use-1 person received HAART, week 32 / is taken into custody - 1 person and tuberculosis - 1 person, week 40 / severe pyelonephritis. Thus, among patients stopped therapy only 9 people received HAART. There were no correlations between antiviral therapy of CHC withdrawal for any reason and using HAART (p Spearman's criterion 0,321)

RETREATMENT OF CHRONIC HEPATITIS C (CHC) IN HIV-INFECTED PATIENTS

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Incidence of liver cirrhosis is much more increased in HIV-infected patients with CHC, from 15% after 10 years of disease up to 65% - after 25 years.

Analyzing the reasons of treatment failure it is necessary to consider host, viral factors, and previous treatment. There are few data about retreatment of co-infected HIV/CHC non-responders for combined antiviral therapy.

Purpose: to study efficiency of therapy with peg-IFN-alpha 2a 180 mkg/week in combination with ribavirin 15 mg/kg/day for 72 weeks in co-infected HIV/CHC non-responders and patients with HCV recurrence after treatment.

Materials and methods: Co-infected patients with CHC in 3 (latent) stage of HIV infection were selected for research: 2 men and 3 women, aged of 28-33 years, history of HIV/CHC is 3 up to 10 years. Three patients didn't response therapy at week 24 and 2 patients had CHC recurrence after end of 48 week. All patients carried HCV genotype 1.

During retreatment patients received pegIFN-alpha-2a 180 mkg/week in combination with ribavirin 15 mkg/kg/days for 72 weeks. We detected HCV RNA presence and viral load by quantitative and qualitative methods at baseline and at weeks 12, 24 48, 72.

All patients included in research had viral load was over 400.000 IU/ml before retreatment. Transaminase (ALT, AST) levels were increased in at all patients before retreatment. Two patients with CHC recurrence after 48 week of antiviral therapy with peg-IFN-alpha-2 b and ribavirin 15 mg/kg/day were included in research in 4 and 6 months after therapy ending (respectively). HCV RNA (according to a quantitative method of PCR) exceeded baseline (before antiviral therapy) in thousands times. P.Barrera, V.Soriano et al. (EASL 2008, abstract 770) showed that rates of recurrence in HIV-infected patients with CHC reach 17%, and late recurrence is registered in 13% of patients. Monitoring of HIV-infection was carried out with control of CD4 lymphocytes count. The median of the CD4 counts was of 532 cells/ml prior to CHC retreatment.

Results and discussion: in Rapid and early virologic response reply occurred in all patients retreated for 72 weeks. After retreatment with Pegasis and ribavirin aviremia

remained to the 72nd week in all patients. Both patients retreated after CHC recurrence reached undetectable HCV RNA at 4 weeks of treatment. Tolerance to therapy with peg-IFN-alpha-2a and ribavirin for 72 weeks was good in general.

Conclusion: Retreatment of CHC with peg-IFN-alpha-2a and ribavirin for 72 weeks in the most "difficult" category of patients with HCV genotype 1 didn't respond to peg-IFN-alpha-2b and ribavirin is associated with increase in SVR rates. SVR at week 72 in treatment with Pegasis and ribavirin could be reached in 57% of patients if HCV RNA isn't detectable at week 12 (Jensen D, et al. 58th AASLD 2007, Abstract LB4. Marcellin P, et al. Hepatology 2008, 48 (4, Suppl), 1147).

This work proceeds because the number of patients didn't respond to "standard" therapy with peg-IFN-alpha-2a and ribavirin significantly increased. Use of new drugs gorups (HCV RNA protease inhibitors) in therapy of CHC gives chance for SVR in the most difficult category of patients with 1 genotype.

RESULTS OF OVERALL INSPECTION OF PATIENTS WITH CHRONIC HEPATITIS B IN SAMARA REGIONAL HEPATOLOGICAL CENTER

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Purpose: to carry out the overall database analysis of patients with chronic hepatitis B)CHB) in Samara regional hepatological center and detect indications for antiviral therapy.

340 patients with CHB, aged from 18 till 76 years (46±7,8), men - 120, women - 240 are surveyed. In the majority of patients (88%) ALT levels didn't exceed the ULN. In other patients ALT levels increased up to 2-3 UL. Ultrasonography performed for all patients and 162 patients showed signs of liver steatosis and cholesterosis of bile ducts and gall bladder. All patients were HBsAg-positive and 35 patients were HBeAg-positive. HBV DNA were detected in 242 patients.

Thus, results of overall examination of patients with CHB demonstrate prevalence young patients (<50 years), females with predominant replication form of CHB (75%) and combination with low degree of cytolysis.

STUDY OF ANTIOXIDANT AND MICROSOMAL ENZYMES IN PATIENTS WITH VIRAL HEPATITIS C, IN ACCORDANCE WITH THE HEPATIC INFLAMMATORY AND VIRAL PROCESS

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Scope: Study the levels of ceruloplasmin, total GST (glutathione-S-transferase) in patients with chronic hepatitis C virus (HCV) depending on the activity of the inflammatory and viral process.

Materials and methods: Study included 150 HCV patients, average age 42,21±2,04. Clinical, biochemical, enzyme immunoassay tests were taken. Control group - 30 persons. All patients were split in 2 groups: 1st (n=102) group was tested for ceruloplasmin, 2nd (n=48) –for total GST. Test results were compared to the inflammatory process activity (ALT, AST) and the viral infection phase.

Results: It was found that ceruloplasmin level (180,42±4,50mg/l) increased compared to the control group (116,42±2,66mg/l)(p<0,001). Based on the observations, a significant excess of the indicator in both minimal process activity (176,30±4,66 mg/l), as well as in the maximum one (190,66±11,30 mg/l), compared to the results from the healthy persons (p<0,01, p<0,01), was encountered. A direct link between the level of ceruloplasmin and the activity degree of hepatic process was spotted (rxy=0,57) and the viral infection phase (rxy=0,56). Total GST (48,78±9,97mm/l) is reduced compared to the group of healthy people (157,0±3,16mm/l)(p<0,001). Similar results occurred while studying this indicator dependant on the activity of the liver inflammatory process, being at a minimum (52,54±10,33mm/l) and maximum (47,23±9,92mm/l) compared to the control group (p<0,001, p<0,001). A direct linkage between the activity of the inflammatory process and the GSTtot content (rxy=0,64) was found.

Conclusions: In HCV C, increased levels of ceruloplasmin and reduced values of GST were found. Changes in antioxidant and microsomal enzymes reflect the imbalance in liver antioxidant system, which favor peroxidation processes intensification, serving as a negative factor in viral hepatitis evolution.

PREVALENCE OF EXTRA-HEPATIC MANIFESTATIONS IN CHRONIC HEPATITIS C: STUDY OF 200 CASES

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Chronic hepatitis C (CHC) is associated with several extrahepatic manifestations. These conditions contribute to more severe course of disease, deteriorate results of antiviral treatment and increase number of serious complications.

Methods: 200 consecutive patients (112 women) with CHC were enrolled in our study. We examined the prevalence of extrahepatic manifestations in patients with CHC and analyzed their associations with clinical and laboratory data.

Results: The mean age of our patients was 46 ± 14.5 years (range 16 to 81 years). Cirrhosis was diagnosed in 71 (35.5%) patients. The average duration of infection was 20 ± 12 years. Genotype 1 was found in 65% of patients, genotype 3 - in 26% of cases, genotype 2 - in 8% and genotype 4 - in 1% of patients.

Clinically significant extrahepatic manifestations of CHC were detected in 47 (23.5%) patients, of whom 11(23.4%) persons had two extrahepatic sighs, 9 (19%) had three and 4(8.5%) patient had four distinct extrahepatic manifestations.

Cryoglobulins were found in 83 (41.5%) patients. Cryoglobulinemia was asymptomatic in 33 (40%) patients. 34 (17%) patients had diagnosed cryoglobulinemic vasculitis. Of them 20 (58.9%) had purpura, 22 (64.7%) patients reported arthralgia, 11 (32.4%) had chronic cryoglobulinemic glomerulonephritis, 11 (32.4%) suffered from peripheral neuropathy, 9 (26.7%) had Shlegren's syndrome.

Overall 48 (24%) patients had renal impairment: 45 (22.5%) within the bounds of cryoglobulinemia and 3 (1.5%) patients had chronic tubulointerstitial nephritis irrelevant to cryoglobulinemia.

The presence of extrahepatic manifestations was correlated with greater age, longer duration of disease and serum rheumatoid factor.

Conclusions: Extrahepatic lesions were mostly associated with cryoglobulinemia.

Associations of extrahepatic manifestations with greater age and longer duration of disease were found in our group of patients with CHC.

COURSE OF CHRONIC LIVER DISEASE AT THE HERPES INFECTIONS

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Objective: To evaluate the effect of herpes virus (HV) – HSV-1, HSV-2, EBV, CMV on the course of chronic liver disease (CLD) of various etiologies.

Materials and methods. In blood serum at 94 patients with CLD of the virus, alcoholic and mixed alcoholic and virus etiology determined IgG and IgM to HSV -1, HSV -2, EBV, CMV (ELISA) and DNA HSV-1, HSV-2, EBV, CMV (PCR). Results. Antiherpetic antibodies (Ab) were detected in 93/94 patients: IgG HSV-1 - in 91.5% of cases, IgG EBV - in 89,4%, IgG HSV-2 - 37,2%), IgG CMV - 48 , 9%. In 88/94 patients with CLD detected Ab to several types of HV. IgM HSV-1 were detected in 3 patients with CLD, IgM HSV-2 - in 20, IgM EBV - in 1, IgM CMV - at 16. Frequency of other markers of HV at CLD had no significant differences. HV DNA was not detected. The majority of patients were recorded mixed infection with HSV-1 and EBV (n = 60, 63.8%), mainly latent and/or persistent flow. HV reactivation infection was established in 34 (36.2%) patients with CLD - in 28 (29.8%) cases as mono-infection, 6 (6.2%) - mixed infections. Latent and persistent infection within HV is not marked influence on the clinical, biochemical and morphological manifestations of CLD, and also on replication of hepatitis B and C. In all patients, the reactivation of HSV-2 infection helped to increase the necrosis-inflammatory activity. At alcoholic cirrhosis most marked reactivation of CMV infection (n = 11, 44%), which shows the progression of increase jaundice and haemorrhagic syndrome, and reactivation of HSV-1 infection at chronic alcoholic hepatitis - the presence of a vesicular rash and decreased albumin (p<0,05) .

Conclusions. CLD revealed a high frequency of infection HV (98.9%) with a predominance of mixed infections (94.6), which exceeds the prevalence of HV in the general population (80-90%). HV reactivation infection were more common in alcoholic liver disease. This points to the usefulness of specific antiviral therapy.

THE CHARACTERISTIC OF PERIPHERAL BLOOD IN NAÏVE PATIENTS WITH CHRONIC HEPATITIS C (CHC)

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Purpose: to specify prevalence and degree of expressiveness of a cytopenic syndrome in patients with chronic hepatitis C (CHC) at their primary visit.

The analysis was carried out for cases of CHC registered in clinic of infectious diseases, SamGMU.

177 patients of age from 19 to 74 years (37,1±10,2 years), men - 52% and women - 48%, were included. Genotype 1b, 3a, 2 were defined in 62,1%, 33,5% and 3,1% of cases respectively , and 2,3% for other options (including 1a, mixed and uncertain). Hematologic abnormalities (according to WHO recommendations) were revealed in 39% cases: light degree – 21%, average degree – 18%. Thus, pancytopenia was observed in 2% cases, two-cell types cytopenia - in 17% cases (RBC + platelets - 3%, RBC + WBC - 3%, platelets + WBC — 11% of cases). Other patients demonstrated cytopenia of one cell type (anemia - 2%, thrombocytopenia - 8%, leukopenia - 10%). Thus, leukopenia and thrombocytopenia were most common - 26 and 22% respectively. The WBC formula was characterized by relative lymphocytosis, monocytosis, decrease in segmented nuclei neutrophils. All patients with hematologic abnormalities have high viral load.

Conclusion: high percent of patients with cytopenia in patients with CHC dictates need of search of adequate adjuvant therapy during standard antiviral therapy.

PROGRESSION OF LIVER CIRRHOSIS IN PATIENTS WITH POLYMORPHIC VARIANT 1846G AND 1846A OF CYTOCHROME P450 2D6 GENE

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Fibrogenesis is a response to many liver diseases of different etiologies. Hepatocyte plays an important role in this process. Detoxification is important function of the liver, which is realized by a xenobiotic metabolism enzymes with the leading role of cytochrome P450. The role of this system in fibrogenesis has been insufficiently studied, with the exception of certain hepatotoxins, including alcohol, carbon tetrachloride, and some medications. Our earlier data on the acceleration of fibrogenesis upon toxic exposures pointed to the need for such research. In this study we investigated the relationship of polymorphic variants of locus 1846 G> A cytochrome P450 2D6 gene (CYP2D6) to the development of liver cirrhosis in 90 patients with chronic viral hepatitis. That association was not observed in patients with viral hepatitis C, B or B+C. However, in the group of patients with cirrhosis of viral etiology combined with additional toxic exposure (alcohol, occupational hazards) a trend toward faster development of cirrhosis was observed in heterozygous genotype CYP2D6*1846G/A carriers compared to homozygous 1846G/G genotype (odds ratio 2,0, 95% CI 0,2 – 2,1).

PREVALENCE OF PARENTERAL VIRUS HEPATITIS IN HIV-INFECTED IN THE SAMARA AREA AND PROBLEMS PREVENTION

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Background: The common routes of transmission of parenteral virus hepatitis and HIV-infection promoted high prevalence of these diseases in Russia due to the lack of information of protection and preventive maintenance methods. Coinfection of hepatitis and a HIV has got the importance of a demographic, political and universal problem.

Objective: to assess the prevalence of virus hepatitis B and C among HIV-infected patients in the Samara region.

Design: Retrospective observational study. Patients were recruited from a HIV clinic «Samara regional AIDS and infectious disease medical prevention centre», observation cards: form 25/u. Standard hepatitis B and C serology (ELISA) was performed.

Results: 840 participants were screened: 402 men (47.9 %) and 438 women (52.1 %) at the age 20–76 years. The mean age was 33.9±7.12 years (M±SD). Diagnosis of chronic virus hepatitis C had 197 (23.5%) patients (129 men and 68 women), diagnosis of chronic virus hepatitis B had 4 patients, chronic hepatitis C+B had 76 (9%), including 59 men and 17 women. Anti-HCV has been found at 264 men and 140 women: among men 65.8 % (95% CI: 61.0-70.5%, Klopfer-Pirson method) and among women 32% (95% CI: 27.7-36.6%). Antibodies to HBcorAg have been assessed in 452 patients, of whom 235 persons were positive: 157 men (61.7%, 95% CI: 54.8–68.2%) and 78 women (47.9%, 95% CI: 41.4–54.5%). HBsAg was found at 15 persons.

Conclusions: High prevalence of HBV and HCV among HIV-positive patients was found out. This demands the optimization of measures of preventive maintenance. Rules of safe behavior and infection prevention by parenteral virus hepatitis are extremely important because hepatitis virus infection causes a significant reduction in quality of life. Decision making process of financing of prevention programs should be based on the deep analysis of the fact that the treatment of hepatitis/HIV coinfectd patients is highly expensive.

A COMPARATIVE ANALYSIS OF DIAGNOSTICS ACCURACY OF FIBROELASTOMETRY AND LIVER BIOPSY OF PATIENTS WITH CHRONIC HEPATITIS C VIRUS

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Target of the present research. To evaluate the information content of liver elastometry, compared to a morphological liver study of the patients with chronic hepatitis C virus.

Materials and methods of the research. The study was conducted during 2 years (2010-2012) with 152 patients with hepatitis C (85 men and 67 women) of KIDCH №8 and KCH№3. The average age scope was 18-60 years old, the disease duration period from 1 till 15 years. All the patients were gone through fibroelastometry with the use of a “Fibroscan” device (EchoSens, France) and through liver biopsy performed with punches (16-18-gauge needles), under ultrasound control. Fibroelastometry was conducted with a measuring elasticity index in kPa. The tolerated interquartile rate (IQR) was not more than ¼ of elasticity index. Fibrosis degrees were measured according to the “Metavir” Score System.

Results. The results of fibroelastometry showed that 44 (28,9%) patients had no fibrosis, 79 (51,9%) patients with chronic hepatitis C were diagnosed with early stages of fibrosis (F1-F2). Advanced stages of fibrosis (F3-F4) were detected in 31 (20,3%) patient, 12 (7,8%) of whom were diagnosed with cirrhosis, confirmed by clinical and laboratory data. The equivalence of the values of fibroelastometry and liver biopsy on a F0 stage was noticed in 23 (52,2%) patients, on a F1 stage - 10 (23,8%) patients, F2 - 6 (17,1%) patients, F3 - 16 (84,2%) patients, F4 - 11 (91,6%) patients. The indicator of diagnostic accuracy of the results equivalence of biopsy and fibroelastometry for F0 equaled to 86,9%, for F1 - 40,0%, for F2 - 66,0%, for F3 - 87,5%, for F4 - 90,0%.

Conclusions. A comparative analysis of the results of liver fibroelastometry and morphological study showed a rather high degree of diagnostics accuracy. The highest degree of fibroelastometry performance was obtained in the diagnosis of the 4th stage of fibrosis. The accuracy of this method, equaled to 90,0%, allows to use it as an alternative to a percutaneous needle liver biopsy for the advanced stages of fibrosis.

THE MARKERS OF HBV- AND HCV-INFECTION IN PATIENTS AND MEDICAL STAFF OF HEMODIALYSIS DEPARTMENTS

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Background: the special place in the route structure of HBV and HCV infections is occupied with patients and staff of hemodialysis units.

Aim: to carry out the epidemiological analysis of testing results for the presence of HBV and HCV markers in patients and staff of hemodialysis departments and to define the prevalence of “occult” and HBsAg-mutant forms.

Patients and methods: 145 patients and 63 medical staff who were controlled in the Moscow Botkin Clinical Hospital were investigated for the presence of HBV and HCV markers in serum samples using a commercial enzyme immunoassay (“Vector-Best”, Russia, «Abbott Diagnostics», USA). S-gene nucleotide sequences were tested with the help of «ABI-3100 PRISM Genetic Analyzer» («Applied Biosystems», USA).

Results: Among the patients and medical staff blood samples tested, 2(1,4%) and 1(1,6%) were positive for HBsAg, respectively. At each of them DNA HBV was defined. “Occult” hepatitis B forms were revealed in 2 (1,4 %) patients and anti-HCV were found out in 13 (9,0 %) of patients, but not in staff. The medical staff examination has shown the presence of total antibodies to HBcAg in 13 (20,6 %) persons and their increase to 31,4 % of cases at the experience of work more than 10 years. From three HBsAg-carriers it was revealed three HBV isolates with S-gene replacements during sequence analysis. All isolates belonged to genotype D, subtype ayw3 and viral load was in a range of 10^{^2}-10^{^3} ME/ml. All isolates had serologically significant substitution in relation to HBsAg 118 aminoacid residue.

Conclusions: the prevalence of “occult” hepatitis B and occurrence of HBsAg-mutant forms has appeared enough high, that testifies to necessity of in-depth molecular-biological researches implementation in this population.

L-SELECTIN AND CHRONIC LIVER PATHOLOGY

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The aim of study is to assess plasma levels of L-selectin in chronic liver diseases.

Material and methods. 198 patients (125 men, 73 women) at age from 23 years to 59 years (27 men, 17 women) were examined: 28 patients with chronic viral hepatitis (CVH) B, 93 patients with CVH C, 62 patients with viral liver cirrhosis (LC), and 15 patients with alcoholic LC. 7 patients with alcoholic liver cirrhosis additionally had signs of acute alcoholic hepatitis. Patients with liver cirrhosis were divided into classes A (39 patients), B (28 patients) and C (10 patients) depending on Child-Pugh criteria. The control group included 54 healthy volunteers at age from 22 years to 55 years. Blood concentration of L-selectin was carried out by means of ELISA.

Results. L-selectin plasma levels were increased in chronic hepatitis and liver cirrhosis without differences between groups. Type, genetic and phenotypic features of viruses, and viral load of HBV and HCV did not influence on content of mediator in blood. Etiology of liver cirrhosis was not associated with elevated plasma values of L-selectin. Combination of alcoholic liver cirrhosis with acute alcoholic hepatitis was characterized by higher content of adhesion molecule in blood. Increase of E-selectin in blood with intensifying of expressiveness of cytolytic syndrome in chronic liver diseases was revealed. Prognostic indicators of liver cirrhosis (classes B and C according Child-Pugh, decompensated portal hypertension, esophageal varices of 2-3 degree, and hypersplenism) did not influence on concentration of L-selectin in blood.

Conclusion. Elevation of L-selectin levels in blood is observed in chronic liver pathology especially in cases of severe biochemical activity of disease. Those results testify to the pathogenetic importance of mediator in development of inflammatory process in liver.

The work was performed as part of the grant of President of Russian Federation № MD-934.2012.7.

RISK FOR DECOMPENSATION, HCC AND LIVER-RELATED DEATH AND THEIR PREDICTORS IN PATIENTS WITH CHRONIC HDV-INFECTION

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Aims: to assess the risk for liver decompensation, HCC and liver-related death and to identify their predictors in patients with chronic HDV-infection.

Methods: patients with serum markers of HDV-infection (anti-D and HDV RNA), treated in E.M. Tareyev clinic from 2002 to 2011, were included in the study. Prognostic factors were assessed using logistic regression analyses. Cumulative probability of survival, risk for decompensation and HCC were calculated by the Kaplan-Meier method.

Results: 102 patients have revealed markers of HDV-infection (mean age 39 years, male 58%). 42 patients (mean age 44.3 years, male 47.6%) with compensated liver cirrhosis developed decompensation during follow-up. First episode of decompensation occurred after mean time 45±33.1 months upon diagnosing liver cirrhosis. The most frequent first decompensation episode was ascites. According to the analysis, low serum albumin, high γ-globulins and high bilirubin levels were predictors of decompensation. Patients with hypoalbuminemia had 50% risk of decompensation at 5 years. 8 (7.8%) patients developed HCC (mean age 50.8 years, male 50%), older age, high serum ALP and AFP being its' significant predictors. 18 (17.8%) cases of liver-related death occurred during follow-up (mean age 44.1 years, male 72.2%), mostly of liver failure (50%) and of HCC (33.3%). High serum bilirubin and low prothrombin were significant predictors of liver-related mortality.

THE STRUCTURE OF CHRONIC HEPATITIS C AMONG SVERDLOVSK REGION HEALTH CARE WORKERS

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Aim: To evaluate features of chronic hepatitis C in Sverdlovsk Region health care workers group depending on virus genotype and the categories of medical profession.

Materials and Methods: We analyzed medical records 145 health care personnel followed up at Sverdlovsk Region Hepatological Center between 2005 and 2012 with chronic hepatitis C. The mean age of patients was 40.9±9.2 years (men - 31 (21.4%), women - 114 (78.6%).

Results: Of all patients (n=145) genotype 1b revealed in 85(58.6%), genotype 3a in 41 (28.3%) and genotype 2 in 19 (13.1%).

According to categories of medical profession the patients were divided in to nurses - 86 (59.3%), medical assistants – 18 (12.4%), doctors - 41 (28.3%), among whom 30 (20.7%) were surgeons and 11 (7.6%) - internists.

Of nurses and medical assistants HCV genotype 1b had 59 persons (40.7%), genotype 3a - 31 (21.4%), genotype 2 – 13 (9%). Among doctors genotype 1b revealed in 26 (17.3%), genotype 3a – 10 (6.9%) and genotype 2 – in 5 (3.5%).

Conclusions: Among Sverdlovsk Region health care workers with HCV hepatitis 59.3% were nurses, probably due to the higher risk of infection compare to other categories of medical profession. More, than 50% of health care workers were infected with 1b genotype.

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HEPATITIS E IN RENAL TRANSPLANT RECIPIENTS

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Background: rather recently in France a few cases of chronic hepatitis related to hepatitis E virus (HEV) infection in solid organ transplant recipients with progression to cirrhosis were reported. There are no data regarding the frequency of anti-HEV in this group of patients in other countries.

Aim: to evaluate the prevalence of HEV-infection markers in renal transplant recipients (RTR) in Russia.

Patients and methods: 330 RTR who were controlled in the Moscow City Nephrological Centre were screened for anti-HEV IgG and IgM in serum samples by ELISA ("Vector-Best", Russia). HEV RNA was determined by real-time PCR («Mediagnost», Germany).

Results: HEV-infection markers have been detected in 30 patients (M:20, F:10), age 52 years (range: 38–72), time after transplantation of 8,7 years (range: 2–27 years). Seroprevalence was 9,1%. Serum samples were positive for anti-HEV IgG in 15 RTR, anti-HEV IgM – in 12 and anti-HEV IgG + IgM – in 3 patients. The samples were negative for HEV RNA in all cases. Among 30 RTR chronic HBV- or HCV-infection was detected in 15 patients. 7 RTR had elevated aminotransferase levels greater than 1.5 times the upper normal limit, which probably has been connected with HBV- or HCV-infection.

Conclusions: the frequency of HEV-infection markers detection in RTR in such nonendemic region as European part of Russia has appeared enough high. It is necessary to note that even in patients with anti-HEV IgM it was not possible to detect serum RNA HEV. Thus, these antibodies cannot be considered as reliable markers of activity of disease, at least, among renal transplant recipients.

CHANGING OF COMPOSITION OF INTESTINAL BACTERIA ANTIGENS IN HOSPITALIZED PATIENTS WITH ACUTE VIRAL HEPATITIS

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Endointoxication by intestinal flora lipopolysaccharides significantly contribute to the damage of the liver in acute viral hepatitis (AVH).

In adult patients with AVH of different etiologies (95 people) it was studied the presence in coprofiltrates (CP) of LPS/O-antigens (O-Ags) of intestinal bacteria (Shigella, Salmonella, Yersinia, Campylobacter, Helicobacter pylori and E.coli O157) in coagglutination.

At admission O-Ags of various intestinal bacteria were found only at 81% of patients, with about the same frequency in the group of 30 patients with cholestatic syndrome and in a group of 65 patients with AVH without cholestasis.

During jaundice period O-Ags of some agents continue to define in the feces, the O-Ags of others- disappear. Of greatest interest are the O-Ags, which appeared in the feces of patients within 2-3 weeks of their stay in the hospital, which could be due to exposure of pathogens or their O-antigen in an organism with food.

Appeared again O-Ags in the feces were found in 30% of AVH patients with cholestasis (in most cases it was the O-Ag of Shigella, Salmonella and Helicobacter pylori) and in 12.3% of AVH patients without cholestasis (mainly O-Ags Salmonella and Helicobacter).

The data indicate that in the context of viral infection and weakened immunity in hospitalized patients with AVH staying in a hospital O-antigens of enteric bacteria put additional pressure on detoxification of the body.

HISTOLOGICAL AND IMMUNOHISTOCHEMICAL MARKERS OF VIRAL INFECTION IN DIFFERENTIAL DIAGNOSTICS OF CHRONIC HEPATITIS

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A feature of modern course of chronic hepatitis B and C (CH-B and C) is the prevalence of forms with minimal activity and often association with negative serological markers of HBV- and HCV-infection by the results of routine screening tests. Purpose of study is to demonstrate the possibilities of pathomorphological differential diagnostics of CH-B and C in such cases.

Liver biopsies were studied in 17 patients with CH with minimal activity and the negative results of ELISA tests for HBsAg and HCV-Ab, as well as by the lack of HBV-DNA and HCV-RNA in PCR. The direct and indirect markers of viral etiology of disease were studied on histological sections, its activity and stage were evaluated. Immunohistochemistry (IHC) study was performed by streptavidin-biotin method using a commercial system LSAB2 (DAKO, USA). Mouse antibodies to HBsAg and NS3-HCV (Novocastra Lab., Great Britain) and rabbit polyclonal antibodies to HbCag (DAKO, Great Britain) were applied.

In 6 studies there were revealed direct histological markers of HBV-infection: nuclear inclusions, diffusing screen and orcein-positive hepatocytes. In the course of IHC study expression of HbcAg was found in all of these observations. In 1 case there were combined histological and IHC (expression of HbCag and NS3-HCV) markers of HBV- and HCV-infection. In 10 observations the histological markers of viral infection were absent, but IHC study found expression of HbCag (4 cases) and combined expression of HbCag and NS3-HCV (3). Histological and IHC markers of HBV- and HCV-infection were detected in 3 cases. According to IHC study the expression of HBsAg was absent in all 17 studied cases.

Thus, taking into account of histological signs of viral etiology of disease and use of IHC markers of hepatotropic viruses can significantly improve the detection of chronic hepatitis B and C in the differential diagnostics of so-called unverified chronic hepatitis.

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**DRUG-INDUCED
LIVER INJURY**



CLINICAL FOLLOW-UP: DRUG-INDUCED HEPATOTOXICITY AT THE PULMONARY TUBERCULOSIS PATIENTS ON BACKGROUND OF COMBINE HEPATHOTROPIC THERAPY

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Introduction. In spite of the substantial progress made in most countries with a high burden of TB, substantial challenges remain in the region. The reported incidence of antituberculosis drug-induced hepatotoxicity (DIH), the most serious and potentially fatal adverse reaction, varies between 2 % and 28 % and may have negative consequences for treatment outcome. But there is no agreement on the clinical approach for cases in whom hepatotoxicity has developed.

Aim. To evaluate the ability of combination of amino-acide containing hepatoprotector glutargin & magnitolazotherapy (MLT) to prevent antituberculosis treatment induced hepatotoxicity.

Materials and methods. Patients with active TB diagnosis were randomized to a drug control group (43 patients) and a trial group (38 patients) on drugs combine therapy by glutargin & MLT. Isoniazid, rifampicin, pyrazinamide and ethambutol for first 2 month followed by continuation phase therapy during 4 month.

Results. Our findings showed that during 6 months in the trial group incidence of DIH signs was less ($p < 0,05$), than in the control. At this case, toxic reactions was in 2,4 times less ($p < 0,05$), and toxic-allergic one – in 3,5 times less ($p < 0,05$), than in the control. Among them clinical and clinical-laboratory signs of liver injury are revealed in 2,5 times less ($p < 0,05$) often, than in control group. In both group they were, mainly, during the first 2 months of treatment. After usage of glutargin with MLT was not revealed cases of a medicamentous hepatitis, whereas in the control group it is registered in 2 (4,6 %) case on 3 and 4 week from the starting of treatment. Pathological changes of laboratory sings of cytolytic, mesenchymal inflammations and disorder of pigmentary exchange have appeared more expressed, than at patients of the trial group.

Conclusion: The combination of hepatotropic therapy glutargin & magnitolasertherapy prevented hepatotoxicity of antituberculosis drug, decrease of clinical signs severity, as well as to preserve the pulmonary tuberculosis patient compliance.

THREE MONTH COURSE OF ATORVASTATIN HAD NO SIDE EFFECTS ON LIVER FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Objectives: Evaluation of the effects of atorvastatin on liver function and lipid profile in patients with rheumatoid arthritis (RA).

Materials and Methods: We examined 24 patients with RA, with a mean age of 56,29 ± 6,96 years, and a mean disease duration of 9,76 ± 6,48 years. The diagnosis of RA was verified accordingly to ACR/EULAR diagnostic criteria of 2010. 79,17% of patients were seropositive. Moderate disease activity of RA was determined in 50% of cases, 50% had very active disease. Systemic manifestations were present in 45,83% of patients. 1-2 radiographic grades were found in 58,33% of patients, 3-4 - in 41,67%. The control group consisted of 22 healthy women. RA patients were randomized to the two treatment groups: I - atorvastatin (Atomax) 20 mg per day in combination with methotrexate 10 mg per week, II - methotrexate 10 mg per week. In the course of the initial study and final examination in 12 weeks physical and instrumental examination of patients, the evaluation of total bilirubin (TB), ALT, AST, cholesterol (Ch), triglycerides (TG), low density lipoproteins (LDL) and high density lipoproteins (HDL) in blood were conducted.

Results: All patients with RA had no significant changes in the studied parameters of the liver function and lipid profiles compared to the control group ($p > 0,05$). As a result of the treatment, the patients with RA in group I, along with a positive clinical effect, had no significant increase of TB, AST, ALT in blood ($p > 0,05$), but a downward trend of Ch and LDL ($p > 0,05$) and a tendency to increase HDL was detected ($p > 0,05$), with a significant decrease in blood TG ($p < 0,05$). In patients with RA in group II, no changes of liver functional blood tests were detected ($p > 0,05$), but a tendency to increase blood Ch and LDL ($p > 0,05$) was found, without changing of the blood TG and HDL ($p > 0,05$).

Conclusion: Atorvastatin (Atomax) is an effective and safe medicine, probably due to its pleiotropic and lipid-lowering properties. Atorvastatin can be recommended for use in clinical practice as an additional drug to the standard treatment of RA.

DRUG-INDUCED HEPATITIS AND PREGNANCY

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The influence of medications on the gestation course and the pregnancy outcome remains one of the most unknown spheres of the clinical pharmacology. Nevertheless, the data of the surveys held shows that 80-90% of the pregnant women take various drugs which could be potential threat of the drug-induced liver injury and may jeopardize the woman's life, the gestation course and the fetus condition.

Therefore the aim of the current research is to study the drug induced hepatitis in pregnant women having been observed in the Mordovia Republic Perinatal Center in 2011-2012. During this period 20 women were detected to have the clinical laboratory picture of drug-induced hepatitis. The number of the medications prescribed was from 3 to 11 including Vitrum Prenatal (16 women), Elevit Pronatal (3 women), Curantil (8 women), Sorbifer Durules (5), Magne B6 (4 women), Vitamin-E (3 women), Fenules (2 women), Iodomarin (3 women), Duphaston (up to 20 weeks of pregnancy — 10 women), Utrogestan (6 women). Moreover, 5 patients were taking Phlebodia during the last trimester. In addition, almost all women were taking anti-spatics (No-Spa, Drotaverine) and had phytotherapy (Brusniver).

The results show the direct correlation between the number of the medications taken and the drug-induced hepatitis activity. For instance, the highest level of the liver transaminase (10 times exceeding the normal level) was detected in the women who was taking 9-11 different drugs. The liver transaminase level was particularly high in those women whose treatment included Duphaston and Utrogestan (especially when combined with Vitrum Prenatal).

We may conclude that the pregnancy means a very careful approach to the treatment prescribed whereas the health of a woman and a fetus mustn't be underestimated compared with the likely outcome of the treatment chosen.

EFFECTIVENESS OF A TREATMENT OF DRUG-INDUCED HEPATITIS WITH A USAGE OF HEPATOPROTECTORS BASED ON APICULTURE'S PRODUCTS IN PATIENTS WITH PULMONARY TUBERCULOSIS

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Apitherapy has been used in hepatology since ancient times.

Objective: to study the effectiveness of modern therapy with a usage of drugs based on apiculture's products in a treatment of drug-induced hepatitis, which developed as a result of polychemotherapy of the pulmonary tuberculosis.

Materials and methods. The study included 60 patients, 30 of them (the main group) had been receiving Hepazyl compositum (JVI Innovation, Austria) with a royal jelly as drug's main component for a month. Then, those patients had been receiving Hepazyl of the same production with a pollen as drug's main component for five months. It also contains silymarin, quercetin, cernitine, artichoke extract. Thirty patients of the comparison group received the preparation of silymarin. Biochemical blood analysis, sonography of the liver and gallbladder were performed before and after treatment. Five patients of the main group underwent puncture liver biopsy before and after treatment.

Results. Upon the treatment with a usage of Hepazyl compositum and Hepazyl we managed to achieve a significant reduction in the evidence of hepatocytes' cytolytic, cholestasis, improvement of synthetic and detoxificative functions of the liver, decrease in the atherogenicity of lipid blood profile. According to the results of ultrasonic histography of the liver, treatment with a usage of those drugs promoted the reduction in the evidence of liver's steatosis, decrease in the frequency of detection of biliary sludge in the gallbladder. According to the results of puncture liver biopsy it was proved that Hepazyl compositum and Hepazyl stimulated reduction in the evidence of such histological changes in the liver as: degeneration of hepatocytes, intracellular cholestasis, there were growing regenerative processes.

Conclusion: drugs Hepazyl compositum and Hepazyl based on apiculture's products are rather effective in a complex treatment of drug-induced hepatitis in patients with pulmonary tuberculosis.

PECULIARITIES OF DRUG-INDUCED LIVER INJURY IN CASE OF SPECIFIC THERAPY OF PULMONARY TUBERCULOSIS

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Purpose: to develop modern method of monitoring of liver in patients with pulmonary tuberculosis passing specific therapy.

Materials and methods: First stage: a retrospective study of 250 case records of 250 patients with pulmonary tuberculosis. The second stage: a comparative prospective study in parallel groups of 50 patients with pulmonary tuberculosis. To assess the functional state of the liver the following was studied monthly: complete blood count and common urine analysis and biochemical tests.

Results: 250 case records were analyzed: 165 men (66%) and 85 women (34%) aged 15 to 73 years, new patients prevailed - 231 (92.4%), who were treated with the standard chemotherapy regimen. It was found that for control of therapy the most significant is study of the dynamics of AST and ALT. This prospective study included 35 men and 15 women, average age - 39.7 years. The comparison group consisted of 30 healthy subjects (18 men and 12 women). Initial excess of AST and alkaline phosphatase (ALP) by 1.2 times was found. At the end of therapy only ALP firmly decreased. Coagulation analysis showed excess of prothrombin index and international normalized ratio by 1.1 times. After treatment activated partial thromboplastin time was firmly changed by 17.6%. CD4 (39, 33 and 33%) and CD16% (38, 36 and 44%) had less variability in the groups of «healthy», «pre-treatment», «post-treatment». Level of CD16% (+64%)T was increased the most significantly with age. As a result of treatment of both men and women level of CD4 D16% decreased and D16% increased. However, these changes in men were less evident.

Conclusions: for control of the safety of pulmonary tuberculosis chemotherapy it is reasonably to study AST and ALT. Preventive measures in relation to hepatotoxic reactions should be taken from the moment of admission. In order to assess efficiency of therapy it is necessary to study CD4 and CD16.

EFFICIENCY OF SUCCINATE-CONTAINING DRUGS AND ADEMITIONIN IN PATIENTS WITH LIVER INJURY AND LUNGS TUBERCULOSIS

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Purpose. Comparative studying of efficiency of hepatoprotective features and assessment of relative risk of a failure (RR) in use of reambirin, remaxol and exogenous ademetonine in patients with drug induced liver injury (DILI) during antituberculous chemotherapy.

Materials and methods. One hundred eighty patients with tuberculosis of respiratory system (diagnosed at the 1st time) are divided into 4 groups (n=45 in each group) and are surveyed: the main group 1 (MG1) - patients receiving reambirin, the main group 2 (MG2) – patients received remaxol, the main group 3 (MG3) – patients received ademetonine and the group of comparison (GC) - patients received 5% glucose solution. Studied drugs were appointed IV 1 time per day for 10 days. The assessment of the laboratory index (LI) of severity (by T.N. Kalachnyuk) and RR with NNT calculation (number of patients who need to be treated) is made.

Results. LI significantly (by 1,7-1,8 times) raised in DILI caused antituberculous drugs. During use of studied drugs there were significant decrease (by 1,3-1,5 times) of LI in comparison with glucose solution, thus most expressed decrease is noted in use of remaxol. At an assessment of RR and the relation of chances the high probability of approach of good outcome is established (LI decrease) during use of each of three studied drugs in comparison with glucose solution, the greatest relative risk (RR) and the relation of chances (OR) are revealed during use of remaxol (1,87 and 2,31 respectively), while NNT coefficient was in 1,6 and 4,4 times lower in comparison with reamberin and ademetonine respectively.

Conclusion. Studied drugs are effective in treating of DILI in patients with tuberculosis. The greatest positive (meanings of laboratory index of severity and indicators of RR and NNT) is reached with remaxol.

POLYMORPHIC VARIANTS OF GENES CYP2E1 AND NAT2 AND SIDE-EFFECTS OF DRUG THERAPY TUBERCULOSIS

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Drug therapy of pulmonary tuberculosis, characterized by long-term use of combinations of drugs in high doses, often accompanied by hepatotoxic reactions. Reaction with moderate increased levels of alanine and aspartate aminotransferase in serum occur in 10-20% of patients with tuberculosis, in 0, 5 - 4% of patients - with a five-fold increase in their level. Their death rate is up to 5% due to functional failure of the liver. Great importance in the development of hepatotoxic reactions has drug metabolism. This is because the metabolism of toxic metabolites may occur. For example, isoniazid has been acetylated by N- acetyltransferase 2 (NAT2) to form a non-toxic acetylisoniazid and hydrolyzed by amidase to form toxic hydrazine. Hydrazine can be acetylated, and then oxidized by the cytochrome P450 (CYP2E1) to the final toxic metabolites that damage proteins, DNA, lipid membranes. We investigated changes in the levels of ALT in patients depending on the carrier alleles causing low rate of acetylation (genotypes NAT2 * 5, * 6, * 7), and the high activity of cytochrome P450 2E1 (genotype CYP2E1 * 7632T / A). The results showed that without genotypes (for the whole group, n = 54 persons) increased ALT above the normal range in the first month is observed in 29% of patients. However, an increase was observed in 47% with genotype NAT2 * 5, * 6, * 7, 50% of those with a high activity of cytochrome R4502E1 (genotype CYP2E1 * 7632T / A) and 75% of those with a combination of these symptoms. Consistent with the metabolic mechanisms, rate of ALT activity increase were 1.53 fold in the whole group, 2.0 and 3.0 in patients with genotype NAT2 *5, *6, *7 and CYP2E1*7632T/A and 5.18 in in patients with combinations of these genotypes.

**METABOLIC
ABNORMALITIES**



THE DEGREE OF LIVER FUNCTION IMPAIRMENT IN CHILDREN WITH WILSON'S DISEASE.

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Purposes: definition of the degree of liver function impairment and its dynamics during therapy in children with Wilson's disease (WD).

Materials and methods. The retrospective analysis of medical histories documents of 101 children with WD (middle age of 12,3±2,9 years) is carried out (79 children with hepatic form, 22 with the mixed form of WD). The degree of liver function (LF) impairment determined by the scale developed and patented in The Federal Scientific Center of Children Health of the Russian Academy of Medical Science.

Results. The degree of LF impairment is decreased by 40,6±1,2%: in the hepatic and mixed forms 41,2±1,4 % vers. 38,6±2,6% (p=0,386). In children with liver cirrhosis (LC) FP is decreased by 48,0±1,7%, without LC – by 35,0±1,4% (p <0,001). In patients with considerable decrease in ceruloplasmin levels LF is decreased by 45,0±1,2%, with normal or insignificant decrease – by 31,1±2,5% (p <0,001). In 6 and 12 months of standard therapy the degree of LF impairment was 39,1±1,2% (p=0,391) and 34,4±1,5% (p<0,001). Thus, in children with hepatic form of WD the degree of LF impairment decreased to 37,4±1,2% (p<0,05) and to 33,4±1,6% (p<0,001). In children with the mixed form of WD decrease in the degree of LF impairment wasn't noted and it made 48,1±2,3% (p<0,01) and 38,8±3,5% (p=0,957), respectively. In children with LC the degree of LF impairment decreased to 42,4±1,7% (p <0,05) and to 36,8±2,3% (p<0,001), respectively. Patients without LC the degree of LF impairment had amounts of 36,4±1,6% (p=0,498) and 31,8±1,8% (p=0,166), respectively Children with considerable decrease in level of ceruloplasmin have 42,1±1,3% and 35,8±1,7% (p<0,001). Patients with normal or insignificant decrease in level of ceruloplasmin have 30,3±2,9% (p=0,856) and 27,4±3,0% (p=0,357).

Conclusion. Function of a liver is reduced by 40,6±1,2% in children with Wilson's disease that corresponds to moderate impairment. The degree of liver function impairment is more significant in patients with severe decrease of level of ceruloplasmin and in patients with liver cirrhosis as the outcome of Wilson's disease. Carrying out standard therapy considerably improves liver function in most cases.

INTERLEUKIN-28B GENE POLYMORPHISM IN PATIENTS WITH CHRONIC HCV-INFECTION

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The search for new reliable predictors of achieving sustained virologic response (SVR) during antiviral therapy (AVT) for chronic HCV-infection is one of the most actual problems of modern hepatology.

Objective: to study an IL-28B gene polymorphism in patients with chronic HCV-infection and to determine its importance in achieving SVR.

Materials and methods. 68 patients with chronic hepatitis C and liver cirrhosis HCV-etiology were examined: 32 men and 36 women. HCV genotype 1 was detected in 40 patients, non-genotype 1 – 28 patients. Mean values of viral load were 4.9±1.2 log10. 14 patients infected with HCV genotype 1b had AVT failure in anamnesis, other 55 patients had never received antiviral drugs. IL-28B gene polymorphisms were studied by identifying oligonucleotide polymorphisms rs12979860 (C>T) and rs8099917 (T>G) by polymerase chain reaction using reagent kits Ltd. “DNA Technology” (Moscow).

Results. Genotype of rs12979860 C/C met in 29.4% of cases, C/T – 51.5%, T/T – 19.1%. Polymorphism of rs8099917 divided as follows: T/T – 56%, T/G – 38%, G/G – 6%. We found no differences in the prevalence of IL-28B gene polymorphisms depending on gender, genotype of HCV, level of viral load, as well as the stage of the pathological process – the degree of fibrosis. In the group of patients with a previous therapeutic failure genotype of rs12979860 T/T met more often than in naive patients (35.7%) and genotype C/C was determined only in one case (7.1%). However, these differences were not statistically significant (p = 0.091 for genotype C/C), that was probably due to insufficiently large values of studied samples.

Conclusion. The data on IL-28B gene polymorphism could be as the predictor of SVR during antiviral therapy, however, the reliability of studied parameters requires further research.

SOME PARAMETERS OF ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE

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The aim of study is to assess the plasma content of endothelin-1 (ET-1) and nitric oxide (NO) as parameters of endothelial dysfunction in patients with nonalcoholic fatty liver disease (NAFLD).

Materials and methods. 142 patients with NAFLD were examined (77 men and 65 women). The mean age of patients was 49±0.9 years, BMI was 32.69±0.47, and values of HOMA-index were 4.13±0.25. Nonalcoholic steatohepatitis (NASH) was detected in 46 patients, hepatic steatosis was diagnosed in 96 cases. The control group included 20 healthy volunteers. Activity of ALAT was 71.29±4.72 U/l in patients with NASH. Blood concentration of ET-1 was carried out by means of ELISA («Biomedica-Gruppe»), NO levels were carried out by means of colometric method («R&D Systems»).

Results. The plasma levels of ET-1 were higher in patients with NAFLD (0.66±0.05 fmol/ml) than in healthy volunteers (0.48±0.05, p=0.037). The blood concentration of ET-1 was normal in patients with steatosis and was elevated in patients with NASH (0.78±0.12 fmol/ml). The ET-1 values in NASH were more than in liver steatosis (p=0.031). The NO levels in blood of patients with NAFLD don't exceed the normal values. The mean NO levels in patients with NASH (47.93±7.31 μmol/l) were higher than in healthy volunteers and patients with steatosis (p=0.038 and p=0.003 accordingly). In 20 patients with NASH reduction of plasma ET-1 levels and activity of aminotransferases was observed (p=0.018) after month of complex treatment including metformin, whereas the dynamics of NO in blood was absent (p=0.08).

Conclusion. Obtained data demonstrate the presence of endothelial dysfunction in patients with nonalcoholic steatohepatitis. The increased levels of ET-1 and NO can be as additional criteria of inflammation, developing in liver during evolution of steatosis into steatohepatitis.

THE LIPID COMPOSITION OF THE MEMBRANE OF RATS HEPATOCYTES WITH DRUG INDUCED HEPATITIS, AND CORRECTION

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The development of drugs induced hepatitis is accompanied by the accumulation of oxidized toxic byproducts in the liver parenchyma, which leads to destructive changes in the membranes of hepatocytes. This explains the need for therapy that stimulates regenerative processes in damaged biomembranes. Means of such action can be accomplished with phospholipid containing drugs. The aim of our work was to research changes in lipid composition and features of membrane hepatocytes in rats by experimental drug induced hepatitis, and a comparison of the effectiveness of corrective drugs based on phospholipids (PL) of soybean (Essentiale forte) and milk (food supplement, dietary supplement FLP-MD).

The results of the research related to the microsomal membrane (MCM) of hepatocytes in rats that remained untreated, resulted in a tendency to reduce the content of total lipids (REG.), mainly due to the fraction of the PL observed against the background of a significant increase in triglycerides (TG), free fatty acids (FFA) and bound cholesterol ester (EHS). In the preparations of the submitochondrial membrane (SMM) of hepatocytes with the absence of changes in the content of OBL was significantly higher in levels of free fatty acids, triglycerides, and EHS. Rats that were treated with the drug essentiale forte in MKM and established a decrease in cholesterol and triglycerides. In reference to SMM hepatocytes animals in this group exhibited a significant reduction in FFA, TG, EHS, which may indicate a lack of endogenous synthesis or heavy use in the regenerative processes. The animals that used the supplements FLP-MD, the MC hepatocytes against the tendency of increased OBL determined an increase in PL and a decrease – in TG and EHS. In reference to SMM hepatocytes against a minor increase in the content of OBL marked increase in the level of PL and a decrease in - FFA, TG, and EHS, which may indicate the action of the membrane-active dietary supplements FLP-MD and intensive involvement of membrane lipid fractions in the reconstruction of their structure.

POLYMORPHIC VARIANTS OF GENES OF ANTIOXIDANT DEFENCE SYSTEM (GSTM1, GSTT1, GSTP1, GSTA2) ARE MARKERS OF HEPATOTOXICITY LUNG TUBERCULOSIS DRUG THERAPY

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Pulmonary tuberculosis - one of the most significant social diseases. In the course of medical treatment of pulmonary tuberculosis are frequent adverse reactions, especially hepatotoxicity (up 47%). In the metabolism of anti-TB drugs are formed reactive metabolites and their cause oxidative stress in the liver, a major role in protecting against liver toxicity may play a glutathione S-transferase (GST), the enzymes of antioxidant protection. In 75 patients receiving daily regimen of TB drugs were determined polymorphic variants 63G> C in exon 5 and 83A> C exon 7 gene GSTA2, 313A> G and 314C> T gene GSTP1, as gene deletion polymorphism of GSTM1 and GSTT1. Determination of markers of hepatotoxicity - serum alanine aminotransferase (ALT) and aspartamaminotransferase (AST) was performed at admission and one month after the start of treatment. Shown that the polymorphic locus 63G> C 5 gene GSTA2 have the most significant impact on the increase in serum ALT and AST during treatment. In patients with genotype 63GG gene GSTA2, ALT levels increased from 14.5 to 68 U / l (p = 0051), whereas in all the studied group, regardless of genotype, from 18 to 27.5 U / L for the first month treatment (p = 0.0051). Also significant are investigated and polymorphic loci gene GSTP1: patients with genotype 313AA ALT levels increased from 17.5 to 32.5 U / L (p = 0.0005) in patients with genotype 341CC from 16.5 to 28.5 U / L (p = 0.000004). Case-traditional role of polymorphisms of genes GSTM1 and GSTT1 was not unequivocal. In patients with a deletion of the gene GSTM1 ALT levels increased from 16 to 28 U / L (p = 0.0009), and then for the presence of GSTT1 gene was more significant (19 - 36 U / L (p = 0.0011)) than its absence (15 - 21 U / l (p = 0.093)).

DYSLIPIDEMIA CORRECTION WITH PATIENTS SUFFERING FROM METABOLIC HEPATIC LESIONS

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This article describes the changes in lipid spectrum and possible treatment of dyslipidemia with patients suffering from postcholecystectomic syndrome.

Research purpose. To develop the nature of metabolic disorders of the liver with patients suffering from postcholecystectomic syndrome and to detect the appliance efficiency of medical resort factors for rehabilitation of this contingent.

Data and methods. The patients were the officers of the FSB. They arrived to undergo spa treatment after cholecystectomy (30 people) and got clinical nutrition according to D-5, warm low mineralized water Essentuki-new (carbonate chloride-hydrocarbonate-sulfate-sodium-calcium water) 3, 5 ml/kg of body weight in 30 minutes before meals 3 times a day and foam licorice baths t 37° c, 15 minutes exposures every other day (8 procedures in a treatment course). Magnet therapy with application of pulses of damped three-phase alternating magnetic field on the unit “UMTI-ZB”-“Kolibri-export” on the upper half of the abdomen in the course of 10 procedures.

Examination: General clinical, biochemical (liver function tests, cholesterol and its fractions, GGT, ALP, MDA, catalase, glucose), ultrasound abdominal examination.

Results: Decrease of pain syndrome from 66.7% to 30%, of dyspeptic syndrome from 53.3% to 23.3%, normalization of the liver size with 63.6% of the patients. Reduction of high bilirubin level from 23,8+1,12 to 17,1+0,08 micromole/l (p < 0.05). ALT activity from 40,2+0,04 to 32,4+0,01 u/l (p < 0.05), AST from 39,9+0,02 to 29,2+0,10 u/l (p < 0.05), cholesterol loss from 7,8+0,22 to 6,0+0,42 mmol/l (p < 0.05), triglycerides from 3,0+0,06 to 2,0+0,08 mmol/l (p < 0.05), LDL 5,59+ 0,09 to 5,0+0,12 mmol/l (p> 0.05), VLDL from 1,53+0,10 to 0,9+0,08 mmol/l (p < 0.05), GGT reduction from 50,1+ 0,03 to 39,9+0,10 u/l (p < 0.05) and MDA from 6,9+ 0,09 to 6,0+0,04 mmol/l (p>0.05). HDL increase from 0,75+0,03 to 1,2+0,08 mmol/l (p < 0.05) Catalase increased from 0,22+0,05 to 0,35+0,02 mAb/l (p < 0.05). The treatment efficiency was 83.3%.

Conclusion: The effect of the medical complex with magnet therapy has shown the improvement of blood circulation in the liver, biliation stimulation, restoring of fat digestion, anti-inflammatory as well as central and peripheral analgesic action.

INTERRELATION OF ENTEROHEPATITIC CIRCULATION OF BILE ACIDS AND GUT ORGANISMS WITH PATIENTS SUFFERING FROM CHRONIC PANCREATITIS

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To keep intestine biocoenosis it is necessary to use exposure methods on sanogenetic processes taking into consideration a huge role of the general macroorganism condition especially liver as a component of metabolic syndrome.

Research purpose: Correlation characteristics of liver choleresis and intestine biocoenosis in treatment with the help of natural resort factors of the patients suffering from chronic pancreatitis.

Data and methods. 30 patients with chronic pancreatitis have been observed.

Examination: Complete-clinical, biochemical (hepatic tests, cholesterol with fractions, alkaline phosphatase, structure of colonic microflora, abdominal ultrasonography) analyses.

Treatment: Diet №5, intake of low-mineralized sulfate-hydrocarbonate calcium-sodium mineral water Slavyanovskiy 250 ml 3 times a day in 30 minutes before meals, mineral baths of the same water t - 37°C during 15 minutes every other day. Course of treatment is 10 procedures.

Results: Reduction of pain syndrome was observed with 63,3% to 40% patients, (p<0,05), of dyspeptic syndrome with 56,7% to 30% patients (p <0,05), meteorism with 83,3% to 40% patients (p<0,05), stool normalization with 2/3 patients. Bilirubin in serum decreased from 26,1+0,09 to 18,0+0,08 micromole/l (p<0,05), cholesterol from 8,0+0,09 to 6,8+0,11 millimole/l (p> 0,05). ALT from 40,1+0,05 to 31,2+0,07 u/l (p<0,05), thyreoglobulin from 2,9+ 0,07 to 1,9+0,11 micromole/l (p<0,05), low-density lipoproteins (LDL) from 5,6+0,12 to 4,8+0,09 mmol/l (p>0,05), but high- density lipoproteins (HDL) increased from 0,7+0,04 to 1,6+0,12 mmol/l (p<0,05). Bifidus and lactobacteria in feces decreased by 73,3%, colon bacillus by 87,7%. The decrease of colon bacilli with changed enzymatic properties and enterococcus with 2/3 patients was detected.

Conclusion: Positive effects summation of applied medical factors helps accelerate enterohepatic circulation of bile acids which restores digestion and stops disorder of large intestine microflora.

INFRARED SPECTROSCOPY OF TISSUES OF LIVER OF RATS POISONED WITH HEAVY METALS

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The use of new methods for the diagnosis of pathologies, identifying various reactions at the molecular level, there is an urgent task. Infrared (IR) spectroscopy is one of these.

The aim of our work was to study the infrared absorption spectra of the components of the liver tissue of rats with intoxicated heavy metals (Cu, Zn, Cd and Pb).

Materials and methods. Investigations were carried out on white male rats nonlinear, same age, weighing 180 - 200 animals were divided into five groups: the first one - intact (control), the second - the animals were administered per os solution of copper sulfate at a dose of 1/10 of the LD50 and the third - animals were administered per os solution of zinc sulfate at a dose of 1/20 of LD50, the fourth - the animals were administered per os solution of cadmium sulfate at a dose of 1/30 of LD50, the fifth - the animals were administered per os lead nitrate solution at 1/50 of the LD50. Absorption spectra were performed on a spectrophotometer «Nicolet 380» with Fourier transformation, the company «Thermo electron corporation» by reflectance attachment of ZnSe and step 4 cm-1.

Results. Found that the IR spectra of intact rat liver tissue differ from the IR spectra of the experimental group of animals and have specific absorption bands. In the studied range of frequencies detected absorption bands with peaks at wavelengths of 1616 cm -1, 1632 cm -1, 1650 cm -1, 1659 cm -1, 1667 cm -1, 1677 cm -1, 1688 cm -1, 1696 cm -1, 2823 cm -1, 2911 cm -1.

Conclusions. Studies of the IR spectra of intact liver tissue and toxicity in rats indicate the presence of various spectral characteristics, which are in the shift of the maxima of the absorption bands, the increase or decrease of the integrated intensity, which can be used for studies of heavy metals in tissues.

CANCER OF THE THICK GUT AND GEPATOBILIARNYE OF DYSFUNCTION

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Urgency. In mortality structure from oncological diseases in the majority of the developed countries, including in Russia, the colorectal cancer takes the second place. The main share (to 50 %) lethal outcomes at this disease is the share of persons of senile age. Existence at such sick accompanying diseases (komorbidnost) often in a dekompensirovanny form, and also an age astenizatsiya are the major prognostic factors of a failure of surgical intervention.

Purpose. To study frequencies, localisations, morphological characteristics, tactics of a cancer therapy of a thick gut, existence of accompanying pathology.

Research materials. In office of a koloproktologiya of RB No. of 2 TsEMP 95 patient's records (for 2011r) with the diagnosis a cancer of a thick gut are studied. The structural and statistical analysis of results of research is carried out.

Results. The following frequencies of occurrence of a cancer are revealed: in a % rectum-36,8, in a thick gut-62,1 of % (from them: in a blind gut-9,47 of %, a hepatic corner-7,36 of %, a selezenochny corner-8,42 of %, in a sigmoidny gut-36,8 of %), a % anus-1,1. Men have 41,1 %, at female-58,9 of %. On a national identity at the radical – at 41 (43,1 %), at not radical – at 54 (56,8 %). On age at men and women as a percentage respectively in intervals of 20-30 years – at 2 (2,1 %), 31-40 years – at 2 (2,1 %), 41-50 – at 16 (17 %), 51-60 – at 20 (21 %), 61 also are more senior – at 55 (57,8 %). At 53 (55,8 %) patients the structure of a tumour had character moderate differentiated adenokartsiny, at 15 (15,8 %) had patients mucous and small differentiated adenokartsiny, 9 (9,4 %) – tubulyarno-fleecy adenoma, 11 (11,6 %) – well differentiated adenokartsiny and 7 (7,4 %) – a perstnevidno-cellular cancer. Operative intervention is carried out at 78 (82,1 %) patients. From them: gemikolektomiya-13 (16,7), the operation Gartmana-15 (19,2 %), hardware anastomosys - 8 (9,8 %), sigmostomiya-11 (14,1 %), transversostomiya-5 (6,4 %), a rectum ekstirpatsiya - 13 (16,7 %). At 10 (12,8 %) patients polyps are removed with a method of an endoskopichesky polipektomiya. The lethality makes – 7,36 % (7 people). From accompanying diseases of ZhKB it is revealed at 20 (21 %) the person. From them the female-12 (60 %), the man - 8 (40 %), the radical - 15 (75 %), not radical - 5 (25 %). Able-bodied age-10 (50 %), young - 2 (10 %), senile - 8 (40 %). On ultrasonography it is revealed: mechanical jaundice – at 5 (5,26 %) patients, kalkulezny cholecystitis – at 20 (21 %), chronic pancreatitis – at 90 (94,7 %), diffuzny changes parenkhima a liver – at 85 (89,4 %), a gepatomegaliya – at 2 (2,1 %).

Conclusions. Thus, the cancer of a thick gut – 62,1 % prevails, from them the cancer of a sigmoidny gut – 36,8 % is most widespread, to a thicket women – 58,9 %, not radical – 56,8 % are ill, in age group 61 and is more senior – 57,8 %. At the majority of patients it is revealed moderate differentiated adenokartsiny (55,8 %). At 10 (12,8 %) patients polyps are removed with a method of an endoskopichesky polipektomiya, the rest – abdominalny operations. From accompanying pathology of ZhKB it is diagnosed for every fourth patient with a colorectal cancer, in a clinical picture dispepsicheskym anifestatsionprevail.

MOLECULAR AND CELLULAR BIOLOGY



THE INFLUENCE OF POLY(ADP-RIBOSE) POLYMERASE (PARP) INHIBITOR 4-HYDROXYQUINAZOLINE ON NECROSIS AND APOPTOSIS OF IMMUNOLOGICALLY COMPETENT CELLS (ICC) IN CONCAVALIN A INDUCED HEPATITIS IN MICE

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The mode of cell death may play a key pathogenetic role, especially in autoimmune diseases. Sufficient level of lymphocyte apoptosis is crucial to maintain immunological tolerance and to limit an inflammatory and immune reactions. On the other hand, necrosis is a source of intracellular autoantigens and might provoke autoimmunity. Cell membrane damage, a hallmark of necrosis, results also in the release of cytotoxic molecules which induce pro-inflammatory responses. It is likely that in situation of intense leukocyte infiltration, necrosis of ICC has been implicated in the initiation and the progression of autoimmune diseases. Prevention of necrotic cell death could exert protective effect. Recent findings have suggested that a DNA repair enzyme PARP-1 is involved in the induction of necrosis. It is activated by DNA damage and forms polymers of ADP-ribose from the substrate NAD⁺. Excessive activation of the enzyme causes a depletion of the intracellular NAD⁺ and ATP. This results in rupture of the plasma membrane and necrotic cell death. The role of PARP-1 in the pathogenesis of autoimmune liver disorders and PARP involvement in the induction of necrosis are still unclear. Concanavalin A (ConA)-induced hepatitis is widely used murine model for T-cell dependent autoimmune liver damage. Here, we studied the influence of PARP-1 inhibitor 4-hydroxyquinazoline (4-HQN) on necrosis and apoptosis of lymph node and spleen cells from mice treated with ConA. ConA administration was accompanied with the decrease in the viability of ICC. Both apoptotic and necrotic death of lymph node and spleen cells were increased. Pretreatment with 4-HQN exerts hepatoprotective and anti-inflammatory effects against ConA-hepatitis. 4-HQN significantly decreased the percentage of necrotic lymph node and spleen cells by 1.8 and 2.0 times, respectively (P<0.001), without a change in apoptosis. Thus our study suggests that PARP has been implicated in the pathogenesis of immune liver injury via induction of necrosis in cells including ICC. PARP inhibition was effective in preventing this pro-inflammatory and immunogenic form of cell death. Our results support potential therapeutic application of PARP inhibitors in the treatment of autoimmune liver disorders.

FREE RADICAL PROCESSES AND EXPRESSION OF REG1A GENE IN RAT HEPATOCYTES UPON LONG-TERM HYPOACIDITY

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Introduction. Long-term gastric hypochlorhydria and subsequent hypergastrinemia are the causes of pathological processes in the gastrointestinal tract, including the hepatobiliary system (Jensen R., 2006).

Aim. It was to determine the intensity of free radical processes and Reg1a gene expression in rat hepatocytes upon long-term hypoacidity.

Material and Methods. Experiments were carried out on white non-strain mail rats. Hypoacidic state was modeled through intraperitoneal injection of omeprazole during 28 days. In hepatocytes, determined the content of hydrogen peroxide using xylenol orange and diene conjugates in the heptane-isopropanol extract - spectrophotometric methods, Schiff bases - fluorimetric method, TBA-active compounds - by reaction with thiobarbituric acid. The level of Reg1a gene expression was determined by semi-quantitative analysis with RT-PCR.

Results. It was shown that in hepatocytes of rats with long-term reduction of gastric secretion of hydrochloride acid, the content of hydrogen peroxide increased 2-fold, while the content of lipid peroxidation products also increased: conjugated diene - 2.2 times, TBA-active compounds - in 1,7 times and Schiff bases - 1.6 times relative to the control. The appearance of Reg1a gene expression in hepatocytes upon long-term hypoacidic conditions was shown in comparison to control.

Conclusion. During long-term gastric hypochlorhydria in liver activated free-radical processes, indicating the development of oxidative stress. The possibility of hepatocytes' neoplasia is considered as a result of the appearance of Reg1a gene expression.

PLASMOCYTOID DENDRITIC CELLS THEIR ROLE IN CHC PATHOGENESIS IN ADULTS AND CHILDREN

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After description the plasmocytoid dendritic cells (PDC) in 1999 new page in the human immune response was opened.

Purpose: to establish PDC role in pathogenesis of CHC in children and adults.

Materials and methods: One hundred sixty one persons: 133 patients in the various phases of CHC (58 of children and 75 adults) are surveyed, 28 people (16 children and 12 adults) - healthy individuals. Determination of quantity of PDC in blood was carried out by a method of a flow cytometry with use of monoclonal antibodies to specific markers of PDC (CD303 and CD123). IFN determination (the producing function of PDC) was carried out by IFA ELISA method, with previous stimulation of ODN2216 and IL3.

Results: Production of IFN in PDC is significantly higher in patients with CHC, than in healthy individuals, and remains higher by all key parameters, defining a natural history of CHC, in adult patients, than in children. The number of PDC is higher in children, than in adults, however is significantly lower, than in healthy individuals. Natural inversely proportional correlation between degree of IFN production and viral load is revealed. IFN level in PDC is high both in adults, and in children with low viral load (461,1±262,2 pg/ml in adults, 153,5±38,07 pg/ml in children), and low IFN-generation corresponds to a high viral load (147,1±59,77 pg/ml and 75,76±20,72 pg/ml, p<0,05). The correlation between IFN production in PDC and cytolysis is shown. The increase in IFN production in adults correlates with aminotransferases levels increase (132,8±42,72 pg/ml with normal levels of ALT, AST, 314,9±137,7 pg/ml with ALT, AST <UNL, p<0,05), but has a feedback in children (146,7±36,73 pg/ml and 86,19±23,64 pg/ml respectively, p<0,05). It is shown that number of PDC in adult patients closely correlates with a stage of liver fibrosis: it sharply decreases from 8,4±0,9 cells/ml in F0-1 to 3,9±0,9 cells/ml in F4 (METAVIR) (p<0,05), and IFN production increases in proportion to a stage of fibrosis (from 68,32±33,21 pg/ml in F0-1 to 291,3±195,9 pg/ml at F4, p<0,05).

Conclusion. The obtained data for the first time show close correlation between quantities of PDC with the key parameters defining a history of CHC. That testifies to an important role of these new immune cells in CHC pathogenesis in adults and children.

INTERACTION OF TL+ WITH SH-GROUPS OF RAT LIVER MITOCHONDRIAL PROTEINS

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Active centres of many mitochondrial enzymes contain SH-groups. In addition the latters also play an important role in keeping of a protein spatial structure. Oxidation of SH-groups of the inner mitochondrial membrane (IMM) facilitates opening the mitochondrial permeability transition pore (MPTP). It was previously shown that Tl⁺-induced opening of MPTP in Ca²⁺-loaded rat liver mitochondria (Korotkov, Saris, 2011). Ions of bivalent heavy metals Me(h)²⁺ (Cd²⁺, Hg²⁺, Pb²⁺, Zn²⁺) possess high chemical affinity to the groups that is one of the reasons for high toxicity of these metals. On the other hand, affinity of Tl⁺ to the SH-groups was significantly lower in comparison to one of Me(h)²⁺ (Perrin, 1979). The reaction of Tl⁺ with SH-groups of mitochondrial proteins is not studied virtually. We estimated the interaction of Tl⁺ c SH-groups of rat liver mitochondrial proteins by their interaction with to 5,5'-dithiobis-(2-nitrobenzoic acid) (Kowaltowski, Castillo, 1997). Our experiments were performed in 400 mOsm medium containing 0-75 mM TlNO₃ and 250-400 mM sucrose or 0-75 mM TlNO₃, 125 mM KNO₃ and 0-150 mM sucrose, as well as 100 μM Ca²⁺ (on occasion). Mitochondria were energized by glutamate plus malate or succinate being I or II respiratory complex substrates, respectively. Visible increase of the concentration of SH-groups in the IMM faction and simultaneous decline of the concentration in the matrix faction were found in the medium containing 50-75 mM TlNO₃. This effect was more potent in the medium containing KNO₃. It was found regardless of the presence of Ca²⁺ or the above respiratory substrates in the medium. The results suggest that the interaction of Tl⁺ with SH-groups of the matrix proteins reduces their solubility in water phase and promotes for part of these proteins to be co-precipitated with the IMM faction. Increase of the co-precipitation in salt medium containing KNO₃ might be due to the greater availability of R-groups of amino acids of mitochondrial proteins for the reaction with ions of Tl⁺.

INFLUENCE OF SORBENTS ON INDICATORS OF FREE RADICAL OXIDATION IN ACUTE ETHANOL INTOXICATION.

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Work purpose: to estimate influence of sorbents on indicators of free radical oxidation in peripheral blood of rats in acute ethanol intoxication.

Materials and methods. Ethanol in a dose of 0,5 LD₅₀ was put into stomachs of 78 rats. Studied sorbents (polysorb, litovit, sapropel) in a dose of 3000 mg/kg were put in stomachs once in 30 minutes after xenobiotic. For an assessment of free radical oxidation processes the hemiluminescent analysis of RBC and blood plasma was used. The blood sampling was made in 24 hours after ethanol intake. Ethanol levels were measured by method of a gas chromatography. Ceruloplasmin (CP) levels in plasma were determined by V. S. Kamyshnikov's method (2003).

Results. In 24 hours after ethanol intake there were no significant changes of intensity of a hemiluminescence of RBC and blood plasma. Intake of ethanol in combination with enterosorbents had no impact on indicators of the hemiluminescent analysis of plasma of blood. With hemiluminescent analysis of RBC it was established that ethanol intake in combination with the polysorb or litovit leads to significant decrease in the maximum value of hemiluminescence intensity, a tendency to decrease light sum of hemiluminescence and light sum after the maximum value of a hemiluminescence. CP levels in acute ethanol intoxication increase almost by 1,5 times in comparison with control (p<0,01). When using studied sorbents (polysorb, litovit, sapropel) blood CP levels didn't differ from control.

Conclusions. Corrective influence of enterosorbents on the main antioxidant of plasma – ceruloplasmin- in acute ethanol intoxication is revealed. Enterosorbents are an effective drug for detoxication in acute ethanol intoxication.

**NON-ALCOHOLIC
FATTY LIVER DISEASE**



COMPLEX RESORT THERAPY FOR NON-ALCOHOLIC FATTY LIVER DISEASE WITH APPLICATION OF BAS “METABOLITE PLUS”

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Research purpose: to study the effectiveness of complex resort therapy for non-alcoholic fatty liver disease (NAFLD) with application of mineral drinking water Essentuki-New in combination with taking BAS “Metabolite plus”.

Data and methods study. 52 patients at the age of 49,8 ± 5,7 years suffering from NAFLD have been examined. 20 (38.5%) of these patients are people with non-alcoholic steatohepatitis, 32 (61.5%) of them are people with liver steatosis. All the patients received spa therapy consisting of clinical nutrition, exercise therapy and internal taking of mineral water Essentuki-New and BAS “Metabolite plus” 1 teaspoon with meals 3 times a day.

Study results. After the treatment most of the patients have improved clinical indices. 87.5% of the patients lost body weight and BBI. 77.3% of the patients normalized liver function tests, 77.5% of the observed decreased total cholesterol, triglycerides and lipoproteids possessing low and very low density (respectively from 6.42 ± 0.1 to 5.52 ± 0.17, from 2.25 ± 0.05 to 1.88 ± 0.11, from 4.17 ± 0.15 to 3.51± 0.18 and from 0.98 ± 0.05 to 0.8 ± 0.05 mmol/l (p < 0.05). The patients suffering from hyperinsulinemia decreased insulin level from 17.8 ± 0.9 to 11.5 ± 0.7 mIU/ml, insulin resistance index HOMA-IR from 4.11 ± 0.19 to 2.58 ± 0.16, (p < 0.05). There has been detected indices improvement of peroxide homeostasis: elevated level of malonic dialdehyde fell from 6.12 ± 0.11 to 3.83 ± 0.12 mmol/l with 77.5% of the patients, and reduced concentration of catalase increased from 11.18 ± 0.54 to 20.21 ± 0.62 mkat/l (p < 0.05) with 75% of the patients.

Conclusion. Complex resort therapy with application of drinking low-mineralized water “Essentuki-New” and BAS “Metabolite Plus” helps to reduce clinical symptoms of the disease, to improve functional liver condition and lipid metabolism, to reduce insulin resistance and to normalize oxidative homeostasis with the patients suffering from non-alcoholic fatty liver disease.

NON-ALCOHOLIC FATTY DISEASE OF THE LIVER AND PANCREAS: FREQUENCY OF COMBINATION

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Problem of abstraction of such an independent nosological form as non-alcoholic fatty disease of the pancreas has been widely debated in the past few years (M. M. Smits, 2011). Like a non-alcoholic fatty disease of the liver, this pathology is developing in patients with obesity, metabolic syndrome.

Objective: to study the frequency of combination of non-alcoholic fatty disease of the liver and pancreas according to the results of computer tomography.

Materials and methods. 180 patients with obesity were examined. All patients underwent computer tomography with an assessment of the organs' density pursuant to the Hounsfield scale. Presence of fatty infiltration of both organs was determined upon the identification of hypodensia. Other computer-tomographic signs of steatosis of the liver and pancreas were also taken into consideration, particularly, steatosis of the pancreas was accompanied by a lobulation and certain lack of clarity of its structure. Density of the pancreas in the regions of its head, body and tail was determined.

Results. Combination of steatosis of the liver and pancreas was detected in 126 (70.0%) patients. Steatosis of the pancreas in conjunction with a normal density of the liver was detected in 45 (25.0%) patients according to the results of computer tomography. The rarest variant that presupposed steatosis of the liver upon the absence of fatty infiltration of the pancreas was diagnosed in 9 (5.0%) patients.

Significant differences of the densitometric density of the pancreas in its head, body and tail were not found.

Conclusion: in the majority of cases, both steatosis of the liver and steatosis of the pancreas are developing in patients with metabolic syndrome.

LIVER CONDITION IN PATIENTS WITH OBESITY ON DIFFERENTIAL THERAPY.

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Obesity currently has become one of the most widespread chronic diseases. The liver is a target with development of non-alcoholic fatty liver disease (NAFLD) in obese patients. NAFLD has stage of steatosis, steatohepatitis, liver fibrosis and cirrhosis.

Aims: to define conditions of hepatic tissue in patients with obesity depending on different therapies.

Materials and methods: Fifteen patients average age of 20-60 years, 5 men and 10 women with varying severity of obesity are observed. All patients were divided into 3 groups: the 1st – control, the 2nd – being on a diet No. 8 and 3 – receiving Ropren (Russian hepatoprotector) in a dose of 3 drops 3 times per day and the reduced diet. Duration of obesity was from 1 year to 10 years. Standard clinical and biochemical laboratory tests are performed, for more exact quantitative and quality standard of steatosis and fibrosis degrees the Fibromax test were carried out in dynamics. For verification steatosis ultrasound was performed (or computed tomography of liver if necessary).

Results. All patients receiving complex therapy have a weight decrease. In patients receiving Ropren and the reduced diet, in comparison with group on a diet No. 8, activity of serum ALT, AST, GGTP authentically decreased, cholesterol levels dropped into normal, in 4 patients degree of fibrosis reduction occurred (due to Fibromax test results). In group of comparison there were no significant changes of liver tests or cholesterol.

Conclusions. Ropren, a biopolymer of polyprenols, allocated of pine and fir-tree greens, promoted reliable improvement of a clinical course of NAFLD, normalization of liver tests and cholesterol levels. Ropren may be recommended for the complex therapy of NAFLD in patients treated of obesity.

NON-ALCOHOLIC STEATOHEPATITIS WITH ACTIVE CYTOLYSIS: PROBLEM OF ADEQUATE “START-THERAPY”

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Non-alcoholic steatohepatitis (NASH) within non-alcoholic fatty liver disease (NAFLD), metabolic and diencephal syndromes plays an increasing role in structure of chronic hepatitis. Special difficulties are presented by a treatment problem in patients with high cytolysis degree in the beginning of treatment.

Aims: development effective and safe start therapy of a cytolytic syndrome in patients with NASH.

Materials and methods: patients with NASH within diencephal and metabolic syndromes aged of 14-50 years were observed. In patients the subclinical steatohepatitis presented, and biochemical cholestasis markers and high cytolysis tests were noted: ALT and AST levels were higher than 10N (350 U/l) in numerous measurements within not less than 6 months. All patients had contraindications to purpose of steroids, metformin and statins. Groups of patients: I - 25 patients treated with ursodeoxycholic acid (Urdoksa, JSC Farmproyekt, Russia), II - 30 patients treated with essential phospholipids (essentialsie-forthe N, Sanofi - Aventis group), III – 29 patients treated with essentialsie-forthe in N + Urdoksa. Diagnostics methods: clinical, biochemical, immunological (markers of viral and autoimmune hepatitis), ultrasonography, MCP, MSKT. As estimated criteria were: ALT, AST, C-RR, AP and GGT.

Results: initial decrease in cytolytic and cholestatic activity is noted in 1-1,5 months of therapy in group III, maximum – in 3 months: up to -25% from basal ALT and AST levels and up to -80% of AP and GGT basal levels. Biliary sludge (originally was registered at 1/3 patients) regressed in all groups in 1 month of treatment.

Conclusions: Drugs Urdoksa and essentialsie-forthe have demonstrated primary efficiency and safety of combined start therapy in cytolytic variant of NASH.

APPLICATION OF PREBIOTIC SUPPORT AND BIGUANIDES IN THE COMPLEX THERAPY OF NONALCOHOLIC STEATOHEPATITIS

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Purpose: Optimization of the complex treatment tactic of non-alcoholic steatohepatitis (NASH).

Materials and methods: 106 patients (mean age, M ± m = 41,2 ± 9,6 years, M / F = 67/39) with NASH and type 2 diabetes. All patients were divided into two randomized groups: a program for the first group of patients (n = 52) in addition to basic therapy included prescription of metformin in individually chosen doses not exceeding 2500 mg / day, and taking of eubikor prebiotic per os 2 packets 3 times daily for a period 3 months, the comparison group (n = 54) received standard therapy with essential phospholipids. All patients underwent examination including dynamic study of general clinical and laboratory and instrumental parameters.

Results. It was found that in Group I patients during the treatment both fasting serum levels of insulin and levels of insulin performed 1 hour after the exercise test, reduced in comparison with the control group. Usage of prebiotic therapy in complex treatment of patients with NASH contributed to a statistically significant increase in major intestinal microflora (Bifidum and Lactobacillus), as well as typical E. coli. At the same time there was the reduction and elimination of Clostridium, Staphylococcus and Candida fungi compared with Group II patients. Against the background of the therapy being carried out in both groups there was a decrease of steatosis degree. However, in group I patients there was a significant reduction of the frequency of its 3rd grade (p <0.04). More significant changes were observed in the analysis of the morphological activity in the groups studied. Thus, in group I there was a decrease of morphological activity, characterized by the disappearance of the marked inflammation and significant increase in patients with minimal disease activity (p <0.02). At the same time in the control group the natural growth of the focal and periportal fibrosis (II stage) was observed (p <0.005).

Conclusion: The use of metformin and eubikor in the complex treatment of NASH contributed to the normalization of carbohydrate metabolism and intestinal microbiota, improve the morphological picture of the disease in the form of lower degree of steatosis, histological activity and the lack of dynamic growth of the stage of fibrosis process in the liver.

EVALUATION OF HYPOLIPIDEMIC EFFECT OF PROBIOTICS IN PATIENTS WITH TYPE 2 DIABETES AND NON-ALCOHOLIC FATTY LIVER DISEASE.

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Introduction. One of the most frequent causes of morbidity and mortality in patients with nonalcoholic fatty liver disease (NAFLD) is cardiovascular disease (CVD). Increased cardiovascular risk in these patients observed due to low high-density lipoprotein cholesterol (HDL-C) level, high triglycerides (TG), small, dense particles of low-density lipoprotein cholesterol (LDL-C) and apoB100 levels.

Materials and methods. We examined 72 patients with type 2 diabetes and non-alcoholic fatty liver disease. All patients divided by us on the way of therapy into 2 groups. The main group (n=45) received oral antidiabetic therapy and multiprobiotic “Symbiter” containing concentrated biomass of 14 probiotic bacteria genera Bifidobacterium, Lactobacillus, Lactococcus, Propionibacterium, within 30 days. Patients of comparison group (n=27) received only hypoglycemic drugs. All patients underwent determination of lipid parameters before and after treatment.

Results. We observed reduction in total cholesterol level on 4.8% (p = 0.001), non-HDL-C on 6.9% (p<0.001), LDL-C on 7.2% (p=0.003) and triglycerides on 10 6% (p= 0.010) after the course of multiprobiotic “Symbiter”. But don't find significant changes on HDL-C level (p=0.085) in main group and for all lipid parameters on the comparison group after treatment.

Conclusion. Multiprobiotic “Symbiter” has moderate hypolipidemic effect and can be used in the treatment of multifactorial type 2 diabetes and NAFLD.

CLINICAL AND PATHOGENIC FEATURES OF CARDIO-RENAL SYNDROME IN NON-ALCOHOLIC FATTY LIVER DISEASE.

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Purpose. Studying of clinical and pathologic features of cardio-renal syndrome at not alcoholic fatty illness of a liver.

Materials and methods. Eighty patients with metabolic syndrome (60 men and 20 women, middle age of 44±11 years) and non-alcoholic fatty liver disease (NAFLD) were observed. Markers of insulinoresistance, plasma leptin and serum adiponectin levels, an albuminuria, thickness of a complex intima-media (TIM) in common carotid artery (CCA) were defined.

Results. In process of increasing number of signs of target organs injury in patients with NAFLD the reliable growth of frequency of detection of chronic kidney disease (CKD) and atherosclerotic injury of carotid arteries, increased albuminuria and TIM of CCA, and also decreased in estimated glomerular filtration rate (eGFR) are registered. \maximal leptin levels appeared in group of 27 patients with CKD, and also directly correlated with an albuminuria degree. Reliable decrease in adiponectin serum levels in 52 patients with atherosclerotic injury of common carotid artery which demonstrated a feedback with thickness TIM of CCA. The last one directly correlated with an insulin, C-peptide level in plasma and HOMA-IR. Adiponectin serum levels directly correlated with De Ritis ratio.

Conclusions. Common formation of CKD and atherosclerotic injury of CCA defined by leptin/adiponectin imbalance is a feature of cardio-renal syndrome in NAFLD.

INCIDENCE OF LIVER STEATOSIS IN PATIENTS WITH ARTERIAL HYPERTENSION AND SUBCLINICAL HYPOTHYROIDISM

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Purpose. To estimate incidence of liver steatosis in at patients with primary subclinical hypothyroidism (SH) in combination with the arterial hypertension (AH).

Materials and methods. The comparative analysis in 101 patients with primary SH in combination with AG (middle age of 52,74±8,47 years) and in patients with an arterial hypertension (111 patients, middle age of 50,04±10,12 years). The BMI in groups was comparable: 32,88±5,44 and 32,71±4,19 kg/m². All patients went through examination and ultrasonography of a thyroid gland, the common carotid arteries and liver. Liver size, echogenicity and a parenchymal stiffness, vascular architectonics, structure of intra- and extrahepatic bile ducts, diameters of portal vein and vena cava inferior. Statistical data are submitted in form of M±SD.

Results. Significant higher degree of dyslipidemia is revealed in patients with SH+AG in comparison with patients with AH (total cholesterol - 5,97±0,96 and 5,61±0,97 mmol/l, p<0,01, triglycerides- 1,65±1,00 and 1,2±0,62mmol/l, p<0,001, LDLP - 3,57±0,78 and 3,31±0,82 mmol/l, p<0,02). A moderate positive correlation between the TSH levels and degree of dyslipidemia (r=0,49) is revealed. AST and ALT levels in patients with SH+AH were significantly higher (ALT - 40,07±22,06 and 25,28±6,64 mmol/l, p<0,001, AST - 29,79±8,53 and 22,50±4,54 mmol/l, p<0,001). Atherosclerotic plaques in carotid arteries appeared in 2,7 times more often in patients with SH+AH than at patients with AH (16,8% and 6,3%). Sagittal liver size were significant in patients with SH+AH, than in patients with AH (170,53±17,36 and 161,61±15,98 mm, p=0,001). US signs steatosis (echogenicity increase, poor vascularization of parenchyma in combination with hepatomegaly) in patients with SH+AH occurred twice more often (74% vs. 38%). Thus, the dyslipidemia and liver steatosis in patients with SH+AH were significantly more often revealed than in patients with AH.

CORRELATION BETWEEN ABDOMINAL FAT DEPOSITES AND LIVER AFFECTION IN METABOLIC SYNDROME

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Aim: To recognize correlations between degree of abdominal fat's deposits and presence of fatty liver in metabolic syndrome.

Materials and methods: 138 patients in age from 40 to 90 years were investigated (64 females and 74 males). We provided anthropometric investigations (height, weight, waist circumference (WC), BMI) laboratory tests (lipid's profile, carbonydrate's metabolism, biochemical blood analysis). The thickness of subcutaneous fat (SF) and intraabdominal fat thickness (IAF) were measured with US-method in the middle between umbilicus and processus xyphoideus. Statistical analysis was provided by use of program Statistica 6.0.

Results: all patients had IHD and arterial hypertension. Disturbances in glucose metabolism were in 90,7% of patients. WC in females was 102,6±1,75sm, in males 100,6±1,4sm, BMI was 28,8±0,4 kg/m². The thickness of IAF was 53,5 ±1,64 mm (10,5-106 mm), it was significantly more in males (p<0,001). The thickness of SF was 12,7±0,38 (3,7-30 mm) and was not significantly more in females. The hepatomegaly was revealed in 36,2% of patients, in 52% - diffuse increasing in density and liver echogenity.

Correlation between IAF thickness and BMI (r=0,44, p=0,000001), WC (r=0,56, p=0,000001), level of HbAlc (r=0,57, p=0,03), level of HDL (r= -0,19, p=0,02) triglycerides (r=0,17, p=0,05) were revealed.

The thickness of SF correlates with BMI (r=0,3, p=0,00016), with WC (r=0,27, p=0,0014), the level of cholesterol (r=0,18, p=0,02), with liver's right lobe size (r=0,19, p=0,02). In males liver's right lobe size directly correlates with IAF thickness (r=0,25, p=0,016).

Conclusion: increase in subcutaneous and intraabdominal fat predictor of liver affection patients with metabolic syndrome.

PRO-INFLAMMATORY CYTOKINES IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) AND LIVER FIBROSIS

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Aims: to study a role pro-inflammatory (TNFα, INFγ and IL6) in liver fibrosis development in patients with NAFLD.

Materials and methods: research was conducted on base of Regional Hospital, Chita in 2010-2012.

The diagnosis of NAFLD is established when: risk factors exist (obesity, carbohydrates metabolism disturbances of different degree), signs on ultrasound, and morphological changes. Fact of liver fibrosis was estimated with indirect elastography. Fifty six patients were included in research. Thirty patients with NAFLD and liver fibrosis. Twenty six patients made control group, healthy individuals too. Cytokines levels in blood serum - TNFα, INFγ, IL6 - were measured by the immunofermental analysis with use of commercial "VEKTOR-BEST" test systems (Russia). For statistical data processing median, 25 and the 75th percentiles, Mann-Whitney's criterion (Statistica 6 program) were used.

Results: Levels of serum TNFα in patients with liver fibrosis (LF) are considerably increased in comparison with control group, p=0,025 (21,18 pg/ml (10,5 pg/ml, 35,33 pg/ml) and 11,52 pg/ml (8,39 pg/ml, 18,01 pg/ml) respectively). Levels of IL6 are also increased in patients with signs fibrosing process in liver tissue in comparison with healthy individuals, p=0,052 (8,23 pg/ml (6,48 pg/ml, 13,35 pg/ml) and 5,92 pg/ml (3,71 pg/ml, 9,88 pg/ml) respectively. INFγ levels in patients with LF (5,48 pg/ml (3,42 pg/ml, 8,32 pg/ml)) practically didn't differ from that in control group (6,93 pg/ml (4,69 pg/ml, 12,04 pg/ml)).

Conclusions. Serum levels of pro-inflammatory cytokines (TNFα and IL6) increase in patients with NAFLD while LF is being forming.

LIVER TUMORS

CHEMOTHERAPY LIVER ALVEOCOCCOSIS

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Liver alveococcosis is a serious problem of surgical hepatology. Characteristics of a parasite: the slow, hidden history of disease, infiltrative growth, invasion along fatty tissue of vessels and ducts to liver porta. Difficulties at treatment of patients with liver alveococcosis: lack of intact liver parenchyma, jaundice existence, background cirrhosis, high number of palliative operations.

Aims: to prove need of adjuvant and neoadjuvant chemotherapy of liver alveococcosis.

Materials and methods: 125 operated patients: men-95, woman-30. Age: 16–79 years. Localization: right liver lobe-92 (73,6%), left-29 (23,2%), bilobal process-4. Two stages in surgical treatment: without neoadjuvant therapy and with pre-operative nemozol administration.

The 1st stage (n=76): right hemihepatectomia-48, two-stage operations-6, cytoreduction-17, opening and drainage of a parasital cavity -5. The 2nd stage (n=49): right hemihepatectomia-30, two-stage operations-1, cytoreduction-2, bisegmentectomia-9, left lobectomia-7.

Nemozol (albendazol) therapy: 1. pre-operative: 400-800 mg/d 28 days, 14 days break, for 3-6 months, 2. post-operative: 800 mg for 3-6 months, then 400 mg up to 1 year, when palliative operation – up to 3 years.

Results: 1st group: complications-9 (11,84%), mortality-4 (5, 26%), recurrence-7 (9,21%), 5-year survival-56 (73,68%). 2nd group: complications-5 (10,2%), mortality-2 (4,08%), recurrence-3 (6,12%), 5-year survival-40 (81,63%).

Conclusions: results allow to recommend not only adjuvant, but also neoadjuvant therapy of liver alveococcosis. Efficiency of pre-surgical administration of nemozol is confirmed morphologically.

HEPATOCELLULAR CARCINOMA IN THE OUTCOME OF CHRONIC DELTA INFECTION

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Aim: To present clinical characteristics of patients with hepatocellular carcinoma (HCC) in the outcome of chronic delta infection living in an endemic region for this infection (Republic Tuva, Russia).

Materials and methods. 318 patients aged 4-77 (39,1±10,6) with chronic delta infection studied by immunological and molecular genetic methods. There were 123 males (38,7%) and 195 (61,3%) women among them, 68 patients were followed long time (from 2009 to 2012).

Results. Chronic hepatitis delta (CHD) was diagnosed in 77,4% (246/318) and liver cirrhosis (LC) - in 22,6% (72/318) cases. All patients infected with hepatitis D virus (HDV) had chronic hepatitis B (superinfection). Progression of CHD to LC was estimated in 14,7% (10/68), decompensation of LC – in 14,7% (10/68) and development of HCC 11.8% (8/68) patients for 4 years in the dynamic observation. It is shown that HCC is formed in a small proportion of patients due to rapid disease progression, the development of decompensated LC and its complications (coma, bleeding) with a high frequency of deaths. The mean disease duration from the first time of HDV infection to HCC was 15–20 years and the average age of the patients with HCC - 43,5±8,4. The diagnosis of HCC was estimated on late stage in all patients when there are multiple lesions in the liver (by ultrasound data). Average ALT level was 48±16,6 U/l, bilirubin didn't not exceed 11,8±1,8 mkmol/l. Replication of hepatitis viruses took place in 4 of 8 HCC cases: HDV RNA was detected in 2 patients, HBV DNA - in 1 case. One patient with HCC died due to bleeding from varicose veins in the esophagus and stomach. Replication of both viruses was determined in this observation.

Conclusion. Chronic delta infection is mainly estimated among persons of young and working age and is characterized by progressive course, rapid development of LC, HCC and high mortality rate in endemic region (Republic Tuva, Russia)

CLINICAL AND LABORATORY FEATURES OF HYPOGRANULAR FORM OF ACUTE PROMYELOCYTIC LEUKEMIA

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Clinical hematology currently achieved undoubted success in promyelocytic leukemia treatment (M3 on FAB classification). However big resistance to therapy is shown in hypogranular variant (GGV) of promyelocytic leukemia. Determination of clinical and laboratory features of this M3 GGV was the purpose of our work. All cases of M3 registered within in 1 year in practice of hematologic department of Regional clinical hospital are analyzed. In total there were 6 cases of acute promyelocytic leukemia registered for the first time, in two cases the hypogranular variant is described in morphology. Four cases of "classical" M3 were characterized by leukopenia, significant low platelets count (<10.000/mkl). Leukocytosis was observed in both cases with hypogranulated blasts (20-30.000 leukocytes/mkl), platelets counts within 25-50.000/mkl. The hemorrhagic syndrome was less expressed in patients with GGV M3. Probably cytoplasm of blasts in this group of patients contained less granules with heparin-like substance. One patient with GGV leukemia had generalization with different organs involvement: liver, intestines, lungs. It is interestingly to research immunocytochemical features of blasts for clinical supervision of M3 with two different in their morphology blast subpopulations. In marrow samples it was observed both hypogranulated, and hypergranulated blast cells. Only blasts with small granulation were observed in samples from peripheral blood. Perhaps, this population was less "kept" by marrow microenvironment. The immunophenotype of subpopulations was identical: CD34-, HLA-DR-, CD13+, CD33+, MPOcyt+. Cytochemical research of membrane myeloperoxidase revealed its high activity on blasts of marrow and quite total absence of active enzyme on blasts in peripheral blood cells.

INTRALUMINAL RADIOTHERAPY AS A PART OF COMBINED TREATMENT OF EXTRAHEPATIC BILE DUCT CANCER

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Objective: to estimate capabilities of intraluminal radiotherapy (IR) as a part of combined treatment of patients with extrahepatic bile duct cancer. Materials and methods: 68 patients with malignant strictures of extrahepatic bile ducts complicated with obstructive jaundice underwent a combined treatment that included percutaneous transhepatic draining of bile ducts, IR with the following reconstruction of the biliary system. Extrahepatic bile duct IR was performed using a Microselectron HDR at 10 mm from the source center. Total radiation dose was 60 iGr. The subsequent bile duct reconstruction was realized by 3 ways: bile duct stenting, leaving a transhepatic drainage, forming a cholangiostoma.

Results: 68 patients underwent the technique developed. At the first step, all the patients were performed a percutaneous transhepatic cholangiostomy. 43 patients further underwent only IR, total radiation dose, 60 iGr. 4 patients underwent IR (total dose 42 iGr) plus distant gamma therapy (total dose, 30-35Gr). 22 patients underwent surgical therapy – hepaticocholedoch resection with the subsequent IR of the lobular duct stump (total dose, 60iGr). 49 patients were further left with a constant transhepatic catheter, 16 patients had wallstent endoprosthesis installed, the transhepatic catheter was removed, 2 patients underwent a reconstruction surgery, 1 had a punction cholangiostomy. The control group (n=34) included patients who underwent only a palliative drainage of the biliary system. Survival rate in the analytic group (n=68) was 100%, 85%, 66%, 46%, 22% for 3, 6, 9, 12 and 24 months, respectively. Survival rate in the control group was 96%, 67%, 23%, 4%, 0%.

Conclusion: the technique developed has let reliably increase the life expectancy of patients.

THE SYSTEMIC APPROACH TO HEPATOONCOPREVENTION

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Background and Aims: To reveal role of some exogenic factors, systemic and local nonmalignant diseases in pathogenesis of hepatocellular carcinoma.

Methods: in 80 patients with hepatocellular carcinoma (HCC) 117 different local and systemic comorbid diseases were studied. Structure of paratumoral liver tissue were investigated by hystology methods. In control group 40 patients with nonparasitic liver cysts (NPLC) was include. The statistical validity of the data was verified by the index OR.

Results: (n - % patients)

Factors	HCC	NPLC	OR
Systemic Diseases:			
Diabetes mellitus type II	11 - 13,7	1 - 2,5	5,5
Hyperalimentation	41 - 51,2	16 - 40,0	1,3
Metabolic syndrome	19 - 23,7	3 - 7,5	3,2
Gallstones	18 - 22,5	2 - 5,0	4,5
Chronic pancreatitis	13 - 16,2	1 - 2,5	6,5
Liver Diseases:			
Viral hepatitis - HBV, HCV	23 - 28,7	2 - 5,0	5,8
Cirrhosis - Child A, B, C	16 - 20,0	1 - 2,5	8,0
Steatohepatosis	15 - 18,7	3 - 7,5	1,9
Chronic Alcoholic hepatitis	8 - 10,0	1 - 2,5	4,0

Different stages of NASH in 16,7%, liver fibrosis – in 40,0%, and periportal lobular inflammation (neutrophilic granuloocytes infiltration) – in 53,3% of these patients (OR - 0,5, - 4,0, - 6,0, respectively) were revealed in paratumoral liver tissue hystologically.

Conclusions: Some systemic and local liver diseases were found in patients with HCC. We suppose they lead to inflammatory and fibrotic changes in liver tissues as a strong ground for hepatocarcinogenesis. In these circumstances long complex oncoprotective treatment of these diseases including ursodeoxycholic acid (Ursolfalk) may be rational.



**LIVER TRANSPLANTATION,
HEPATIC INSUFFICIENCY**

Keeping of waiting list for liver transplantation and post-operative monitoring of patients who received donor organ, in Nizhny Novgorod

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In Nizhny Novgorod liver transplantation (LT) from postmortem donor is performed from 2009. The waiting list (WL) for LT is maintained from 2007, the number of patients in it constantly changes (15 to 74). In December 2012 WL included 55 patients, among them 34 women and 21 men, average age - 46.3±22.6 years (range 19 to 60 years). The number of patients with viral liver cirrhosis (LC) was 16 (29.1%) patients.

During the period from 2009 to 2012 26 LT was performed from postmortem donors (including 3 patients with viral LC and one – liver and kidney transplantation). Mortality in the early postoperative period was 19.2% (5 persons). Causes of mortality: PATE, fulminant hepatic failure, sepsis, necrotizing pancreatitis. From 2007 in WL the mortality of patients was 36.

After liver transplantation all patients once per every three months perform biochemical analysis, study of the concentration of immunosuppressive drugs in the blood, ultrasound + USDG of transplant.

The patients received the following immunosuppression schemes: drugs tacrolimus or cyclosporine (6 patients) + mycophenolates (17 patients) + glucocorticosteroids (4 patients). Three-component scheme of immunosuppression is associated with autoimmune causes of LC. The single component scheme is administered to patients with the development of leukopenia or ulcerative colitis. Overall structure of immunosuppression includes drugs cyclosporine in 6 (23.1%) patients, drugs tacrolimus in 20 (76.9,8%) patients. Conversion of immunosuppression drugs was not.

Thus, only complete comprehensive study of patients allows you to thoroughly select patients for entering into WL for LT, to identify indications and contraindications, to decrease significantly complications in post-transplant period. Detailed monitoring of patients after liver transplantation helps to identify possible complications at an early stage, to prevent their further development and progression.

The 7-year experience of the orthotopic liver transplantation (OLT) in Academician V.I. Shumakov Federal Center of Transplantology and Artificial Organs (FCTAO)

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Introduction: For the 5-year period (2006-2011) it was performed 918 orthotopic liver transplantations (OLT) in 38 centers in Russian federation: 503 (54.8%) cadaveric transplantations, 395 (45,2%) – living relative donors. The summary number of OLT for the 5-year period increased for +116 OLT (+131,8%).

Aims: to study evolution of OLT, indications for PLT, complications and recipients and graft survival in the Federal center of transplantation and artificial organs for the 7-year period.

Materials and methods: One hundred was performed for 94 patients (+6 retransplantations) in FCTAO in 7-year period of 2004-2011. Average age was 43,8±13,3 years, follow-up period was 6-84 (45,6±2,4) months. Indications for OLT in waiting list was: chronic hepatitis C – 24%, chronic hepatitis B – 15% (totally viral hepatitis – 29%), hepatocellular carcinoma (HCC) – 8%, primary biliary cirrhosis – 21%, primary sclerosing cholangitis – 6%, alcoholic cirrhosis – 9%, autoimmune cirrhosis – 9%, liver polycystosis - 1%, Badd-Chiari syndrome - 4%, miscellaneous - 6%. The predominant class of Child-Turcotte-Pugh score was B (49%), average meaning in MELD score was 17±7 (range of 9-41.5). Retransplantation was performed for 6 (6,4%) recipients, (4-in early postoperative period).

The total 1-, 3- and 5-year survival after OLT was 89, 87 and 87%, respectively. The 1-, 3- and 5-year graft survival was 85, 82 and 70%, respectively. There were no cases of intraoperative death. Five (5,3%) recipients died in the early postoperative period. The survival after a retransplantation is significantly lower, and is up to 50% (in comparison with to 90% in recipients with one OLT). The 1- and 3-years survival in HCV- positive recipients is much lower: 70 and 76% vs. 93,1% and 93% in HCV-negative recipients, respectively. OLT due to HCC was performed in 8 patients of age of 56,75±11 years. Recurrence occurred in 2 recipients who were out of Milan criteria and died in 11 and 13 months. The 1- and 3-years survival was 86 and 68%, respectively.

Results: Number of OLT has significantly increased in period of 2004-2011 years in Russia, and data show good recipients and graft survival. The 3-year survival in HCV-positive recipients and with HCC out of Milan criteria is worse (up to 76% and 68%, respectively).

EXPERIENCE OF TREATING HEPATITIS C RECURRENCE IN POSTTRANSPLANT PERIOD.

Recurrence of HCV after OLT in HCV RNA – positive recipients is universal and outcome of such patients is worse than in HCV – negative recipients. It is well known that up to quarter of these recipients develop allograft cirrhosis during 5-10 years after LT. Treating of recurrent hepatitis C with a combined antiviral therapy (AVT) is the one option at present time, but it limited controversial frequency of sustain virological response (SVR) and it is still speculatable when to start with antiviral treatment and how to modify immunosuppression within it. Increasing numbers of patients with HCV – related cirrhosis, severe and unpredictable occurrence recurrent hepatitis C and poor outcome of HCV – positive recipients still remain dramatic trouble on the field of liver transplantation. Within 8 years (12/2004-12/2012) in our center was performed 138 OLT to 132 recipients. Most common indication - HCV-associated cirrhosis 31(23,5%), in 6 cases complicated by hepatocellular carcinoma(HCC). 19.4% of patients died: 3-recipient in the early post-transplant period, a 3-to long-term period of observation. 14 patients (45.2%) conducted AVT with PEG IFN + ribavirin. Starting date of the AVT - from 40 days to 28 months after OLT. Overall SVR rate was 64.3%. 4 patients with genotype 3a developed a rapid virological response (RVR), early virological response (EVR) and SVR was subsequently registered in 3 patients. In one recipient with genotype 1b was registered RVR, EVR was present in 4 cases, partial early virologic response (pEVR) - in 3, a slow virologic response (Sl.VR) - in 2 patients. End to treatment virologic response(ETVR) at the conclusion of AVT reached in 7 patients, while SVR only in 6. In all patients AVT conducted during immunosuppressive monotherapy: 10-tacrolimus, 4-cyclosporine A. In no case was a rejection of liver graft. Adverse events of AVT after OLT were anemia, thrombocytopenia, leukopenia, in 2-cases during the treatment patients developed infectious complications (biliary liver abscess - 1, right-sided pneumonia), in the one patient registered acute psychosis. The results indicate that AVT after OLT can change the prognosis HCV RNA-positive recipients, to be safe and effective, but requires the identification of the optimal timing of treatment.

SUSTAINED VIROLOGIC RESPONSE IN THE TREATMENT OF HCV- INFECTION AFTER LIVER TRANSPLANTATION

However, the increase in HCV-positive recipients, severe and unpredictable return for HCV-infection require AVT after orthotopic liver transplantation (OLT), depending not on the period of time after the operation, but on the overall status of the patient, the severity of the return of hepatitis C, stage of fibrosis, the presence of surgical and / or infectious complications, renal function status, severity of cytopenia. In the period 12/2004-12/2012 at our center performed OLT to 31 HCV-positive recipient. Of the 14 patients who carried AVT with PEG IFN + ribavirin, 9 (64.3%) achieved a sustained virological response (SVR). AVT in patients who achieved SVR, began a period of 2, 7, 12, 15 months after OLT on monotherapy with tacrolimus or cyclosporine A. Course of the recurrence ranged from mild to severe (1 case of fibrosing cholestatic hepatitis C). In four patients with rapid progression of fibrosis F0-F2 for 6 months. At the beginning of the AVT opportunistic infections and surgical complications were absent. No patient had no diabetes, 5 hypertension was present. Glomerular filtration rate (GFR), as an indicator of renal function, were in the range 61-105 ml / min, hematological parameters: Hb 87-144g / l, RBC 2,9-5,07, WBC 1,4-3,7, NEU 30-68%, PLT 57000-341000. Three patients had genotype 3a, 6-1b. In one case, the AVT lasted 72 weeks in the form of a slow virologic response, in the other treatment was discontinued at week 6 in mind persistent increase in serum bilirubin despite negative HCV RNA at second week of treatment. In the remaining patients treated consistent protocol regarding genotype of hepatitis C virus (24-48 weeks). In one case, the AVT was stopped after the early virological response (EVR) at 15 weeks, because of an abscess of the right lobe of the liver. After 3 months, the level of viremia was 2.8×10^7 IU / ml. Retry after 8 months had led to a EVR and SVR. Analyzing AEs in patients with SVR, we checked that the highest frequency (100%) met thrombocytopenia and neutropenia, anemia was reported in 78%, psychiatric disorders occurred in 22% patients, infection complication was diagnosed in 11%.

CHOLESTATIC LIVER DISEASES

CHOLESTASIS TREATMENT IN PREGNANT WOMEN BY USING URSODEOXYCHOLIC ACID

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Aim of study. To study the efficiency of cholestasis treatment in pregnant women (CTiPW) by using ursodeoxycholic acid (UDCA) as a main medicine.

Materials and methods. During advisory and diagnostic physician's appointments conducted in the perinatal center there have been patients identified with clinical and laboratory symptoms typical for cholestasis in pregnant women: the levels of cholesterol, bilirubin, alkaline phosphatase, transaminases, coagulogram's indicators and markers of hepatitis B and C. An ultrasound examination of the abdominal cavity has been performed. Correction was carried out with UDCA ("Ursolfalk" or "Ursosan") 0.25 - 4 times a day for 1-2 weeks, after state improvement - 2-3 times a day for up to 1 month and more (prophylaxis).

Results. CTiPW with symptomatic course (skin itch) has been conducted in 20 cases. It was noted that in 12 (60%) patients this condition was not detected or suspected in domiciliary medical facilities: in 4 (20%) an "allergy" was treated, in 3 (15%) - "pruritus gravidarius", in 5 (25%) - the condition was unclear. During UDCA treatment in the first week of therapy itching was cured in 16 (80%) patients, a significant reduction in cholesterol from 7.25 ± 0.34 to 6.51 ± 0.32 ($p = 0.047$) and insignificant reduction of alkaline phosphatase and transaminases have been established. One month later the absence of itching has been registered in all 20 (100%) of women, the level of cholesterol was 6.0 ± 0.3 . All patients approved the improvement of health. There were no adverse effects on the course and gestation outcome.

Conclusions. UDCA is proved to be a highly effective and safe medicine for cholestasis treatment in pregnant women. In the primary stage of health care delivery to pregnant women the cholestasis is often unrecognized or non-diagnosed correctly.

CHOICE OF TYPE OF LITHOEXTRACTION IN CHOLEDOCHOLITHIASIS

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The number of patients with choledocholithiasis constantly increases. Endoscopic papillosphincterectomy (EPS) as "the gold standard" for concrements in bilious ducts leads to destruction of Oddi's sphincter and violation of autonomy of a biliary tree. Ajar cholangioduodenal fistula causes cholangitis.

Aims: to estimate a technique of sanitation of a biliary tree with preservation of its autonomy.

Materials and methods: 5588 patients with gall-bladder stone disease (GBSD) were observed in the Center in the period of 2002-2012, with operated 5345 of them. Choledocholithiasis accompanied or was isolated in 367 (6,86%) patients. 2 stages were experienced: with wide use of forming biliodigestive anastomosis (till 2004) and after, with choledochoscopy (mini-access) or laparoscopic. At the first stage 105 patients with choledocholithiasis are operated. There was performed 29 biliodigestive anastomosis, 45 EPS, 31 choledocholithotomy with drainage by Ker (with use of choledochoscope-31 of them). At the second stage 262 operations are executed and 12 anastomosis formed. The others (250) are operated from mini-access in M.I.Prudkov method (187) and laparoscopic (75). The choledochoscopy, a lithoextraction were made in all cases. Choledochoscope OLYMPUS with a diameter of 4,1 mm was used. It allowed to make a revision of a biliary tree till subsegmentary branches.

Results: There were no complications and mortality at the stage II, as well as recurrence choledocholithiasis in 7-year period of follow-up.

Conclusions: using of choledochoscope keeps autonomy of a biliary tree, allows to make a sanitation of bile ducts with high degree of confidence, by mini-access and a laparoscopic and to lower an intra-operative traumatization. The confidence of full revision allows to avoid biliodigestive anastomosis forming.

COMPARATIVE CHARACTERISTICS OF THE CAUSES OF POSTCHOLECYSTECTOMY SYNDROME

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Purpose of study: analysis of the causes of postcholecystectomy syndrome (PCES) formation.

Materials and methods. The study included 401 patients after cholecystectomy, with diagnosed postcholecystectomy syndrome (average age $57,2 \pm 8,3$ years, men - 99, women - 302 in a ratio of 1:2.9). Clinical-anamnestic data and results of laboratory and instrumental methods of study conducted according to the standards of delivery of health care for patients with cholelithiasis were analyzed. Average duration of cholelithiasis was $25,5 \pm 2,5$ years.

Results. It was determined that in 43,2% (n = 173) there were complaints of biliary-dyspeptic nature. The presence of abdominal pain was found in 35,7% (n=143) patients, among them the pain in right hypochondrium was in 83,2% (n = 119), other sites – in 16,8% (n=24). Based on conducted examination before surgical intervention, and during the postoperative period presence of diseases of the upper gastrointestinal tract was detected in 94,3% (n = 378): superficial gastritis in 95.8% (n = 362), gastric ulcer and duodenum ulcer - 11,1% (n = 42), duodenogastric reflux - 40,2% (n = 152), with the development of reflux gastritis - 10,8% (n = 41). Hepatobiliary pathology was found in 71,1% (n = 285) patients, including biliary dyskinesia – in 97,5% (n = 278), choledocholithiasis – in 1,7% (n = 5), disorder of Oddi's sphincter – in 30, 8% (n=117), papillitis – in 5,9% (n=24). The presence of biliary-dependent pancreatitis was found in 6,3% (n = 18) of patients, including those with exocrine insufficiency in 3 patients (1.1%).

After the study, based on laboratory and functional parameters 384 (95.8%) patients continued treatment by gastroenterologist, since pain and dyspepsia were caused by biliary dyskinesia, duodenogastric reflux. Among organic pathology of biliary tract, the most common reason of bile outflow disorder was stenosis of the distal part of common bile duct - 17.9% (n = 14). Other reasons of PCES in patients were as follows: constrictive papillitis 8,9% (n = 7), choledocholithiasis - 6,4% (n = 5). 17 (9.8%) patients required re-hospitalization for invasive treatment: endoscopic papillosphincterotomy - 16,7% (n = 13), choledocholithotomy - 3,8% (n = 3), stenting of the biliary ducts - 3.8% (n = 3), applying choledochoduodenostomy - 1,3% (n = 1), choledochoenteroanastomosis -

1,3% (n = 1), choledochojejunostomy - 1,3% (n = 1).

Conclusions. Clinical manifestations of postcholecystectomy syndrome depend on the causes of the outcome of cholecystectomy, as well as early detection and treatment of diseases duodenopancreatobiliary zone in the immediate and long-term postoperative period.

STUDYING OF MUTATIONS IN GENES OF IRON METABOLISM IN PRIMARY BILIARY CIRRHOSIS (PBC).

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One of the most actual problems of medicine today is cirrhosis. The global distribution is noted, as the evidence tendency in incidence and number of patients with chronic liver diseases of mainly efficient age increase [Grigoriev P. Ya. Yakovenko A.V. 2004, Ivashkin V. T. 2009]. Much attention is paid to search the genetic markers of multifactorial diseases. We studied clinical-genetic associations of mutations in genes of iron ,etabolism in patients with primary biliary cirrhosis (PBC) in the Republic of Bashkortostan. Accumulation of iron in an organism is toxic practically for all cells and tissues. Recently researchers around the world obtain new data about even small amounts of iron can serve in a liver as factors of increase in severity or progressing of "non-haemochromatosis" liver diseases. Small amounts of iron can accumulate owing to heterozygotic mutations in a gene of haemochromatosis (HFE) [Herbert L. Bonkovsky, 2002]. It is also possible that mutations in HFE gene influence development and progressing of liver diseases irrespective of process of iron deposition. That could be explained to that a product of HFE gene is a protein of the major histocompatibility complex (MHC) type I which can break reaction of the immune answer [Herbert L. Bonkovsky, 1999, 2000].

For detection of molecular and genetic risk factors of appearing of mutations determination of rate of mutations of C282Y, H63D, S65C of a HFE gene and mutations of Y250X of a gene of a receptor transferin2 (TfR2) was carried out.

Mutations of C282Y of HFE gene in patients with PBC are not revealed (in control group-3,3%). Apparently, this mutation doesn't play importance in pathogenesis of PBC.

The analysis of incidence of mutation of H63D in HFE gene showed that this mutation in a homozygous state occurred statistically significantly more often [7,14% and 0%, $c^2=3,81$, $p=0,051$, OR=53,44 (95% C.I. 5,38-531,08)]. H63D mutation in a heterozygotic state almost is twice more often found, however distinctions didn't reach the statistical importance in patients with PBC (21,43% and 11,7%, $p>0,05$). Incidence reduction without a mutation to 71,43% (88,3% in control group) was characteristic for patients with PBC.

Interesting data are obtained at research of a mutation of Y250X of a gene of a receptor

COMPARATIVE ESTIMATION OF THE COURSE CHOLELITHIASIS IN PATIENTS OBESE AND NORMAL WEIGHT

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Purpose – to analyze of the course of cholelithiasis (GSD) and the perioperative period in patients with obesity and normal weight/

Materials and methods. Conducted physical examination of 239 patients GSD, of which 84persons (group 1) with normal weight, 65 (group 2) with overweight, 90 people with obesity (group 3). Patients were examined in the perioperative period.

Results. Groups differed by sex and age composition: men were respectively 27,7%, 47,7%, 8,4%/ Age up to 40 years in group 1 was in 38,5% of patients, in the 2nd – at 13,85%, in the third only 8,8%, age of other patients was 40 – 84 years. In all the groups in ½ cases calculous cholecystitis was acute and ½ - chronically. More than ½ of patients (53,6%) of group 1 had a small period GSD (<5 years), in the 2nd and 3rd group – only 1/3 of cases. Eating disorders have established in a history of all patients, but the patients of group 1 was f restrictive type with frequent periods of complete starvation, the use of different diets, "separate" feeding. For patients with GSD and obesity is characterized rare receptions calorie food and eating in the evening (and night) for many years. Hypercholesterolemia was found only in group 3 patients, in the absence of obesity high cholesterol were observed in isolated cases. Tactics of surgery, course of the perioperative period had no significant differences. Average koykoden was equal in all groups. Severity of cytolytic syndrome in acute calculous cholecystitis was lower than in chronic, respectively $59,64 \pm 1,0$ U/ml and $112,22 \pm 1,7$ U/ml, $p<0,001$, especially for obesity (respectively in patients group 3: $126,03 \pm 2,8$ U/ml and $431,26 \pm 4,6$ U/ml).

Conclusion. The rapid increase in the frequency of surgical interventions for calculous cholecystitis is caused by the fact that at present the GSD occurs often in people with normal weight and normocholesterolemia at the young age, including men. The main risk factor for GSD with normal body weight – the restrictive type of eating disorders, for stout people is overfeeding. Cytolysis is greater in the obese people. Operational tactics and perioperative period are without significant differences.

transferin2 (TfR2). Y250X mutation is revealed in a heterozygotic state in patients with PBC [7,14% is revealed, $c^2=10,57$, $p=0,0012$, OR=10,57 (95% C.I. 0,64-173,65)].

Thus, results of researching the HFE gene showed that H63D mutation in a homozygous state in a HFE gene is statistically significantly more often and is the risk factor for PBC development.

EXPERIENCE OF URSODEZ' USE IN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS

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Aims: an assessment of safety and efficiency of Ursodez use in treatment of patients with primary biliary cirrhosis (PBC).

Materials and methods. 7 women with PBC entered into research (age of 44 -71 years) with PBT history from 2 to 6 years. PBT is confirmed with biochemical tests, immunological (AMA) and instrumental methods. Overlap syndrome (PBC/AIH) was observed in 4 patients. All patients received various medicines with orsodeoxycholic acid (UDCA), one patient received prednisolone and two patients - budenofalk. Ssince April, 2012 Ursodez" (the pharmaceutical company "Northern Star", St. Petersburg) in a dose of 15 mg/kg/day within 12 weeks was appointed as a form of UDCA. Dynamic of clinical symptoms (fatigue, pruritus) in points from 0 to 5, biochemical tests (total bilirubin and fractions, ALT, AST, GGTP, AP, cholesterol, total protein, albumin and γ -globulins) at the 4th, 8th and 12th weeks was estimated. Side effects during therapy were registered too.

Results. Fatigue decreased from average value $2,0 \pm 0,2$ to $1,2 \pm 0,2$ points ($p<0,05$) in 12 weeks of Ursodez use in patients. The average value of point assessment of pruritus decreased a little, though changes weren't statistically reliable – from $3,1 \pm 0,6$ to $2,2 \pm 0,5$ points ($p>0,05$). The average total bilirubin levels at the beginning of supervision didn't exceed the cut-off ($19,0 \pm 3,1 \mu\text{mol/l}$) and its decrease at the 12th week of therapy was insignificant ($14,4 \pm 1,5 \mu\text{mol/l}$, $p> 0,05$). At the same time increased bilirubin levels dropped into normal at the 12th week of Ursodez use in three patients. Reliable decrease of GGTP [from $154,3 \pm 57,8$ U/l to $62,8 \pm 15,3$ U/l ($p>0,05$)] is besides noted. Other cholestasis markers authentically didn't change. Interesting there was a fact decrease in activity of inflammatory process. The average level of ALT decreased from $1,9 \pm 0,3$ UNL to $1,2 \pm 0,1$ UNL ($p<0,05$). Ursodez tolerance was similar to that of other drugs from the group.

Conclusions. Ursodez" as a form of UDCA showed efficiency in treatment of patients with PBC, good tolerance and may be recommended for wide use.

**CIRRHOSIS
AND COMPLICATIONS**



THE EXPERIENCE OF MANAGEMENT GROUP OF LIVER CIRRHOSIS PATIENTS WITH INDICATIONS FOR ITS TRANSPLANTATION

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One of important tasks of decompensated liver cirrhosis patient management is careful patient assessment before listing for liver transplantation, because its success demands optimal patient and time of the operation selection. The structure of pathology which is accepted as contraindication for listing liver cirrhosis patients, and waiting list patient dynamics analysis is of crucial importance, but the experience of this work in Russia is modest.

Materials and methods: Patients with end stage chronic liver disease with the indications for it transplantation admitted to the hospital liver unit from 2005 to 2010 (n=618) were included.

Results: After assessment according to accepted protocol of all patients with indications for it transplantation 196 (31.7%) of them were listed. The group of patients, who decline the operation included 57 (9.2%). Group of patients, in whom contraindications for liver transplantation were detected after clinical assessment, included 365 patients (59.1%). Among often findings, preventing from listing cirrhotic patients were alcoholism - 79 (21.6%) and cardiovascular system diseases - 51 (14.0%). Too severe decompensation, as a result of the late medical appeal, did not permit listing of 19 (5.2%) patients. Besides the disease progression this cases were complicated by infectious processes. Another 93 (25.5%) patients were not listed due to liver process stabilization. In spite of the fact that all this patients had sever decompensation of liver cirrhosis at the time of admission and were legal for listing on Child – Pugh and MELD score, the effective conservative treatment resulted in process stabilization and its regress in a number of cases.

Conclusion: The problem of decompensated liver cirrhosis patient listing for liver transplantation is a complicated decision, demanding full patient assessment, it should be made only after some period of the patient follow up, helping to conduct complete medical examination and to estimate the degree of decompensation reverse as the effect of conservativ

RENNIN-ANGIOTENSIN-ALDOSTERON SYSTEM AND DEVELOPMENT A RESISTANCE TO NONSELECTIVE BETA-BLOCKERS(BB) PORTAL HYPERTENSION(PH) WITH CIRRHOSIS

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As is known, the secondary hyperaldosteronism and activation RAAC with cirrhosis leads to deterioration of current of PH and development of complications, and also can lead to depression of efficiency of therapy of a PH by BB.

Aim: To study the influence of activity RAAS on the hemodynamic response to BB of PH in patients with cirrhosis.

Methods: 32 patients with cirrhosis (mean age 56 ±3,0) were studied. All patients were divided into two groups: the 1st group (n = 18) were administered with propranolol 40 mg titrated up, the 2nd group (n = 14) were administered with propranolol +spironolactone 100 mg. There were no significant differences on a degree of Child-Pugh in both groups (mean score 6,9). Hepatic venous pressure gradient (HVPG), renin and aldosteron plasma levels were measured before and after 4 weeks of treatment.

Results: Propranolol significant reduced HVPG at 10 patients 1st group (15,1±14,6 %,p=0,04). 8 patients 1st group were resistance to BB therapy(mean change of -1.7 ± 2.4 mm Hg).Aldosteron and renin plasma levels a prior to the beginning of therapy was significant above (942±534 vs 575±468 (p=0,047) and 590±439 vs 475±536 (p=0,51)) in the resistance BB group. There was a significant reduction in the HVPG in the propranolol + spironolactone group (-5.7 ± 3.9 mm Hg, p=0,02) as compared to the 1st group. 11 of 14 patients 2nd group significant reduced HVPG (p=0,003). 3 patients were resistance to BB and had aldosteron plasma levels exceeded norm in 2 times. At an estimation of interrelation between aldosteron plasma levels and a negative effect of therapy propranolol with method ROC- analysis, taps relative risk of a negative effect of therapy at patients with aldosteron plasma levels from 300 ng/ml and more = 1,75 (1,03-2,95, 95%DI), p=0,03 (sensitivity of 85,7 % and specificity of 55,6 % (AUCROC=0,651, p=0,1).

Conclusion: It is necessary to perform screening for detection of patients with high-aldosteron plasma levels in treatment resistant PH . With the purpose of rising of effect to treatment PH patients with baseline plasma aldosteron level above 300 ng/ml expediently in addition to appoint aldosteron antagonist.

PREVALENCE OF LIVER CIRRHOSIS IN GASTROENTEROLOGICAL PATIENTS

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Aims: The aim of the study was to learn the prevalence and etiology of liver cirrhosis (LC) in gastroenterological patients and causes of death in patients with alcohol and mixed (alcohol and viral) liver cirrhosis

Methods. We studied medical histories of all the gastroenterological patients, who were hospitalized in 2011 year.

Results. There were 1225 gastroenterological patients hospitalized in 2011 year. 116 (9,4%) patients had LC (male-71, female-45), mean age 48,7±12,7 yrs. 33 gastroenterological patients died. 25 (75,7%) died of LC, mean age 55,3±11,6 yrs.

Etiology of LC	Case		Died	Mortality,%
	n	%		
Alcohol	81	69,8	21	25,9
Mixed (alcohol and viral)	18	15,5	3	16,6
Others	17	14,7	1	5,8

Clinical forms	Case		Died	Mortality,%
	n	%		
Decompensated LC	79	68,9	3	3,7
Acute alcohol hepatitis (AAH) in patients with LC	36	31,1	21	58,3

Causes of death: acute liver failure in patients with AAH and LC – 17 patients, variceal hemorrhage – 3, comorbidities (hepatorenal insufficiency, acute encephalopathy and suicide, acute heart failure)- 5.

Conclusion: The prevalence of LC in gastroenterological patients was 9,4%. The most frequent cause of LC was alcohol (69,8%), mixed (alcohol and viral) etiology had 15% of patients. The mortality in patients with LC was 21% (25,9% in patients with alcohol LC, 16,6% in patients with mixed LC). The main cause of death was acute liver failure in patients with AAH and LC.

CASE REPORT: PORTAL VEIN THROMBOSIS COURSE IN LIVER CIRRHOSIS PATIENT

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Portal vein thrombosis is frequent liver cirrhosis complication with the incidence from 7 to 16% according to different data, increasing with the disease progression. Among liver transplantation waiting list patients this complication develops in 30%. In case of thrombosis of the portal vein or in the branches of the portal vein within the liver itself the possibility of liver transplantation can be estimated only after complete patient evaluation in terms of thrombosis extension.

Patient B. 48 y.o., male, has being followed up in Sverdlovsk Regional Hepatological Center for HCV associated liver cirrhosis, Child C (11 points), MELD - 17, portal hypertension (ascitis, splenomegaly), hypersplenism and listed for liver transplantation science 2010. The maintenance therapy included: diuretics, hepatoprotective medicine, PPI, rifaximine, lactulose, albumin i/v when indicated. From August 2011 deterioration of health started from abdominal pain, fever up to 37.7C, increase in the volume of stomach and the patient was admitted to the hospital liver unit. Serum blood tests reviled total bilirubin elevation up to 134 mcmol/L, hypoalbuminemia 28 g/L, INR elevation – 1.45 and thrombocytopenia 62x109/L. Portal, splenic and superior mesenteric vein thrombosis for the first time detected on abdominal CT in September 2011. For this reason sulodexide250 U t/d was administrated. Positive dynamic was found on control abdominal CT (January 2012) with thrombosis extension decrease showing only parietal thrombus in the portal and splenic vein.

Conclusion: In case of portal vein thrombosis in liver cirrhosis patient maximal early starting of the anticoagulant therapy may lead to thrombosis lysis and/or its recanalization. This effect is of paramount importance for keeping the cirrhotic patient alive and keeping the possibility of liver transplantation in the future.

POTENTIAL OF RADIOLOGICAL DIAGNOSING OF OSTEOPOROSIS AS LIVER CIRRHOSIS COMPLICATION

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Osteoporosis is one of life threatening complications of chronic liver disease in its terminal stage, which is often underestimated, whereas its significance determined by its consequences: vertebrae and peripheral skeleton fractures with decrease of life quality, patients invalidisation and mortality increase.

Aim of study: to determine the incidence of this complication in the group of liver cirrhosis patients with the signs of decompensation by using radiomorphometry diagnosing of osteoporotic corpus vertebrae deformations among patients with liver cirrhosis of different etiology.

Results: 89 cirrhotic patients were examined (64 female and 25 male, mean age 49.7±4.7), mean Child – Pugh score 9±2.4, MELD 13±4.1. According to etiology of liver disease all the patients were divided into groups: 32 patients (36%) – choletstatic cirrhosis, 35 patients (40%) – virus associated cirrhosis, 22 patients (24%) – alcohol liver cirrhosis. All the patients were examined by using radiomorphometry of thoracal Th4-Th12 and lumbar L1-L4 vertebrae. Osteoporotic corpus vertebrae deformations were found in 33 patients (37.1%), in 1 patient (1.1%) the signs of Shoerman-Mau disease, in 17 patients (19.1%) – osteochondrosis of vertebral column, in 1 (1,1%) deforming spondylolysis and in 37 patients (41.6%) no pathology found. No significant difference in the incidence of osteoporosis between different etiological groups was registered.

Conclusion: Among liver cirrhosis patients with the signs of hepatological decompensation examined by using radiomorphometry of vertebral column the incidence of osteoporotic corpus vertebrae deformations is as high as 37,1%. Higher incidence of this complication probably can be revealed in complex liver cirrhosis patient examination using other methods of osteoporosis detection.

DYNAMICS OF PORTAL BLOOD FLOW IN CIRRHOSIS

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The purpose of research - assessment of the impact the combination of standard therapy of liver cirrhosis with antihypertensives on the dynamics of portal blood flow.

A total of 24 patients with CP at the age of 29 to 58 years, with disease duration of 11 months to 10 years. The diagnosis was confirmed by clinical, laboratory and instrumental studies. Control (I group) - basic therapy CPU, II group - basis kardinorm + (2.5 mg / day), III group - base + ramipril (5 mg / day). Patients determined linear change (HP), volume (OS) rates in the portal (BB), splenic (SV) veins for 3 groups of patients.

Results: CPU most frequently, according to our research, in males (37.5%) aged 30 to 50 years (60%). LSVV concerning data on admission for groups I to 2,4%, II group at 7,4%, III group by 11.2% on the data control group - an increase that figure by 3.5% in group II and 4.9% in group III, respectively. LSSV increased data concerning admission to the group I to 4,3%, II group at 9,6%, III group by 15.4% on the data of the control group - an increase that figure by 4.1% in group II and 6.1% in group III, respectively. OSVVV increased data concerning admission to the group I to 5,1%, II group at 9,7%, III group by 16.2% on the data of the control group - an increase of 4.5% in group II and 3.7 % in group III, respectively. WWTP increased data concerning admission to the group I to 6,1%, II group at 8,3%, III group by 16.1% on the data of the control group - an increase of 3.6% in group II and 3.6 % in group III.

Conclusions: When the antihypertensive drugs (kardinorm (2.5 mg / day), ramipril (5 mg / day)) in the scheme of standard therapy showed a significant improvement in CPU speed parameters blood flow in the BB and CB. Kardinorm (2.5 mg / day) increased the LSVV by 7.4% in the NE - 9.6%, OSVV - by 9.7%, NE - 10.3%. Ramipril (5 mg / day) increased the LSVV by 11.2% in the NE-15, 4%, OSVV - by 16.2%, in the NE - 18.4%. A more pronounced effect on the performance results of portal blood flow provided ramipril (5 mg / day), which shows the usefulness of a combination of standard therapy with antihypertensive agents for the treatment of patients with HC.

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The purpose of research - assessment of the impact the combination of standard therapy of liver cirrhosis with antihypertensives on the dynamics of portal blood flow. A total of 24 patients with CP at the age of 29 to 58 years, with disease duration of 11 months to 10 years. The diagnosis was confirmed by clinical, laboratory and instrumental studies. Control (I group) - basic therapy CPU, II group - basis kardinorm + (2.5 mg / day), III group - base + ramipril (5 mg / day). Patients determined linear change (HP), volume (OS) rates in the portal (BB), splenic (SV) veins for 3 groups of patients. Results: CPU most frequently, according to our research, in males (37.5%) aged 30 to 50 years (60%). LSVV concerning data on admission for groups I to 2,4%, II group at 7,4%, III group by 11.2% on the data control group - an increase that figure by 3.5% in group II and 4.9% in group III, respectively. LSSV increased data concerning admission to the group I to 4,3%, II group at 9,6%, III group by 15.4% on the data of the control group - an increase that figure by 4.1% in group II and 6.1% in group III, respectively. OSVVV increased data concerning admission to the group I to 5,1%, II group at 9,7%, III group by 16.2% on the data of the control group - an increase of 4.5% in group II and 3.7 % in group III, respectively. WWTP increased data concerning admission to the group I to 6,1%, II group at 8,3%, III group by 16.1% on the data of the control group - an increase of 3.6% in group II and 3.6 % in group III. Conclusions: When the antihypertensive drugs (kardinorm (2.5 mg / day), ramipril (5 mg / day)) in the scheme of standard therapy showed a significant improvement in CPU speed parameters blood flow in the BB and CB. Kardinorm (2.5 mg / day) increased the LSVV by 7.4% in the NE - 9.6%, OSVV - by 9.7%, NE - 10.3%. Ramipril (5 mg / day) increased the LSVV by 11.2% in the NE-15, 4%, OSVV - by 16.2%, in the NE - 18.4%. A more pronounced effect on the performance results of portal blood flow provided ramipril (5 mg / day), which shows the usefulness of a combination of standard therapy with antihypertensive agents for the treatment of patients with HC.

NEW APPROACHES TO CORRECTION PORTAL HYPERTENSION IN PATIENTS WITH LIVER CIRRHOSIS

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Objective: To study the influence of drugs of β-blockers and and - ACE to correct GHG syndrome in cirrhotic patients.

A total of 24 patients with CP at the age of 29 to 58 years, with disease duration of 11 months to 10 years. The diagnosis was confirmed by clinical, laboratory and instrumental studies. Control (I group), basic therapy CPU, II group-basis kardinorm + (2.5 mg / day), III group-basis + ramipril (5 mg / day). Patients determined by the degree of GHG compensation stage, changing size of the liver, spleen, and the dynamics of high-speed performance of portal and splenic veins.

Results: Ultrasound signs of PG were found in 87.5% of patients. Cirrhotic patients with PH grade of 25%, Class C - 75%. Size of the liver of patients were increased in 91.7% of cases, reduced - in 8.3% of normal size were found. FFW right lobe: the II group increased by 6.8% compared to the data on admission, by 4.2% compared to group I, in group III increased by 12.4% compared to the data on admission, by 8.5% relative to the I group. IRR of the right lobe of the liver - for III group - increased by 7.1% compared to the data at admission and by 4.1% compared to I group. Dlinnik enlarged spleen about the data on admission for groups I to 2,9%, II group at 3,7%, III group by 5.9% on the data I group - an increase of 3.1% in Group II and 3, 9% in group III, respectively. The diameter of the spleen: III for the Group increased by 2.6% compared to the data at admission and by 2.9% compared to I group. Kardinorm (2.5 mg / day) increased the LSVV by 7.4% in the NE - 9.6%, OSVV - by 9.7%, NE - 10.3%. Ramipril (5 mg / day) increased the LSVV by 11.2% in the NE-15, 4%, OSVV - by 16.2%, in the NE - 18.4%.

Conclusions: The prevalence of patients with PH P indicates that the need for hospitalization, and conducting emergency intensive care occurs in complicated CPU. When the antihypertensive drugs in the treatment scheme of GHG in cirrhotic patients was considerable correction size of the liver and spleen, indicating intensification of the microcirculation in the studied organs. A more pronounced effect on correction GHG provided ramipril (5 mg / day), contributing to an improvement in renal blood flow as a factor involved in the formation of GHG CPU.

DYNAMICS OF PORTAL BLOOD FLOW IN CASE OF LIVER CIRRHOSIS

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Purpose of study – assessment of effect of the combination of the standard therapy of liver cirrhosis (LC) with antihypertensives on the dynamics of portal blood flow.

Materials and methods: 24 patients with LC at the age of 29 to 58 years, with disease duration of 11 months to 10 years were examined. I group (control), wherein patients received basic treatment (BT) of LC, which included hepatoprotectors, antioxidants, diuretics, vitamins, II group - BT + kardinorm (2.5 mg / day), III group - BT + ramipril (5 mg / day). Change in linear (LS) and volume (VS) speed of blood flow in the portal vein (PV), and splenic vein (SV) was determined in patients.

Results: According to our study the LC most frequently was in men (37.5%) aged 30 to 50 years (60%). Against the background of therapy by means of ultrasound and Doppler sonography the following dynamic changes were detected: in patients intaking the basic drugs (I group) the LSPV and LSSV increased by 2% and 4%, respectively, VSPV in this group rose by 5% and VSSV by 6%. In case of inclusion of antihypertensive drugs into the scheme of standard therapy of LC there was significant improvement in speed parameters of blood flow in PV and SV. Kardinorm (2.5 mg / day) increased the LSPV by 7.4%, in SV - 9.6%, VSPV - by 9.7%, in SV - 10.3%. Ramipril (5 mg / day) increased the LSPV by 11.2%, in SV-15, 4%, VSPV - by 16.2%, in SV- 18.4%. Thus, compared to the control group, LSPV and LSSV increased in group II by 3.5% and 5%, respectively, in III group – by 5% and 6%. In case of adding kardinorm and ramipril to therapy the VSPV and VSSV also tended to increase in comparison with controlling data, in II group - by 4.5% and 3.6% respectively, while in III group - by 4% and 3 , 6%.

Conclusions: ramipril (5 mg/day) had more pronounced effect on speed parameters of portal blood flow, which shows the usefulness of a combination of standard therapy with antihypertensive agents for the treatment of patients with LC.

NEW APPROACHES IN CORRECTION OF PORTAL HYPERTENSION IN PATIENTS WITH LIVER CIRRHOSIS

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Purpose of study: to study the influence of the drugs of β -blockers and ACE inhibitor on correction of portal hypertension syndrome (PH) in patients with liver cirrhosis (LC).

Materials and methods: 24 patients with LC at the age of 29 to 58 years, with disease duration of 11 months to 10 years were examined. I group (control), wherein patients received basic treatment (BT) of LC, II group - BT + kardinorm (2.5 mg / day), III group - BT + ramipril (5 mg / day). Degree of PH, PG decompensation stage, presence and occurrence of complications, changes in sizes of liver and spleen were determined in patients.

Results: According to our study the LC most frequently was in men (38%) aged 30 to 50 years (60%). US-signs of LC were detected in 88% of patients. Patients with LC with PH of Class B were 25%, C Class - 75%. Frequent complications: edematous ascitic syndrome - 100%, hepatic encephalopathy II-III degree - 95%, bleeding from the varicosity of the esophagus and the stomach - 67%, syndrome of hypersplenism - 62%. 92% of patients had an increase in liver size, normal size was not detected, and in the remaining cases the size decreased. Significant changes in the right lobe anterior-posterior dimension: were not detected in patients of group I, in groups II and III it increased by 7% and 12%, respectively. As for control values this indicator increased by 4% in group II and 9% in group III. Significant increase in inferior-superior dimension (ISD) of the right lobe (by 7% relative to the data at admission and by 4% relative to the control group) was only observed in patients in group III. APD and ISD of the left lobe of the liver were not significantly changed. Length of spleen was increased for group I by 3%, II by 4%, III group by 6%, as for data of I group - an increase by 3% in group II and by 4% in group III, respectively. Increase in dimensions of length were not reliable.

Conclusions: in case of inclusion of hypotensive drugs into scheme of PH treatment in patients with LC there is significant correction of liver and spleen dimensions. Ramipril (5 mg/day) had more pronounced effect on correction of PH.

FETAL HEMOGLOBIN CONCENTRATION IN LIVER CIRRHOSIS WITH PULMONARY HYPERTENSION

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Objective: to study changes in the level of Fetal Hemoglobin (HbF) in patients with Liver Cirrhosis (LC), depending on the presence of Pulmonary Hypertension (PH).

Methods. The concentration of HbF in the blood was studied in 98 patients with LC (56 men and 42 women aged 35 to 60 years). Application Control Group (CG) - 30 donors. For quantitative analysis of HbF developed and patented a way to rocket electrophoresis in agar gel. All patients underwent determination of the diameter of the pulmonary artery (PAD) and mean pulmonary artery pressure (PAP) using an ultrasonic scanner «ALOKA-5500 Prosound» (Japan).

Results: the content of HbF levels in patients with LC averaged $2.98 \pm 0.07\%$ of total Hb ($p < 0.001$ compared to control), and the excess of the normal concentration of HbF had in 72 patients. Compare values HbF in LC patients by gender showed that the content of HbF% in men was significant lower ($p < 0.001$), than in women (respectively $2.8 \pm 0.09\%$ and $3.35 \pm 0.1\%$). Increased average concentration of HbF% in women can be explained by higher compensatory capabilities of the female body, which are retained in spite of the LC development and its complications. In 49 patients with LC reported signs of PH, and an increase in PAD above 25 mm Hg PAP, of which 12 cases - within 30 to 35 mmHg in this sub-index of HbF averaged $3.02 \pm 0.03\%$. In 49 patients PAP was ≤ 25 mmHg, and the level of HbF - an average of $2.86 \pm 0.01\%$ of total Hb. The revealed distinctions between compared subgroups were statistically authentic.

Conclusion. Increased level of HbF in the blood as a marker of tissue hypoxia in adults with LC is associated with the presence of PH. Increased PAP is a consequence of hemodynamic changes in the pulmonary circulation in LC. PH can lead to a breach of the oxygenation of blood and the development of tissue hypoxia. HbF promotes a better adaptation than adult Hb to chronic hypoxia, which develops with LC.

EFFICIENCY ENDOSCOPIC SCLEROTHERAPY OF ESOPHAGEAL VARICES IN PATIENTS WITH LIVER CIRRHOSIS

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AIMS. Evaluate the efficacy of endoscopic sclerotherapy (ES) esophageal varices (EV) in patients with liver cirrhosis (LC).

PATIENTS AND METHODS. From 2006 to 2012 19 patients (10 men and 6 women) with LC in order to prevent a recurrence of bleeding from EV was performed 88 sessions of ES. 17 of them, it was held on as planned, the two - the next day after a conservative stop bleeding from EV. Everyone suffered from 2 to 6 sessions, during which 2-3 veins were sclerosal. Typically, the procedure is carried out under local anesthetic lidocaine. Sclerosant (most often - 1-3% aethoxysklerol, at least - 3% fibro-vein) of 2 ml were injected both intra- and paravasal. In 17 cases emerged bleeding from the puncture site was successfully halted by Blackmore tube.

RESULTS. In 2 patients was marked good effect ES 2-3 days after conservative stop bleeding from EV. Later they came to repeat courses, while not having relapses. Of the 17 planned patients received 12 sessions of repeated ES, 5 - after one and then not treated and their fate is unknown. In 8 patients with 3% aethoxysklerol effect was noted "trainspotting": vein slept almost immediately after the introduction of these drugs. Of hospitalization for repeat sessions of ES is 2-6 months. The efficiency was higher for shorter interval. For example, when applying 2 months rebleeding of EV were not noted. In three cases, there was a regression of them with F3 to F2, one - after 5 courses ES large varices were transformed into a slightly extended network trunks. In 3 patients emerged ulceration of the mucous membrane of the esophagus was effectively cured by anti-ulcer therapy. Recurrent bleeding occurred in three patients, two of them varices spread to the stomach. This was the indication for partial mesocaval bypass in two cases, and the distal splenorenal bypass in one.

CONCLUSIONS. ES is an effective method of preventing recurrence of bleeding from EV in cirrhotic patients.

THE USE OF METADOXIL IN PATIENTS WITH ALCOHOL LIVER CIRRHOSIS

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Aims: The aim of the study was to learn the effects of Metadoxil (Laboratori Baldacci S.p.A, Itali) in patients with alcohol liver cirrhosis (ALC). We examined encephalopathy according to the numeral test, distal polyneuropathy according to the Neuropathy Symptomatic Score (NSS), liver fibrosis measured by the Bonacini score, quality of life evaluated by the Health Status Survey (SF-36), biochemical tests and class of cirrhosis according to the Child-Pugh score before and after the study.

Methods: We included 23 patients with ALC, Child-Pugh class A– 8, class B – 11, class C -4. Male - 18, female - 5, mean age $52,3 \pm 9,3$ yrs. All the patients received Metadoxil 500 mg 3 times a day, for 4 weeks, they also received treatment of portal hypertension and hyperaldosteronism.

Results: Statistical comparison showed significant decrease in the total bilirubin level from $49,9 \pm 33,1$ to $34,8 \pm 27,2$ ($p = 0,02$) and GGT from 255 ± 160 to $170,4 \pm 141,3$ ($p=0,02$), there was a tendency to decrease in ALT (in 1,3 times), AST (in 1,5 times), alkaline phosphatase, significant decrease of Child-Pugh score from $8,8 \pm 2,2$ to $8,0 \pm 2,2$ ($p=0,002$), significant decrease of NSS from $2,07 \pm 1,3$ to $1,2 \pm 0,9$ ($p=0,02$). Quality of life improved: there was significant increase of Physical Functioning (PF), Role-Physical Functioning (RP), Mental Health (MH) Vitality (VT) by SF-36. There were no significant differences in numeral test and Bonacini score before and after the study.

Conclusion: Our study showed efficacy of Metadoxil in treatment of ALC. Metadoxil significantly improved quality of life, biochemical tests, and symptoms of distal polyneuropathy in patients with ALC, it also decreased Child-Pugh score of liver cirrhosis. Tolerance of Metadoxil was good in all patients.

PORTOSYSTEMIC SHUNT PLACEMENT – AS A “BRIDGE” PRIOR TO LIVER TRANSPLANTATION

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In recent years occurrence of liver cirrhosis (LC) increases. Radical treatment of LC is liver transplantation (LT). However, due to the shortage of donor organs in Russia - portosystemic shunt placement (PSSP) remains actual.

The purpose of the study. Study of short-term and long-term results of surgical decompression of the portal system in terms of shortage of donor organs for LT.

Materials and methods. The study involved 950 patients with portal hypertension of various genesis, of which 137 were operated, which amounted to 14.4%. There were 66 men (48.2%), average age $43,6 \pm 11,03$, women - 71 (51.8%), average age $45,7 \pm 10,3$. In most cases, the cause of the portal hypertension was LC of different etiology - 106 patients, 31 patients were with subhepatic block of portal system.

Results and discussion. Among 106 operated patients with LC class A involved 10 (9.4%) persons, class B - 80 (75.5%), Class C - 16 (15.1%). In the course of PSSP we carried out term-lateral splenorenal anastomosis by type « side-to-end» with diameter of 12-13 mm. With this type of anastomosis there is sufficient decrease in portal pressure without worsening effects of hepatic encephalopathy and prevention of bleeding from PSSP.

Since 2009, our center performed 26 LTs, of which 5 (19.2%) for patients passed surgery PSSP in a period of 3 to 7 years after surgery. At the same time the separation of portosystemic shunt was not carried out. Any effect on the post-operative period after liver transplantation was not observed.

Survival rate, calculated using the Kaplan-Meier method, for patients passed surgery of PSSP in 1 month was - 89.8%, 1 year - 85%, 3 years - 79.3% 5 years - 78.1%. Recurrence of bleeding of varicosity of esophagus and stomach after PSSP was observed in 9 (6.6%) patients in the first year after surgery.

Conclusion. In terms of the shortage of donor organs the PSSP is the operation of choice, allowing prevent bleeding of varicosity of esophagus and stomach and increase the life of patients on the waiting list.

THE SIGNIFICANCE OF ETIOLOGY IN SEVER DECOMPENSATED LIVER CIRRHOSIS PATIENTS SURVIVAL PROGNOSIS

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Survival prognosis in sever liver cirrhosis decompensation is highly important in clinical practice. Cirrhosis decompensation demands urgent hospitalization and intensive care. It is not established now whether liver disease etiology plays role in decompansation severity. Child and MELD scores are wide used for survival prognosis estimation and the higher its level, the higher possibility of patient’s death.

Aim: To estimate the influence of liver disease etiology on survival prognosis in the group of decompensated liver cirrhosis patients admitted to the hospital by using Child and MELD scores.

Results: 87 decompensated liver cirrhosis patients with different etiology were included in the study. In the group of virus associated cirrhosis $n=52$ (59.8%) the mean Child score was 10.4 ± 1.2 and MELD 18.2 ± 6.5 . Among patients with cholestatic cirrhosis $n=10$ (11.5%) the mean Child score 10.4 ± 2.1 , MELD 16.3 ± 1.8 . In the group of alcohol cirrhosis $n=25$ (28.7%) mean Child was 10.8 ± 1.6 and MELD - 19.6 ± 6.1 .

Conclusion: The highest Child and MELD score at the time of admission were revealed in the group of alcohol liver cirrhosis patients. So the most unfavorable etiology factor of liver cirrhosis decompensation is alcohol compare to viral and cholestatic etiology.

STUDY OF CORRELATION OF THE HEPATOPRIVE SYNDROME PARAMETERS WITH OF STUDIED PARAMETERS IN PATIENTS WITH CIRRHOSIS AND CHRONIC LIVER INSUFFICIENCY.

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Purpose: study correlation of parameters of the hepatoprive syndrome (HS) with other studied parameters and clinical and laboratory data in patients with liver cirrhosis (LC) and chronic liver insufficiency (CLI).

Materials and methods. Eighty patients with LC of various etiology, class B and C on Child-Pugh scale (41 men and 39 women), middle age $54,95 \pm 1,09$ years, with clinical and laboratory data of CLI are surveyed. Parameters of the main clinical and laboratory hepatological syndromes, serum levels of macroelements (Na+) are studied. The correlation analysis (according to Pearson) of HS parameters with bilirubin level, Na+ and assessment LC with Child-Pugh and MELD score was made.

Results: Direct correlation of a hypoalbuminemia with low sodium levels ($r=0,298$, $p < 0,01$) and with a hypocholesterolemia ($r=0,484$, $p < 0,001$) and feedback correlation of albuminemia with total bilirubin levels ($r=-0,407$, $p < 0,001$), with ascites ($r=-0,533$, $p < 0,01$), with class of Child-Pugh (to $r=-0,569$, $p < 0,001$) and MELD score ($r=-0,403$, $p < 0,001$) is established. The prothrombin level directly correlates with sodium ($r=0,212$, $p < 0,05$) and with a cholesterol levels ($r=0,326$, $p < 0,05$) and feedback correlates with bilirubin level (of $=-0,573$, $p < 0,001$), ascites ($r=-0,393$, $p < 0,01$), and Child-Pugh class (to $r=-0,584$, $p < 0,001$) and MELD score points ($r=-0,672$, $p < 0,001$). The HS parameters directly correlates with each other.

Conclusions: Correlation analysis revealed in patients with liver cirrhosis and chronic liver insufficiency a direct dependence of the HS parameters with low sodium levels and a feedback with a hyperbilirubinemia, cirrhosis class by Child-Pugh and points of MELD score. Low sodium levels and hyperbilirubinemia are estimated as negative predictive factors for patients with liver cirrhosis and chronic liver insufficiency.



OTHER DISORDERS

ENDOSCOPIC PAPILOSPHINCTERTOMY IN PATIENTS OF ELDERLY AND SENILE AGE

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A significant proportion of patients that require EPST are persons of elderly and senile age, in who have a number of peculiarities connected with carrying out the survey. The majority of these patients have severe concomitant pathology, limiting the possibility of premedication, anesthesia, and the duration of the endoscopic procedures. EPST in the analyzed group of patients was conducted in 184 patients, which amounted to 69.4% of all EPST performed during this period of time. The group consisted of 53 (28,8%) men and 131 (71,2%) women. Age: 64 (34,8%) patients - 61 – 70 years, 81 (44,0%) patients - 71 - 80 years, and 39 (21,2%) of the patients were older than 80 years.

The content of bilirubin in the blood plasma was not increased only in 8.6% of the patients. Atypical localization of holes in MDP was diagnosed in 29 (15,8%) patients. In 14 (7,6%) of them papilla hole was located in parapapillar diverticulum of duodenal intestine and in 15 (8,2%) patients - in the rim of diverticulum, which significantly complicated the implementation of EPST.

The diameter of the common bile duct in 4.7% of patients was less than 6 mm, in 16,0% - from 7 to 10 mm, in 43.2% - 11-15 mm, in 26.6% -16-20 mm, and in 9.5% - 21-25 mm.

The cause of jaundice was stones in common bile duct in 140 (76.1% of patients), 21 (11,4%) - microcholelithiasis, in 1 (0,5%) - tumor in common bile duct, in 2 (1,1%) patients with adenoma of MDP, in 2 (1,1%) - tumor of the pancreas and in 10 (5,4) patients –stricture of terminal part of common bile duct. In 8 (4,4%) patients the cause of the jaundice has not been determined.

In elderly and senile age of the patients there has been diagnosed higher concentration of bilirubin in the blood, the greater diameter of the common bile duct, more frequent atypical location of holes in MDP, making it difficult to facilitate EPST.

POSSILITIES OF PROBIOTIC THERAPY OF THE PATIENTS WITH INTESTINAL DYSBIOSIS IN COMBINATION WITH CORONARY HEART DISEASE

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The purpose of the research is to study the effect of probiotic therapy on the clinical course of coronary heart disease of patients with intestinal dysbiosis.

Materials and methods. We observed 65 patients with CHD in combination with intestinal dysbiosis. To diagnose, all patients were examined according to the alleged disease record. In terms of the appointed therapy patients were divided as follows: the first group (n = 32) patients received standard therapy of CHD, the second group (n = 33) patients received additionally probiotic bifiform 1 capsule 3 times daily during one month in order to correct intestinal dysbiosis.

Research results. Before treatment, the coprogram of all patients detected creatoreya, steatorrhea, impaired digestion of fiber was noted. After treatment, the decrease tendency in the creatoreya and steatorrhea was observed in patients treated by probiotic therapy, whereas in the comparison group data remained at the same level (p <0.05). Thus, the inclusion in the standard CHD therapy schemes of the correction means of intestinal microflora reduces the severity of scatological changes in patients with coronary heart disease associated with intestinal intestinal dysbiosis. In the analysis of complaints by the cardiovascular system in patients with coronary heart disease associated with intestinal dysbiosis was observed positive clinical dynamics of recourse against the physical manifestations of coronary heart disease. There was a significant decrease in frequency of pain of the heart, reducing breathlessness and palpitations in patients of 2nd group.

Conclusion. Thus, the inclusion in the standard CHD therapy schemes of the corrections of intestinal microbiota contributes not only to reduce the severity of scatological change, but also relief of clinical symptoms of coronary heart disease.

HOW CAN WE OBTAIN FIBROSIS OUT OF LIVER STIFFNESS AND BIOCHEMICAL TESTS?

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Background: Liver stiffness (measured by transient elastography (Fibroscan®)) is one of the newest and most verified noninvasive imaging based methods for the assessment of liver fibrosis. Fibrotest® is a marketed biochemical score with also a lot of well documented studies behind. We aimed to verify how these two tests are correlated with liver biopsy and with each other.

Methods and Patients: We analyzed retrospectively 230 patients for which we had available liver biopsy (LB), Fibroscan (FS) and Fibrotest (FT) and complete blood count performed in an interval of maximum one week. The patients were suffering either of B hepatitis or of C hepatitis.

Results: Best correlation was found between FS and biopsy (r=0.854, p<0.001). FS and LB were also well correlated (r=0.715, p<0.001), while FS and FT were poorer correlated (r=0.449, p<0.001).

Taken by etiology, the correlations maintain, but are stronger in C hepatitis: LB and FS (r=0.854 versus r=0.843, p<0.001 and p<0.001 for C respectively B hepatitis), LB and FT (r=0.776 versus r=0.551, p<0.001 both), FS and FT (r=0.516 versus r=0.0.278, p<0.001 versus p<0.005 for C respectively B hepatitis).

Liver stiffness was significantly correlated with the results of alpha 2 macroglobulin, GGT, ALT, AST, serum glucose level, and inversely correlated with haptoglobin, cholesterol and platelet count (r = respectively 0.375, 0.415, 0.255, 0.383, 0.281, -0.204, -0.247, -0.305, all with statistic significance, with p lower than 0.002).

When combined, FS and FT have an AUROC of 0.92 in predicting significant (>2) fibrosis.

Conclusions: Both noninvasive methods performed well in predicting separately the fibrosis. Used together they have an even higher sensibility and specificity.

ARTERIAL HYPERTENSION FREQUENCY IN WOMEN WITH GALLSTONE DISEASE

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Aim. To determine arterial hypertension (AH) frequency and grade in women with gallstone disease (GSD) in an open clinical study.

Materials and methods. In an open clinical study using the continuous set there were included 26 women with GSD (mean age 49,9±1,6 years) admitted to the surgical department for routine laparoscopic cholecystectomy. The diagnosis of GSD was confirmed by ultrasound. The control group consisted of 8 women with stable hypertension with verified absence of GSD by ultrasound. All patients with AH (diagnosed in accordance with the recommendations of ESH/ESC (2007) and RSMH/RSSC (2008)) received continuous antihypertensive therapy with ACE inhibitors and angiotensin II receptor antagonists, beta-blockers, calcium channel blockers, diuretics. Blood pressure was defined as the average of the two blood pressure measurements by Korotkov mercury sphygmomanometer performed in the sitting position, after fifteen minutes rest, every five minutes. Statistical analysis was performed by SPSS (11,0).

Results. AH was found in 11 (42.3%) patients with GSD. The average age of women with GSD combined with AH and women with GSD without AH did not differ (52,5±2,3 and 48,5±3,5 years, p> 0,05). Age of AH in women with GSD combined with AH and hypertensive patients without GSD was similar: 12,2±3,2 and 10,9±4,8 years respectively (p> 0,05). Prevalent AH among the examined patients with GSD was grade 3 (90,9%), grade 2 AH was identified in 9,1% of cases. Grade 3 AH was detected more frequently in women with GSD combined with AH compared to women with AH without GSD (90,9% and 62,5% respectively, p = 0,1).

Conclusions. AH was found in 42,3% of women with GSD, and AH grade 3 prevailed in women with GSD combined with AH.

PAIN AND DYSPEPTIC SYNDROMES FREQUENCY IN WOMEN WITH GALLSTONE DISEASE COMBINED WITH ARTERIAL HYPERTENSION

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Aim. To estimate abdominal pain and dyspeptic syndromes frequency in women with gallstone disease (GSD), combined with arterial hypertension (AH).

Materials and methods. In an open clinical trial using the continuous set there were included 26 women, of which 11 patients with GSD in combination with AH and 15 patients with GSD without AH. Both subgroups were similar for age (52,5±2,3 and 48±2,1 years respectively, p>0,05). The diagnosis of GSD was confirmed by ultrasound. All patients with AH (ESH/ESC (2007) and RSMH/RSSC (2008) criteria) received continuous antihypertensive therapy. Statistical analysis was performed by SPSS (11,0).

Results. painful form of GSD in all patients with GSD combined with AH was marked (in patients with GSD without AH painful form of GSD occurred in 13,3%, p <0.05). In 18,2% of women with GSD combined with AH cholelithiasis was complicated by obstructive jaundice in anamnesis (against 6,7% of women with GSD without AH, p>0,05). Women with GSD combined with AH more often used spasmolytics and analgesics compared to women with GSD without AH (p=0,008). increasing of abdominal pain after laparoscopic cholecystectomy compared with the preoperative period, was noted by 18,2% of women with GSD combined with AH and 13,3% of women with GSD without AH (p>0,05). Dyspeptic symptoms (nausea, heartburn, belching air, food or acid regurgitation, bloating and rumbling in the abdomen) occurred in women with GSD with and without AH equally often (p>0,05).

Conclusions. painful form of GSD in women with GSD combined with AH was found in 100% of cases, these patients had significantly more frequent analgesics use than patients with GSD without AH. Dyspeptic syndrome occurred equally frequently in women with GSD with and without AH.

CLINICAL OBSERVATION OF THE LIVER'S FORM ANOMALY DURING 10 YEARS

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We managed to make a dynamic observation of patient G. with the anomaly of the liver that occurs rarely. Riedel's lobe is one of the variants of such anomalies.

In 2002 forty five-year-old patient was delivered to the hospital with a complaint about heaviness in the right subcostal area and in the right part of meso- and hypogastrium. He had been disturbed by such a pain for 6 years. He was treated without any clear effect in connection with a chronic cryptogenic hepatitis with a minimal activity, chronic cholecystitis. Pylorostenosis took place in the neonatal period. There weren't any abdominal injuries. Palpation identified that the entire right part of the abdominal cavity was occupied with a dense formation of a size 10x15 cm. Vertical cylindrical painful formation of a size 7x3 cm was being palpated in the right iliac area. One-and-a-half increase in ALT and alkaline phosphatase was detected. Markers of viruses B and C were negative ones.

Sonography, CT, scintigraphy of the liver revealed additional liver lobe, which occupied the right part of the abdominal cavity up to the opening into a small pelvis. Fibrogastroduodenoscopy indicated additional Vater's papilla. Cholecystography showed that gall bladder descended into the small pelvis, it was enlarged, had several constrictions, and there was a diverticulum at its bottom. Dopplerography displayed atypical structure of the portal system's veins in a form of separate trunks, arcual anastomoses between those trunks and the hepatic veins. Puncture liver biopsy demonstrated chronic hepatitis with a minimal activity.

In 2010 cholecystectomy was performed in connection with a cholelithiasis. Puncture biopsy from the both parts of the liver was performed once again after the patient's re-admission to the hospital in 2012. Increasing inflammatory infiltration in portal tracts, the amplification of the dysplasia of hepatocytes were found in the upper part of the liver. Chronic cholangitis with a sclerosis around the bile ducts was being developed in the lower part of the liver.

Clinical diagnosis: chronic hepatitis with a minimal to moderate activity on the background of the anomalies of the liver (additional portion). Removed gall bladder.

APOE GENE POLYMORPHISM AND PAIN AND DIARRHEA SYNDROME IN PATIENTS WITH METABOLIC SYNDROME AND WITH GALLSTONE DISEASE COMPLICATED BY BILIARY-DEPENDENT CHRONIC PANCREATITIS

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Purpose. To evaluate occurrence of alleles of gene of apolipoprotein E (Apo E) and possible association with pain (PS) and dyspeptic syndrome (DS) in patients with metabolic syndrome (MS) in combination with gallstone disease (GSD).

Materials and methods. 106 patients were examined, including 67 patients with MS (ATP-III, 2001) in conjunction with GSD and 39 patients with MS in combination with GSD complicated by biliary-dependent chronic pancreatitis (bHP). Polymorphism of the encoding part of gene of APOE was studied by PCR. Statistical processing of data was performed using the program SPSS (11.0).

Results. Among examined patients with MS and GSD the APOE ε2 allele was detected in 9.0% of persons, ε3 - in 76,2%, ε4 - in 14.8%. Patients with MS and GSD complicated by bHP, the occurrence of corresponding allele was 7.7 %, 76.9% and 15.4%. Among the patients with MS and GSD the carriers of allele ε2 had positive association with the PS in the right hypochondrium (p <0,05), heartburn (p <0,05), bitter taste in the mouth (p <0,05), while the ε4 allele carriers had positive association with bitter taste (p <0,05), bloating (p <0,05), nausea (p <0,05). Patients with MS and GSD complicated by bHP had positive association of allele ε4 with the PS in the left hypochondrium (p <0,05), with a PS in the right hypochondrium (p <0,05), nausea (p > 0, 05).

Conclusions. The occurrence ε2, ε3, ε4 allele of APOE in patients with MS and GSD is 9.0, 76.2 and 14.8%. Among the patients with MS and GSD the presence of ε2 allele is associated with the PS and DS, and the presence of allele ε4 - only with the DS. In patients with MS and GSD complicated by biliary-dependent CP, ε4 carriers are associated with pain syndrome.

ANALYSIS OF RISK FACTORS CONTRIBUTIS TO THE DEVELOPMENT OF CHOLELITHIASIS

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Purpose: To study the risk factors and to determine their significance in the development of gallstone disease (GSD).

Materials and methods. The study involved 396 patients with a first (pre-stone) stage of cholelithiasis. There were 156 men and 240 women aged 22 to 70 years. The diagnosis was verified on the basis of echographic study of the gall bladder, duodenal multifractional tubing and study of the biochemical composition of bile. In addition to carefully study the anamnesis data, all patients underwent anthropometry (to determine the type of constitution and body mass index - BMI). For all studied factors was calculated their relative risk (RR) for gall stone formation - the ratio of a/n1 b/n2, where a - the frequency of occurrence of this factor among patients, b - the frequency of occurrence of this factor among the control group, n1 - the number of patients, n2 - the number of the control group, which consisted of 50 healthy volunteers aged 20 to 50 years.

Results of research. We found the following values of RR (in points): BMI more than 26 - 4.57, more than three pregnancies ended or incomplete delivery - 4.62, hypodinamya - 4.25, non rational nutrition (violation diet, overeating or starvation, using a lot of animal fat) - 3.94, age older than 45 years - 3.67, female gender - 3.16, frequent stress situations, conflicts in the family, at work - 2.8, genetic burden of CL-2, 05, the hyperthemic type of constitution -2.15, smoking - 1.56, alcohol using - 1.25.

Conclusion. The most significant in the development of cholelithiasis are such social and hygienic factors as high BMI, the lack of nutrition, hypodinamya, from the medical and biological factors the greatest importance in the development of cholelithiasis have multiple pregnancies and delivery. The obtained data will allow to reveal patients with high risk of cholelithiasis and begin early prophylactic and treatment and to prevent the development of cholelithiasis.

AGE-RELATED CHANGES OF LIVER STIFFNESS IN NORMAL RATS ACCORDING TO THE METHOD OF ULTRASONIC SHEAR WAVE ELASTOGRAPHY.

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Ultrasound shear wave elastography (SWE) is the newest biophysical method for noninvasive quantitation of liver stiffness (LS), which strongly correlates with the accumulation of connective tissue in the liver (fibrosis).

Materials and methods: We first studied age-related changes of LS in normal rats (n=30) which were divided on 3 groups: I - 3-month (n = 10), II - 12-month (n = 10) and III - 20-month animals. SWE was performed using Ultima PA ultrasound machine (Radmir, Ukraine), with a 10–5 MHz linear transducer in the right and left lobes of rat liver. To assess the functional state of the liver we examined levels of serum enzymes: ALT, AST, total, indirect and direct bilirubin. In the samples of liver tissue determined the content of total lipids and triglycerides and morphometry was performed.

Results: A valid LS determination (success rate of at least 60%) was observed in 96.6% animals of different age groups. The intraobserver reproducibility of SWE was excellent - ICC 0.889 (95% CI 0.778-0.946). We observed statistically significant increasing of LS between 3-month and 20-month rats (p=0.010), but its value in each group do not exceed normal or reference range. This can be seen as age-related drift of liver tissues - especially its connective tissue elements. Another possible reason is accumulation in the liver parenchyma total lipids, or some of their subclasses with age.

With age activity of transaminases was significantly decreased (p <0,001) on 27.5% and 36.1% in 12-month and 20-month respectively, compared with 3-month animals. The concentration of total lipids in the liver of rats increased with age, while the content of triglycerides decreased significantly. It is noted that with age there is suppression of the functional properties of the liver parenchyma. Conclusion: Ultrasound shear wave elastography is a new objective biophysical method to obtain information about the state of LS in laboratory rats. In normal rats LS is in the range 4.0–5.7kPa.

FEATURES OF HISTORY OF CHRONIC PANCREATITIS

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Aims: to carry out the analysis of history of different forms of chronic pancreatitis (CP).

Materials and methods. The analysis of clinical histories of 85 patients [39 – chronic pseudotumor pancreatitis (CPP), 21 – chronic calcificating pancreatitis (CCP), 25 – chronic infiltrative and fibrous pancreatitis (CIFP)] treated in gastroenterological department of A.Novak Uzhgorod regional clinical hospital.

Results. Among observed patients there were: women - 25%, men - 75%. Ratio of men/women at CPP - 5,5, at CCP – 6, at CIFP – 1,08. In CPP 61,5% of patients had disease duration from 6 months to 5 years. In CCP and CIFP duration of a disease made from 1 month to 10 years. There were no correlation between current features of CP and disease duration. In clinical presentation of CPP pain occurred in 82% of patients, fatigue and weakness – 56%, weight loss – 44%, an unstable stool – 36% of patients. In CCP pain occurred in 76%, fatigue and weakness – 57%, weight loss – 52%, an unstable stool – 48% of patients. In CIFP pain occurred in 84% of patients, fatigue and weakness-68%, 44% - an unstable stool, 40% - abdominal distention. Gastopathy revealed on endoscopy in 56, 52, and 40% of cases in CPP, CCP, and CIFP respectively.

Conclusions:

1. Chronic calcificating and infiltrative and fibrous pancreatitis observed in 5,5-6 times more often in men than in woman.

2. Pain appears as a symptom in 76-84% of patients and is a dominating symptom in different forms of chronic pancreatitis. In chronic pseudotumour pancreatitis and calcificating pancreatitis (CCP) 44-52% of patients a significant weight loss is notable. The unstable stool is equally expressed in all patients with chronic pancreatitis.

3. A gastopathy appears in 40-56% of patients with chronic pancreatitis (more often in CPP).

EFFICIENCY RATING OF PREVENTIVE BALNEOFACTOR ACTION IN TOXIC LESIONS IN THE EXPERIMENT

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There have been carried out experimental researches of preventive influence of mineral waters of different chemical composition on animals (rats, mice) while forming the models of subacute toxic lesions by carbon tetrachloride and formalin in combination with ethanol.

Data and methods: Experimental animals took mineral waters such as “Yessentuki №17” and “Krasnoarmeiski new” 1,5ml per 100 g of body weight once a day during 21 days. The animals were also given oral introduction of succinic acid in the form of 1% aqueous solution and drank freely daily during 21 days. Subacute toxic lesions were modeled within 21 days: 1. Carbon tetrachloride (CT) per os 0,4 ml per 100 g of animal weight every other day. 2. Combined model - introduction of 40% formalin solution per os 0,4 ml per 100 g of animal weight every other day and simultaneous daily free drinking of 10% ethanol solution by the animals. Clinical (leukocytes, leukogram), and biochemical blood values (glucose, creatinine, AST, ALT, cholesterol, alkaline phosphatase, crude protein) were studied. The analysis of the main and small populations of mice lymphocytes venous blood was carried out with the help of cytofluometry method using the following panel: CD3+CD19-, CD3+CD4-, CD3+CD8 +, CD3+Angezim I-AK MHC, CD3+NK (Beckman Coulter, USA). Histologic study was also conducted.

Results: At histologic research of lesion degree by the studied factors there has been detected their similar impact on rat organism. Data of clinical, biochemical and immunological indices of animals' blood confirm the direction of metabolic disorder changes under the influence of mineral waters of different chemical composition and mineralization – native “Yessentuki No. 17” and “Krasnoarmeiski new” and their complexes with succinic acid.

Conclusion: It was the first time when new experimental data of preventive effects of mineral waters with animals having metabolic disorders and suffering from subacute toxic lesions of various geneses have been obtained. It has also been shown that low-mineralized waters in severe pathologies can be applied in modifications but it is not advisable to use average mineralized water.

EXPERIENCE OF THERAPY WITH “REZALYUT PRO”

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Aims. To investigate effect of the drug “Rezalyut pro” in lowering cholesterol levels and hepatoprotection.

Material and methods. Forty patients (28 women, 12 men) aged from 25 to 55 years, who demonstrated aminotransferase levels increase (≤ 2 N), a hypercholesterolemia of different types (Fredriksen), in $\approx 50\%$ -increase γ - GT, in the absence of hepatitis B or C markers in outpatient status. All patients appointed the drug “Rezalyut pro” 2 capsules 3 times per day for 4-8 weeks.

Results and discussion. In control research aminotransferases levels turned into normal in 45% patients, significant positive dynamics noted in 35%, in 20% patients biochemical tests worsened. Decrease of total cholesterol (TC) level occurred in 40% of patients, LDLP - in 60%, triglycerides (TG) - in 25%, HDLP levels increase –in 40% of patients who have mainly IIb type of hyperlipidemia. Fifty percent of patients demonstrated improvement of γ - GT: in 15% of patients positive dynamics is noted. Dynamics of biochemical tests considerably varies in comorbid liver injury and disturbance lipid metabolism (metabolic, hormonal, drug etc.) that it is necessary to consider at purpose of complex therapy (ursodeoxycholic acid (UDCA), statins etc.). The smallest effect is noted in patients with subnormal ($\leq 1,5$ N) aminotransferase levels, high levels of TC (2-3 N) and very high TG levels (> 3-4N) with signs of cholestasis (increase of alkaline phosphatase, γ - GT).

Conclusions: 1. It is necessary to consider type of hyperlipidemia when starting hypolipid therapy 2). The most successful treatment is noted in patients with type IIb of gradation. 3). The drug “Rezalyut pro” combining properties of a hepatoprotector with lowering lipids levels effect and is rather effective in treatment liver injury in combination with a hypercholesterolemia. 4). Combined therapy (“Rezalyut pro” + UDCA, “ Rezalyut pro “+statins) yields the best results in more short-term terms with the steadiest effect.

ROLE OF COMBINED THERAPY WITH HEPATOPROTECTOR ROPREN AND POLIPROTEN “NEFRO” IN TREATMENT AND PREVENTION OF COMPLICATIONS OF CHEMOTHERAPY IN PATIENT WITH RECTAL CANCER WITH LUNG METASTASIS.

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Aims. To study dynamics of a clinical presentation and biochemical test in the combined therapy with new domestic hepatoprotector Ropren and the product of the increased biological value (PIBV) Poliprotten of “Nefro” in in patient with rectal cancer and lung metastasis.

Materials and methods. There was a 56 y.o. patient, addressed in Lenmedtsentr for body weight correction (weight 88 kg, height 163 cm, BMI 33,1), who complained to discomfort in the right upper quadrant, aching pain in the lumbal and sacral region, tendency to constipation, unexplained fatigue in the evenings. Examination showed an increased ALT level (55 U/ml). The Fibromax test demonstrated signs of steatosis, other test appeared to be normal.

An ultrasonography revealed hepatomegaly (mainly of the right lobe). Infiltrative mass in rectum, with contact bleeding and rigid walls was found during colonoscopy. Histologically - low differentiated rectal adenocarcinoma. Secondary changes in lungs are revealed by chest CT. Distant radiotherapy was carried out (dose of 50 Gr at 04.04.12), and followed by operative care - an abdominal-peroneal rectum extirpation 31.08.12 [p T4N1M1 (lungs)] and further courses of chemotherapy.

Ropren and the diet enriched with PIBV Poliprotten “Nefro” were added to therapy. From the moment of receipt in Lenmedtsentr (9 months of chemotherapy with Ropren 3 drops 3 times per day) patient feels well, have an active living, her status condition considerably improved. Tolerance of all types of therapy (radiotherapy, operation, chemotherapy) is well too. ALT levels after 2 months of Ropren administration appeared to be normal and remains steadily without change.

Conclusions: this case testifies to efficiency of the combined application of a hepatoprotector Ropren and PIBV Poliprotten “Nefro” and expediency of further studying of the therapy offered by us, as for the purpose of prevention of toxic liver injury in chemotherapy, and for the purpose of development of the standard of treatment of oncological patients. This therapy can be appointed in the early preoperative period and precede any therapy concerning a colorectal cancers.

RESEARCH OF INCIDENCE ЖКБ AT DIABETES ON THE EXAMPLE OF POLICLINIC OF NO. OF 1 G OF YAKUTSK

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Urgency. The World Health Organization reports that now in the world of 6 % of the population are sick with diabetes, these are about 284,7 million people. Forecasts for the future are unfavourable, according to experts, the number of patients will steadily grow, and by their 2030 there are already 438,4 million. It is known that the disease of ZhKB meets at any age, at women in 2-7 times, is more often than at men. In 51,7 % gallstones appear during pregnancy and at 25 % after the delivery (Himal H. S., 1996), and as is accompanying pathology at diabetes.

Purpose. To study incidence of a zhelchekamenny illness (ZhKB) at diabetes on an example of polyclinic of No. of 1 g of Yakutsk.

Research materials. As materials of research out-patient cards of an endocrinological office of polyclinic of No. of 1 g of Yakutsk are taken.

264 out-patient cards of patients with the diabetes, being on the dispanserny account (2012) are worked: from them it is revealed 20 (7.6 %) patients with ZhKB (19 women and 1 man) at the age from 35-40 years 1 (5 %) the person, from 50-60 years 10 (50 %) the person, 60-70 years 5 (25 %) person, 70-80 years 4 (20 %) person. All patients have a diabetes of the II type. Radical inhabitants - 6 (30 %), not radical - 14 (70 %). Duration of a disease of ZhKB over 10 years.

Results. At ultrasonic research are revealed mechanical jaundice - 1 (5 %) the patient, kalkulezny cholecystitis - 20 (100 %), chronic pancreatitis – 10 (50 %), diffuzny changes parenchymy a liver - 6 (30 %), a hepatomegaliya - 3 (15 %), fatty hepatosis – 4 (20 %). Clinical manifestations of ZhKB in a look: a pain syndrome at 18 (90 %), manifestations of a biliarny dispepsiya at 10 (50 %) patients, violation of a motility of a thick gut it is diagnosed at 16 (80 %) patients. Superfluous mass of a body and obesity at 15 (75 %) the person. At laboratory research increase of level of GGTP, ShchF, glucose is defined. The maintenance of ALT, nuclear heating plant - within norm. Treatment concerning ZhKB has been carried out: laparoskopichesky HE – 3 patients, conservative litolitichesky therapy by preparations of bilious acids - 12 patients, refusal of treatment – 5 patients.

Conclusions. ZhKB is diagnosed for every seventh patient with diabetes, in a clinical picture dispepsichesky manifestations prevail, late identification demands the purposeful diagnostics promoting timely identification of ZhKB, to carrying out the differentiated adequate therapy by the patient.

LIVER INJURY IN PATIENTS WITH NFLAMMATORY BOWEL DISEASES

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It is known that one of the systemic manifestations of inflammatory bowel disease (IBD) is a liver injury of various kinds: steatohepatitis, autoimmune hepatitis, sclerosing cholangitis.

The purpose of study is determination of occurrence and nature of liver injury depending on the form of IBD.

Materials and methods. 44 patients with IBD were examined: 28 (63.3%) with ulcerative colitis (UC), 16 (36.7%) with Crohn's disease (CD). Diagnosis was established on the basis of clinical-laboratory and endoscopic data. Liver injury was indicated by change in liver function tests, increased liver size and its structure by ultrasound. Markers HBV-, HCV-infection, ANA, AMA were identified.

Results. Among the patients with ulcerative colitis the steatohepatitis was detected in 7 (25%) patients, including 2 patients (28.5%) with total colitis, and 1 (14.5%) with subtotal colitis and 4 (57%) patients with proctosigmoiditis. BMI of patients with liver injury was 19,97 \pm 2,1 kg/m2, without injury - 24,9 \pm 3,2 kg/m2 (p <0,05). Activity of necrotic and inflammatory process (NIP) in the liver was low: ALT - 55,7 \pm 14,3 U/l, bilirubin - 22,72 \pm 9,6 mmol/l, alkaline phosphatase - 622 \pm 223,4 nmol/centiliter, gamma globulins - 20,42 \pm 1,9%. Steatohepatitis was diagnosed in 7 (43.8%) patients with Crohn's disease: in 5 (71.4%) – with ileocolitis and 2 (28.6%) with terminal ileitis. BMI of patients with liver disease was 17,34 \pm 2,8 kg/m2, without injury - 19,26 \pm 2,5 kg/m2 (p > 0,05). Activity of NIP in the liver was higher in patients with ulcerative colitis: ALT was 98,2 \pm 40,5 U / l (p <0,05) U / L, bilirubin - 18,92 \pm 15,4 mmol / l (p > 0, 05), ALP - 1086 \pm 520,8 nmol/centiliter (p > 0,05), gamma globulin - 20,58 \pm 1,1% (p > 0,05). None of the patients with IBD had signs of autoimmune hepatitis, sclerosing cholangitis.

Conclusion. Liver injury in the form of steatohepatitis in terms of underweight were more prevalent in case of Crohn's disease - in 43.7% of patients, more rarely – in 25% patients with UC, and the activity of hepatitis was higher in case of Crohn's disease, especially cholestasis syndrome than with ulcerative colitis.

ASSESSMENT OF PATIENTS IN THE REMOTE PERIOD AFTER CHOLECYSTECTOMY FOR CHOLELITHIASIS

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The frequency range of clinical manifestations in the remote period after cholecystectomy about gall - stone disease is 20 to 86 % which coincides with the literature data. A significant reduction in the incidence of biliary pain syndrome and dyspepsia. Significantly increased frequency of constipation and heartburn.

Such dynamics of symptoms accompanied by an increase in quality of life (SF-36).

No significant differences in the quality of life in patients undergoing cholecystectomy for cholelithiasis compared to the group not operated patients there.

CHARACTERISTIC OF HISTORY OF TOXIC HEPATITIS IN PROFESSIONAL FIELD

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The quantity of substances capable to affect a liver in production conditions is estimated in thousands. The group of hepatic poisons is allocated. It is shown that clinical manifestations in professional poisonings depend both on accompanying somatic diseases, addictions, and from previous intoxication and liver injury. In some intoxications (lead, benzene, fluorine) signs liver injury develop in parallel with another severe clinical symptoms. In other cases prevailing clinical signs of other organs may overshadow symptoms liver pathology. If signs of liver injury don't dominate, then severity of clinical presentation depends on selective effect of toxic chemical.

The term "toxic hepatitis" is standard in professional pathology though the concept "hepatitis" is a little conditionally since there are no significant laboratory and morphological signs liver inflammation. Therefore sometimes apply the term "toxic-and-chemical liver injury". Certain authors use the term "toxic hepatopathy" which is used for acute poisonings with so-called hepatic poisons (dichloroethane, four-chloride carbon and so forth), with some natural poisons (death-cup, male fern), drugs (paracetamol, acrichin and so forth). Further studying of toxic hepatitis of a professional etiology has great practical value in solution of correlation disease/profession, examination of working capacity and development of treatment-and-prophylactic schemes.

Functional dyspepsia associated with Helicobacter pylori in overweight and obese patients and its drug-free modalities

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The purpose of this study was to investigate the impact of non-drug treatment methods, namely acupuncture, in patients with functional dyspepsia (FD) associated with Helicobacter pylori within the context of overweight and obesity. The study was conducted in 46 patients with a verified diagnosis of FD associated with Helicobacter pylori, 73.9% of whom were overweight and 26.1% were obese. Pain syndrome was observed in 58.7% of individuals with FD associated with Helicobacter pylori in the context of overweight and obesity. Postprandial distress syndrome was present in 41.3% of patients. Ages of the patients ranged from 16 to 45 years. The duration of the disease varied between 12 months and 4 years. The study group included 26 patients who were prescribed eradication therapy in accordance with the Maastricht consensus-3 recommendations. The patients were additionally placed on a hypocaloric diet tailored to each individual and received auricular acupuncture with stimulating two main points (AR 18,17) in a single session for 30 minutes, and the remaining additional points (AR 22, 28, 51, 55, 87) for 10-12 minutes. This was combined with a scanned laser beam therapy projected on the celiac plexus where a scanning width was 4'4 cm, on the tender point with a laser spot for 4 minutes, for the paravertebral zone Th5-Th8 the scan width was 6 cm and exposure duration was 7 minutes. Extremely High Frequency puncture was applied to distant points of systemic effect (GI 4, GI 11, E 36, C 7, TR 5, MC 6, RP 6, RP 9, F2, F 3) where the exposure time varied in each individual case from 10 to 20 minutes per one acupuncture point. The total exposure time per procedure varied from 20 to 40 minutes. The course of treatment consisted of 10 to 15 procedures. The control group consisted of 20 examinees who received symptomatic treatment and eradication therapy depending on the clinical type of FD.

The treatment resulted in a positive impact and high clinical efficacy of reflexotherapy in reducing body weight and successful eradication of Helicobacter pylori in patients with FD associated with overweight and obesity.

EFFICIENCY OF THE COMBINATION OF REPLACEABLE HORMONOTHERAPY AND PREPARATION URSOSAN AT THE ESTROGEN'S DEFICIENCY CONDITIONS AT WOMEN IN MENOPAUSE

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The replaceable hormone therapy (RGT) in the combination with a natural estrogen and progesterone are gained now considerable distribution combination for treatment of the estrogen's deficiency syndrome (EDS) caused by natural or artificial menopause. At the same time long application an estrogen-progesterone combinations as RGT besides positive shifts in homeostasis can cause quite often undesirable collateral violations of liver's function. Considering it, at women with DE, application of the preparations possessing cyto – and hepatoprotective, antioxidant action pathogenetic would be reasonable. In this regard a preparation of the choice is Ursosan. Being well be absorbed in intestines, at intake, it is built in membrane hepatocyte, stabilizes its structure and protects hepatocyte from damaging factors. Replacing unipolar bilious acids, forms the nontoxic mixed micelles, reducing cholesterol synthesis in liver and its absorption in intestines, formation of cytotoxic T – lymphocytes. 70 women are included in research with EDS, needing in long RGT. Patients were divided in 2 groups, by 35 people. Both groups were identical on age (41+7, 5 years), therapeutic and gynecologic diseases, and disease duration. In both groups patients received RGT for 6 to 24 months. Patients of the first group in addition to RGT received a preparation Ursosan on 2 capsules for the night. The patients accepting Ursosan, transferred RGT more favorably, and at the majority of patients of the second group were noted weight in the right hypochondrium, bitterness in the mouth and dyspepsia, gastric indigestion, frustration that served as a cause of failure from a hormone therapy. As required carried out biochemical analyses – blood control for determination of activity hepatic transaminase.

Therefore, the preparation Ursosan is recommended to be used at patients with liver's and biliary tract's pathology, that needing in long RGT.

AMINO ACIDS IMBALANCE IN PATIENTS WITH CHRONIC PANCREATITIS

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Aims: To study serum levels of free amino acids (AA) in patients with chronic pancreatitis (CP).

Materials and methods: Twenty four patients with CP were observed in one hospital in Uzhgorod. Among the surveyed patients men - 16 prevailed, age of 43,1±2,8 years, women was - 8, age of 44,7±4,6 years. Measurement of free amino acids serum levels by one-dimensional descending chromatography on paper method (I.M.Khays, K.Matsek, 1962, T.S.Paskhina, 1964) except standard examination methods was performed in all patients.

Results and discussions. All patients observed had different degree pain in the upper abdomen, and also signs of dyspeptic syndrome (nausea, vomiting, an eructation, a meteorizm) and astenovegetative syndrome. Patients also complained of increase in frequency of stools (on the average up to 3-4 times a day). In patients with CP dysproteinemia signs occurred: decrease of albumin levels (to 35,9±2,7%) and increase of γ - and α 2-globulins levels (to 33,5±2,1% and to 9,3±0,9% respectively) were shown.

These changes were accompanied by abnormal serum levels of free amino acids with primary increase of glutamine, treonine, lysine, histidine, thyrosine, triptophane, methionine, valine that is explained by decrease in individual degradation of AA. In parallel decrease of serine, asparagine, glycine, alanine are noted.

Changes of proteins metabolism develops against the expressed trophological insufficiency in patients with chronic pancreatitis.

Conclusions: In patients with chronic pancreatitis the blood serum dysproteinemia appeared, that is accompanied with of abnormal levels of free amino acids.

EXPERIMENTAL BIOCHEMICAL ANALYSIS OF THE HEPATOPROTECTIVE EFFECT OF THE DRUG GENERATED FROM BIOMASS OF GINSENG CELL CULTURE

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The purpose of this study is to research the effect of the drug generated from biomass of ginseng cell culture on biochemical manifestations of experimental toxic hepatitis caused by priming of mature nonlinear male rats with toxic doses of carbon tetrachloride (a three-day intramuscular injection of 50% of Solutio oleosa in a dose of 0.2 ml/100 g). In the preliminary phase the alcoholate was prepared from biomass of ginseng cell culture by percolation. Then it was de-alcoholized by evaporation till calomel state, followed by restoration of the original volume with distilled water. This aqueous ginseng preparation was injected to experimental rats through esophageal bougie for three days before their priming with hepatotoxin and for three days along with it at the doses of 2.5, 5 and 10 ml / kg (in equivalent of alcoholate).

The severity of the pathological process in the liver in the control and preparation series was estimated by the values of the dynamics of the activity of several enzymes - aspartate aminotransferase, alanine aminotransferase and gamma-glutamyl transpeptidase in blood serum determined with the use of standard sets manufactured by «LACHEMA» (Czech Republic).

These results indicate on the presence of moderate hepatoprotective effect in preparation of biomass of ginseng cell culture to the effect on liver tissue of carbon tetrachloride. This is manifested in a less degree by hyper-enzymes, especially by the values of aspartate aminotransferase and gamma-glutamyl transpeptidase. At the same time the more significant effect was manifested at doses of 5 and 10 ml / kg. Given the pathogenic feature of carbon tetrachloride hepatotoxic effect due to the initiation of free radical processes in its biotransformation, it is likely that the established hepatoprotective effect is based on the evident antioxidant activity of ginseng, which expands the pharmacodynamic characteristics of this drug.

POSSIBILITY OF NON-INVASIVE SCREENING ASSESSMENT OF PATIENTS WITH BILIARY TRACT DISEASES AND HELICOBACTER PYLORY INFECTION IN A CENTRAL DISTRICT HOSPITAL

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In recent years there is a growth in patients with associated biliary tract and stomach diseases. Therefore, early non-invasive screening diagnostics of these pathologies is relevant.

For the period from January 2011 to March 2012 based on State-financed health institution "Uren Central District Hospital" 73 patients with pathology of the biliary tract (biliary dyskinesia and chronic cholecystitis) were examined including 17 men (average age 48,4 ± 13, 6 years) and 56 women (average age 56,6 ± 7,7 years). All patients passed: ultrasound of the abdomen by apparatus «Siemens Sonoline G40» and fibrogastroduodenoscopy by apparatus «Fujinon FG-1Z» by standard methods.

In case of US of the abdomen additional ultrasound examination without filling the stomach with water was performed, measuring the thickness of the muscular layer. In case of fibrogastroduodenoscopy the forceps gastric mucosa biopsy was performed, followed by express-test for urease activity of Helicobacter pylory (Hp).

Group of persons ("Healthy") in the amount of 30 people (8 men (average age 44 ± 10,7 years) and 22 women (average age 53 ± 5,3 years)) without biliary tract disease and the absence of infection Hp was also examined.

It is found that in the "healthy" group the thickness of muscular layer of the stomach by ultrasound data was 3,8 ± 0,14 mm, in case of fibrogastroduodenoscopy the gastritis was diagnosed without evidences of mucous atrophy, urease test - negative.

In the group of patients with the presence of biliary tract disease the muscular layer of stomach was 5,002 ± 1,74 mm. In all cases in the course of fibrogastroduodenoscopy the patients were diagnosed with gastritis without signs of atrophy. It is noted that the thicker muscle layer of the stomach, the higher is urease activity of Hp.

Thus, the presence of increase in thickness of the muscle layer of the stomach in a patient with biliary tract disease according to US-examination over 3 mm allowed to suspect the presence of Hp infection in the central district hospital and promptly refer the patient to perform fibrogastroduodenoscopy followed by forceps gastric biopsy and conducting express-test for urease activity.

Comparative assessment of antioxidant properties of different samples of monofloral pollen in the model of tetrachloromethane hepatitis

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In this paper there is a comparative assessment of the severity of antioxidant effect of monofloral pollen of different botanical origin. With this purpose the classic experimental «free radical» model of tetrachloromethane hepatitis characterizing by significant increase in the activity of the quantitative parameters of lipid peroxidation activity is used, which allows for a correct comparative analysis of the severity of antioxidant activity.

The experiments were performed in adult nonlinear male rats, in which toxic hepatitis was caused by three-day intramuscular injection of 50% Solutio oleosa of tetrachloromethane at a dose of 2 ml / kg. As for preparation series of rats during 10 days prior to the injection of tetrachloromethane, and for three days along with it the newly prepared suspensions of pollen of dandelion, cornflower, clover and fireweed at a dose of 250 mg / kg each was administered. Assessment of the intensity of lipid peroxidation was performed in homogenates of liver tissue by determining the concentration of malonic dialdehyde, activity of NADPH-induced and ascorbate-induced peroxidation.

All assessed samples of monofloral pollen assisted to decrease in the degree of intensification of free radical processes in the liver tissue induced by carbon tetrachloride. At the same maximal degree of antioxidant activity was noted in cases of application of the pollen of dandelion and clover, some smaller - in animals which accepted pollen of cornflower and minimal protective effect was in the series of administration of fireweed pollen. Obtained results enable to recommend the use of just a dandelion pollen and clover as a food additives in case of «free radical» pathologies in general and toxic hepatitis, similar by mechanism of development to tetrachloromethane, in particular.

HEPATOCELLULAR INSUFFICIENCY AS A COMPLICATION IN LIVER DISEASES

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The term "hepatic insufficiency" (HI) is an often used term which doesn't have accurate definition. It unites various violations of liver function: from mild abnormalities to severe (up to hepatic coma) conditions. It is functional non- anatomic concept. Constant morphological signs are absent. "Minor" HI, or a hepatodepression (hepatodepressive syndrome) and "major", or obvious HI with symptoms of "hepatic encephalopathy" are distinguished. Major HI divides into hepatocellular and portal-caval forms. The clinical presentation of hepatocellular insufficiency is identical and doesn't depend on an etiology in different CLD. Neurologic abnormalities (hepatic encephalopathy), weakness, anorexia, jaundice, ascites, abnormalities in azotemia and electrolytes, coagulation system, skin and endocrine changes, etc. are characteristic. Clinical manifestations of chronic HI are usually combined with symptoms of CLD which lead to function decrease. Bilirubin and ALT, AST levels increase. Increase of creatinine, electrolytic disturbances testifies to involvement of kidneys in pathological process (a hepato-renal syndrome).

Laboratory researches show a hypoalbuminemia, low cholinesterase, sodium, prothrombin, cholesterol levels, moderate anemia, lengthening of time of bleeding and coagulation time.

Stages of precoma, a threatening coma and coma are distinguished in development of hepatic coma. Combined therapy should be started before first signs of HI appear.

HEPATOPROTECTIVE EFFECT OF LYZOCYME DURING INTRAGASTRAL USE NANOWOLFRAMIUM IN RATS

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Purpose: assessment of influence of lyzocyme hydrochloride (LH) on a morphofunctional condition of liver in rats receiving nanoparticles of wolframium (nano-W) of different dispersion.

Materials and methods. Histology of liver tissue from 23 rats (Vistar line) in which a suspension nano-W (received by a plasma method, with sizes of particles of 60 nanometers (nano-W60), tungsten - carbon furnace charge with a size of particles of 15 nanometers (nano-W15)) in doses of 50 mg/kg was once entered in stomach. LM was also put in 3 hours prior to nanoparticles. Intact animals served as control group. Research is conducted on the cuts painted by Mayer's hematoxylin and eosin, with a hemi-quantative analyze of results.

Results. In liver of rats received nano-W, in 72 h. the same pathomorphological changes appeared being like acute toxic hepatitis and are the most expressed after application nano-W15. Double decrease in level of endogenous lyzocyme in blood serum is thus noted.

Protective influence of LM on morphofunctional liver condition in rats received nano-W is revealed. After LM and nano-W15 application expressiveness of acute hepatitis decreased from moderated to minimal/moderate: signs of granular and vacuole hepatocytes cytoplasm dystrophy significantly decreased, there were no focal and bridging hepatocytes necroses and tissue eosinophilia, decreased lymphocytic infiltration in portal tracts. Morphology of liver tissue in animals received nano-W60 and LM was according to physiological standard. Lyzocyme levels in blood serum in all animals received LM and nano-W remained at the level of control.

Conclusions. Nanoparticles of nano-W15 and nano-W60 at single intragastral application in a dose of 50 mg/kg induce patomorphological changes in liver tissue in rats, that are the most expressed after nano-W15 intake. The considerable hepatoprotective effect of single preventive application LM is revealed.

PROGNOSTIC SIGNIFICANCE OF BIOCHEMICAL MARKERS OF LIVER DAMAGE

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Purpose: To clarify the prognostic significance of certain biochemical parameters in patients with chronic liver disease.

Materials and Methods: The analysis of biochemical parameters in 120 patients with chronic liver disease. Of these, 46.7% had cirrhosis of the liver (alcoholic etiology - 21.5%, mixed - 11.5%, unspecified - 3.2%, virus C - 3.2% in the virus - 1.6%, autoimmune - 5.7%), chronic hepatitis - 53.3% (alcoholic etiology - 26.6%, mixed - 9.2%, unspecified 8.3% - virus - 6.7%, autoimmune - 1.7%, toxic - 0.8%). The observation group were 60 patients with lethal control group - 60 issued with improvement. Assessment of the importance of risk factors was carried out by determination of the relative risk (RR) and etiologic fraction (EF).

Results: Patient Monitoring Group had the following significant differences from the group of comparison, more severe hypoproteinemia (30,14 ± 1,24 and 38,4 ± 0,72 g / L), hyperbilirubinemia (143,8 ± 31,4 and 29,6 ± 6,9 mmol / l), increased creatinine (183,6 ± 36,7 and 30,9 ± 20,9 mmol / l), decreased fibrinogen (2,9 ± 0,3 and 3,9 ± 0,2 g / l), PTI (63,4 ± 2,3 and 79,7 ± 1,6%), cholesterol (3,4 ± 0,3 and 4,6 ± 0,2 g / l), proteinuria (0, 7 ± 0,1 and 0,3 ± 0,1 g / l). RR of death in the MCP I was 0.02, MCP II - 0.75, MCP III - 29.5. In assessing the dynamics of laboratory parameters during treatment was associated with a negative impact on the prognosis of further improving the AST from baseline (EF 83.5%), reduction of PB (EF 81.0%), increase in total bilirubin (EF 78, 5%), increased ALT (EF 74.0%), lower albumin (EF 69.0%) and total protein (EF 62.7%).

Conclusions: Biochemical markers of a poor prognosis of liver disease, deterioration are synthetic and detoxifying the liver, hyperasotemia. Worsening in the dynamics of cytolytic syndrome indicators synthetic and detoxifying the liver indicates a further deterioration of prognosis.

OVERALL ASSESSMENT OF LIVER FIBROSIS IN PATIENTS WITH CHRONIC LIVER DISEASE (CLD).

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Purposes: to study possibilities of noninvasive diagnostic methods for liver fibrosis in patients with CLD by studying serum markers of fibrosis and results of duplex vessels scanning in abdominal cavity.

45 patients with CLD confirmed with: questioning (CAGE questionnaire), history and examination data (S. Sherlock, 1995), blood tests (dyslipidemia, adnormal carbohydrate metabolism) and ultrasonography by methods are surveyed. Exclusion criteria: serious accompanying somatic diseases, fibrosing processes of any other localization, surgeries on vessels of an abdominal cavity. Serum levels of apolipoprotein A-1, haptoglobin and alpha2 - macroglobulin are studied, duplex scanning of splenic and hepatic arteries and a portal vein are carried out, stiffness of liver tissue was determined by elastography in all patients.

Results showed significant correlation between serum levels of fibrosis markers stiffness of liver tissue at F2-F4stage. Haemodynamic indicators, including indexes of a pulsation of splenic and hepatic arteries significantly correlate with liver stiffness at F3-F4 fibrosis stage.

Conclusions: on the basis of overall assessment of serum fibrosis markers and results of duplex scanning of arteries of an abdominal cavity a method of noninvasive diagnosing of fibrosis may be introduced for patients with CLD.

SEVERE HEPATIC INSUFFICIENCY, AS A MANIFESTATION OF SYSTEMIC ASPERGILLOSIS

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Background and aim. Acute aflatoxicosis rarely diagnosed in humans. However, one should consider the possibility of its development in a patient with jaundice. Present a case of systemic aspergillosis, flowing under the "guise" of decompensated liver cirrhosis (LC) with the development of sepsis.

Case description. Patient M., 47 years old. Disease duration 6 months. Acute onset of the disease - with jaundice, dyspepsia, severe weakness, hectic fever. During hospitalization - coma I, intense jaundice, dyspnea, anasarca. In the lungs, breathing weakened, tachycardia, hypotension. Percussion is not enlarged liver and spleen were not palpable. In the analysis of anemia (red blood cells - 2.62 x 10⁶ / m), leukopenia (1.2 x 10³ / m), granulocytes (91%), thrombocytopenia (19 x 10³ / m), hyperenzymemia (2.5 standards), hyperbilirubinemia and 26 standards (direct bilirubin > 10 standards), total protein - 41 g / l, albumin - 23.3 g / l, prothrombin - 26.3%, INR - 2.43. By CT scan - polysegmental bilateral pneumonia, hydrothorax, portal hypertension, ascites. Blood culture was negative. Bronchoscopy: on the back wall of the trachea revealed ulcerative defect of 2 cm installed sepsis without identifying the primary tumor to the development of severe organ failure, secondary hepatopathy ended in death. Autopsy - signs of septicemia, with damage to internal organs (brain, heart, kidneys, lungs) - necrosis of the vascular wall and bleeding into the surrounding tissue. Electron microscopy autopsirovanny liver tissue were found in the fields of the mycelium of the fungus germinal form, as well as the typical structure of hyphae Aspergillum fumigatus (A.f.). In crops bronchial washings obtained after the death of the patient, in a lot of (A.f.).

Conclusion. The patients in the presence of clinical decompensation cryptogenic LC in differential-diagnostic algorithm is appropriate to include systemic mycoses.

SOCIAL PREDICTOR OF UNFAVORABLE OUTCOME IN LIVER PATHOLOGY

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Purpose: To clarify the role of social factors in the occurrence of adverse outcome in patients with liver disease.

Material and methods. The analysis of a number of social factors in 120 patients with chronic liver disease. Of these, 46.7% had cirrhosis of the liver (alcoholic etiology - 21.5%, mixed - 11.5%, unspecified - 3.2%, virus C - 3.2% in the virus - 1.6%, autoimmune - 5.7%), chronic hepatitis - 53.3% (alcoholic etiology - 26.6%, mixed - 9.2%, unspecified 8.3% - virus - 6.7%, autoimmune - 1.7%, toxic - 0.8%). The observation group were 60 patients with lethal control group - 60 issued with improvement. Assessment of the importance of risk factors was carried out by determination of the relative risk (RR) and etiologic fraction (EF).

Results: Among surveyed in the intervention group were 33 men and 27 women in the control group - 35 men and 25 women. Average age at death was 49,5 ± 1,5 years, issued with improvement - 46,0 ± 0,2 years. RR of death in men with chronic liver disease was 0,9 (EF -11.0%), women - 1.15 (EF 13.0%), residents of the village - 1.1 (EF 9.0%), city - 0,9 (EF -11.0%). Unfavorable outcome in patients who are not married, was significantly higher (EF 66.0%) than married (EF -203.0%). In the patient population most common etiological factor is a history of alcohol use (RR 5.1, EF 80.4%), acute alcohol intoxication (RR 6.5, EF 84.6%), including the background of HBV-and HCV-infection.

Conclusions. Poor outcome in patients with liver disease usually occurs in middle age increases the probability of marriage is marital status, with significant gender differences were found. It is for this population tend to alcohol abuse, which is the main etiological factor for the development of liver disease deaths.

DEATH IN HEPATITIS PATIENTS: ROLE OF COMORBIDITY

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Purpose: To clarify the effect of comorbidity on the outcome of disease in patients with Hepatitis.

Materials and Methods: The analysis of the existing comorbidity in 120 patients with chronic liver disease. Of these, 46.7% had cirrhosis of the liver (alcoholic etiology - 21.5%, mixed - 11.5%, unspecified - 3.2%, virus C - 3.2% in the virus - 1.6%, autoimmune - 5.7%), chronic hepatitis - 53.3% (alcoholic etiology - 26.6%, mixed - 9.2%, unspecified 8.3% - virus - 6.7%, autoimmune - 1.7%, toxic - 0.8%). The observation group were 60 patients with lethal control group - 60 issued with improvement. Assessment of the importance of risk factors was carried out by determination of the relative risk (RR) and etiologic fraction (EF).

Results: The analysis of comorbidity in patients with chronic liver disease pneumonia was diagnosed in 36.7% of patients in the observation and 3.3% - compared (RR 16.8, EF 94.1%), atherosclerosis - 26.7% and 0 % (RR 21.5, EF 95.4%), pancreatitis - 26.7% and 58.3% (RR 0.2, EF -525.0%), COPD - 18.3% and 0% (RR 13.3, EF 9.25%), kidney disease - 18.3% and 6.7% (RR 1.6, EF 37.5%), cholelithiasis - 13.3% and 28.3% (RR 0, 39, EF -156.4%), diabetes - 10.0% and 6.7% (RR 3.1, EF 67.7%), hypertension - 10.0% and 15.0% (RR 0.63 EF -59.0%), ischemic heart disease - 8.3% and 5.0% (RR 1.73, EF 42.2%), gastric ulcer and duodenal ulcer - 6.7%, and 8, 3% (RR 0.79, EF -26.6%), respectively. Among these comorbidities significantly increased risk of death atherosclerosis (EF 95.4%), pneumonia (EF 94.1%), COPD (EF 92.5%), nephropathy (EF 67.7%), ischemic heart disease (EF 42. 2%), diabetes mellitus (EF 37.5%).

Conclusions: In the structure of comorbidity, exacerbate liver disease, the most adverse effect on the prognosis have pneumonia, COPD, atherosclerosis, coronary heart disease, diabetes and kidney disease.

CASE REPORT: IRON-DEFICIENT ANEMIA AS LEADING SYMPTOM IN LATENT COELIACIA.

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View at coeliacia as an illness of childhood has currently changed. Cases of atypically proceeding and latent forms of this disease when the disease is diagnosed for the first time in adults are noted more often.

The 36 y.o. woman addressed to the hematologist of Regional hospital with complaints of expressed weakness, faintness, short-term syncope, and taste perversion. Within the last 15 years hemoglobin level fluctuated from 60 to 90 g/l. Patient noted that administration of iron preparations led to the expressed dyspepsia. Hemoglobin levels could be increased only with RBC mass transfusions.

The complex laboratorial examination was performed. Anemia was hypochromic and microcytic. Reticulocytes count was 1,2%. Refractory anemia with ring-shaped sideroblasts was excluded by marrow morphology with staining for hemosiderin. Hemoglobinopathy, membranopathy, sickle-cell anemia, porphyric metabolism abnormalities were excluded. Serum iron level at the time of visit was 3,16 mmol/l, ferritin level - 15 mkg/l.

Except typical complaints due to anemia patient complained to artralgiias. In biochemical tests AST and ALT levels appeared raised in 1,5 time. After careful history analyzing it was found out that the patient completely excluded cereals from her diet they provoked dyspeptic reactions, and the same reaction occurred after every tableted drugs use, including iron containing drugs. Significantly high level of anti gliadine antibodies was revealed in patient, however duodenum morphology was nonspecific.

Patient followed the gluten-free diet that had allowed maintaining hemoglobin within 100 – 110 g/l.

CLINICAL CURRENT GOOD-QUALITY STRIKTUR OF BILIOUS CHANNELS

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Urgency: Good-quality stricture extra hepatic bilious channels (VZhP) are, as a rule, a consequence of a trauma of a bilious tree during a holetsistektomiya. Traumas of VZhP occur in 0,5-1,4 % of cases. Taking average frequency of a trauma of VZhP for 1 %, in Russia annually 600-1000 people suffer from similar complication, in the Republic of Sakha (I) annually meet at 11-20 people, the majority of them in the postoperative period develop стриктуры, quite often demanding long treatment, the repeated medical and diagnostic actions, often bringing to a serious invalidizatsiya of patients.

Research objective: studying of a clinical current good-quality stricture extra hepatic bilious channels.

Materials and methods: The analysis of a clinical current of 119 patients with good-quality cicatricial stricture extra hepatic bilious channels from 1993r on 2003r is carried out. Women of all bylo:-89, men vsego:-30. From them be elderly: to 39age-8, 40-49age-25, 50-59age-63, 60-69age-22, 70-79age-1, 80 also is more senior. Radical-86, not radical-33.

Results: At 86 (72 %) the person стриктуры are revealed after an "open" holetsistektomiya, still at 33 (28 %) - after a laparoskopichesky holetsistektomiya. Clinical manifestations: postoperativeanorexia, nausea, vomiting were observed at 36 (30 %) patients, belly-aches were at 78 (65,5 %). Holesticheskyjaundice at 32 (26,8 %), a skin itch at 24 (20 %). Podpechenochny abscess it is revealed at 3 (2,5 %). By results of ultrasonography it is revealed: development fibrozawas observed at 13 (11 %) patients. Retsidiviruyushchy inflammation of a gall bladder (Sharko's intermittiruyushchy biliarny fever) has developed at 5 (4,2 %) the person. Biliarnycirrhosis at 6 (5 %). The increase and consolidation of a liver was observed at 48 (40,3 %). Biliarny hypertension at 18 (15 %). Biochemical research of serum of blood has revealed at 68 (57 %) patients increaseof activity alkaline phosphate, GGTP and level of bilious acids.

Conclusions: Good-quality stricture extra hepatic bilious channels develop owing to a surgical trauma, generally during an "open" holetsistektomiya at 86 (72 %) patients, are more often at persons of a female 89 (75 %), able-bodied age 72 (60,5 %). The disease is characterised by the long anamnesis from 5 to 10 years. In a clinical picture the pain syndrome 78 (65,5 %), then dispeptichesky manifestations at 36 (30 %), holestatchesky jaundice at 32 (26,8 %), first of all, prevails.

STUDY CHOLELITHIASIS IN PATIENTS WITH VARICOSE DISEASE
EXAMPLE POLYCLINIC № 1 YAKUTSK

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Purpose: to study incidence of ZhKB at patients with a varicose illness on an example of policlinic of No. of 1 g of Yakutsk.

Research materials. As materials of research out-patient cards of a surgical office of policlinic of No. of 1 g of Yakutsk are taken.

Are worked 162 out-patient cardssick with a varicose illness, from them it is revealed 21 (7.6 %) patients with ZhKB (20 women and 1 man) at the age from 35-40 years, Aborigines - 14 (30 %), not radical - 30 (70 %).

Results. The varicose illness is observedat 56 % of women of able-bodied age, 12 % - invalid. Men: the able-bodied - 26 % and invalid - 6 %. Thrombophlebitis of venous insufficiency of the bottom extremities, meet at 62 % of adult population, at persons 65 years frequency of trophic ulcers are more senior increases in 3 times and more, reaching 3-6 %. Approximately at a quarter of the population 60 years are more senior and thirds of the population are more senior than 70 years there are gallstones. Statistics testify that 10-15 % of the population have stones in bilious ways. At patients with HVN destructive forms of the sharp cholecystitis, being characterised high frequency of complications and a lethality much more often develop. The main reasons for complications, are – serdechnososudisty insufficiency (10-15 %), hepatonephritic insufficiency (3-5 %), tromboemboliya (14-16 %).

Conclusion. Thus, CL diagnosed in 12.9% of patients with varicose veins, the clinical picture is dominated by dyspeptic symptoms in 11% of cases. Given that patients with CVI is much more likely to develop destructive forms of acute cholecystitis, characterized by high rates of complications and mortality, early detection is necessary GSD, a clinical examination of patients with varicose veins is important not only to detect and localize the organic changes in the superficial veins and trophic skin changes, but also to identify possible comorbidities biliary area, as this information enables us to establish a complete diagnosis and determine the treatment policy and the continuation of the differential adequate therapy patients.

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COMPLICATIONS OF DIFFUSE LIVER DISEASE AND GENDER
DIFFERENCES IN THEIR DEVELOPMENTTyaptirgyanova T.M.¹, Yakovleva Z.A.², Dohunaev V.V.²*1Meditsinsky Institute NEFU im.M.K.Ammosova,
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Modern lifestyle, diet, and frequent use of alcohol significantly damage the liver tissue, which is why developing and diffuse changes of the liver parenchyma. Recently took and viral lesions that are often overlooked and thus passed from person to person. There are so many different techniques aimed at diagnosis of various pathological conditions of the liver. Currently, in vivo morphological study of the liver widespread in clinical practice.

Objective: To examine gender differences in the development of complications of diffuse liver disease in women (F) and males (M).

Materials and methods. We have studied the morphological study of the liver tissue u180 patients with chronic diffuse liver disease (DLD). Men was 66.7% -33.3% of women. All patients were operated for cholelithiasis in Belarus № 2 of the Center for Emergency Medical Aid Yakutsk. At the age of 16-20 years - 19 people, 21-40 years - 51 41-60 - 57 61-70 - 37, over 70 - 16.

Results. In the group of patients with PCR's included patients with hepatitis-100chel. and biliary cirrhosis, 80 patients. The preliminary diagnosis of chronic hepatitis B by morphological study was confirmed in only 40% of patients. In 43% of patients with chronic hepatitis morphologically verified in clinical diagnosis was modified to assess the extent of the activity of the process: 25% were diagnosed with a lighter, and 15% - more severe stage of liver disease of the total number of patients. In the history of a 9.4% F and 15% M has previously transferred viral hepatitis (44chel). Chronic hepatitis drug met in 8 women. In the remaining 48 patients diagnosed alcoholic hepatitis-26, 7% of all PCR's, including the M-16.7% F-10%. Biliary cirrhosis, we identified 80 patients (44.4% of all PCR's): -17 F (9.4%), M - 63 (35%). Cholecystitis suffered more than 6 years - 27 people from 10-15 years - 29 people and more than 15 years - 24 people. Complications of diffuse liver diseases with the development of portal hypertension and edematous-ascitic syndrome identified: esophageal varices (EW) 1stepeni the M-10.6% and F-32, 7%, and 11 degrees, the M-40, 8% and M-13, 8%, 111-degree of M-48, 6% and F-22.7%. A history of variceal bleeding: among the M-9.9% of K-4, 08%. Refractory ascites occurs in 36.6% M and 14.2% G. Hepatomegaly expressed at M-32, 8% of K-16, 4%. Violations of the protein-synthetic function of the liver: hypoalbuminemia of

M was observed in 27.6%, and among the F-y 48.9%. The decrease in prothrombin index (PTI) was detected in 32.1% M and 70.4% F, fibrinogen - 27.8% and 57.9% M J. hyperbilirubinemia occurs in 50.6% M and 89.8% F, including bilirubin more than 100 micromol / L in 36.4% M and 60.8% G.

Conclusions.

1. Men in two more complications arise in the form of portal hypertension and variceal bleeding.

2. Violations of the protein-synthetic liver function and hyperbilirubinemia more common in women (48.9% protiv27, 6%).

PREVALENCE OF ECHINOCOCCOSIS IN SAKHA REPUBLIC (YAKUTIA).

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Relevance: Echinococcosis - a dangerous parasitic disease of man. In Russia, the highest morbidity echinococcosis registered in Bashkortostan, Tatarstan, in the Sakha Republic (Yakutia), the republics of the North Caucasus, Krasnodar and Altai, Krasnoyarsk and Khabarovsk, Tomsk, Omsk, Magadan, Amur regions and the Chukotka Autonomous District.

High frequency spread of disease, the difficulty of active detection of the disease at an early stage, related to the clinical picture and erased a high percentage of permanent disability cause the relevance of echinococcosis for health.

Objective: to study the prevalence of hydatidosis in the Sakha Republic (Yakutia).

Materials and Methods: The analysis of statistical data of the National Republican cabinet parasitological hospital № 3 and case histories of patients who were treated at the Department of Surgical Gastroenterology Republican hospital № 1 NCM from 2004 to 2012.

Results of the study: The 01.01.2012g. is followed up by 140 patients with hydatidosis. Of these, 30 (21.4%) - the inhabitants of the city of Yakutsk. The remaining 110 (78.6%) were registered in 22 regions of the country: 13 people in Suntar area, 11 in Ust-Maya region, 10 people in the Aldan region, Namsky 9 people in the area, with 8 people in Verkhnevilyuisk, Kobyayskom, Nyurbinskaya areas by 7 people in Olyekminsky, Olenek, Churapcha areas, 5 people in Amga, Ust-Aldan region, 4 person Viliuisk, mountains, 3 person Tattinsky, Verkhnekolymsk areas, 2 people in Lower area, 1 person in Verkhoyansk, Lensky, Mirny, Moma, Tomponsky areas.

During the study period from 2004 to 2012. hydatid disease occurs in all age groups: 18-19 years, 4 people, 20-29 years, 14 men, 30-39 years, 13 men, 40-49 years, 14 men, aged 50-59, 20, 60 years and over-45 people. Analysis of the age structure of the disease has shown that the disease is most frequently encountered in the age groups 50 to 59 and over 60.

Distribution:

By sex: women-76 (54.3%), men-64 (45.7%),

-On a national basis: Yakuts, 63%, 15%, Russian, few people-10%, others 12%,

FREQUENCY OF OCCURRENCE OF DISEASES OF DIGESTIVE ORGANS
AT ATHEROSCLEROSIS OF VESSELSTyaptirgyanova T.M.¹, Stolyarova A.B.¹,
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Atherosclerosis – one of the most actual diseases of XXI centuries which is one of four most frequent diseases and causes of death. It is known that more than in 90 % of cases the death from cardiovascular diseases is caused to IBS and brain strokes in which development the main role belongs to atherosclerosis.

Work purpose: to reveal frequency of occurrence of defeat of ZhKT at atherosclerosis of vessels of a brain, coronary vessels and aortas.

Research materials: the analysis of 358 protocols (194 women and 164 men at the age of 29-83 years) openings of persons of urban population (314) 84,4 % and country people (44) 12,2 % which have died of different forms of diseases and atherosclerosis (atherosclerosis of vessels of a brain – (182) 50,8 %, atherosclerosis of coronary vessels – (238) 66,4 %, aorta atherosclerosis – (294) 82,1 % that has made 26 % from total number of the openings (1373) which have been carried out in pathoanatomical department of RB № 1 – NTsM of Yakutsk for 2010-2012 is carried out.

Results: defeats of a digestive path from among the general died patients, are revealed such as a tumour of kardialny department of a stomach with transition to a gullet – at (19) 5,3 % of cases, chronic gastritis – at (38) 10,6 %, a sharp ulcer and a stomach erosion – at (44) 12,2 % of patients, ZhKB – at (130) 36,3 % of cases. Changes from a liver and a pankreatobilliarny zone meets in the form of cirrhosis - at (14) 3,9 % of patients, hepatitis B or C - at (37) 10,3 %, chronic pancreatitis - at (213) 59,4 % of cases. More often they met at women at the age of 51-83 and the quantity them as much as possible increased after 60 years. Persons of not radical nationality were surprised in 2 times more often.

The main reasons for death was cardiogenic shock – at (66) 18,4 % of cases, sharp warm insufficiency – at (67) 18,7 %, hypostasis and brain swelling – at (112) 31,2 % of cases,

Conclusion: Thus, accompanying defeats of a digestive path at atherosclerosis meet a look sharp ulcer эрозивных defeats of a stomach (44) 12,2 % of cases, from a pankreatobilliarny zone at atherosclerosis the greatest from all number of the died 358 patients was a zhelchekamenny illness (130) 36,3 % of cases and chronic pancreatitis (213) 59,4 % of cases.

-Localization of the pathological process: in the liver, 72 (52%), lung-53 (38%), other (spleen, brain, heart) -15 (10%).

Over the period 2010 to 2012 on the pulmonary hydatid cyst in 9 patients (6.4%) received ehinokoktomiya.

Conclusion: Thus, the incidence of hydatidosis is high almost the entire territory of the Republic of Sakha (Yakutia). Most common among residents of areas-78, 6%, at the age of 50 to 60 years and older, by sex - women (54.3%), on a national basis - the Yakuts (63%). Most often, the disease process is localized in the liver (52%).

ENDOSCOPIC STENTING ESOPHAGUS IN INOPERABLE PATIENTS

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PURPOSE: To study the characteristics of esophageal stenting in patients with esophageal cancer with the use of stents in different versions.

Materials and methods. During the period from 2009 to the present time we have endoscopic stenting 6 patients for cancer of the esophagus. Age range of patients from 70 to 93 years. All had grade 3-4 dysphagia after chemotherapy and radiotherapy. Most patients were installed nitinol stents MI Tech (Korea), were also used stents firm Wilson Cook (USA). In one case, a stent mounted with anti-reflux valve, the indication for its installation was a cancer esophagogastric junction. Before the patients underwent endoscopic stenting and radiopaque study to determine the nature and extent of the restrictions, and climbed biopsies to determine tumor histology. The introduction of the stent made after premedication (atropine, Relanium) under local anesthesia with the patient on his left side. Esophagoscopy and after the introduction of the strings, under endoscopic control is installed proximal edge of the stent in a compressed state, then he straightened and pushed into the lumen of the esophagus. Radiological control with contrast medium (76% Urografin) is held on the first day after the procedure to assess the patency of the esophagus and the ground level of the prosthesis.

Results. In 5s patients already on the next day after stenting appeared possible to receive the liquid and solid food, and after 3-5 days the phenomenon of dysphagia disappeared. Complications of self-expanding stents installation was not. In the early period after stenting in 1 patient there was pain. Among the late complications after 8 months from stent in 1 patient revealed a continued growth of tumor tissue, which caused stenosis of the lumen of the esophagus above the stent. Patients underwent stenting of this stent in the stent.

Conclusions. Thus, given the low invasiveness of endoscopic stenting, this manipulation is the method of choice for the palliative treatment of patients with inoperable cancers. Application of the method arthroplasty reduces the time of hospitalization. Thus one of the most obvious benefits and advantages of stenting is to preserve the possibility of oral nutrition, which significantly improves the quality of life of patients.

PH-METRY FEATURES IN YOUNG OVERWEIGHED PERSONS HAVING SYMPTOMS OF HEARTBURN

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PURPOSE: To study the parameter characteristics of the 3-hour pH-metry in overweighted patients in the age of 20 - 45 having heartburn.

Materials and research methods: In the study there were 29 overweighted patients having complaints of heartburn (study group - SG), a clinical comparison group (CCG), consisting of 18 standard patients with complaints of heartburn. Body weight index was estimated for all the patients, a three-hour Ph-metry was implemented by the apparatus Gastroskan-5. Statistical treatment was carried out with IBM SPSS Statistics, significant difference was determined by the Mann-Whitney test.

Results: Alkaline reflux was detected in 18 patients (62%) of the SG and 6 patients (33%) of the CCG, while acid reflux was detected in 11 persons (38%) of the SG and 12 persons (67%) of the CCG. The comparison of the groups showed that the alkaline reflux was more common in patients of the SG, significant differences were determined between the acidity rate in an esophagus at rest and during stimulation ($p < 0.05$). At the same time, a statistically significant difference in Ph-metry in the body of the stomach, antrum, duodenum in two groups was not found. In patients of the groups with acid reflux significant differences were determined in the esophagus at rest and during stimulation ($p < 0.05$), in forestomach at rest and after stimulation ($p < 0.05$). Lower rates of Ph were found in the SG. Acidity differences in two groups in the body and antrum of the stomach, and duodenum were not found.

Conclusions: In overweighted patients complaining of heartburn alkaline reflux is more common, while patients with normal weight have acid reflux. Our results demonstrate that patients need to be treated for heartburn in a different way considering the body weight.

THROMBOSIS PORTAL AND SPLENIC VEIN IN PATIENT WITH HEREDITARY THROMBOPHILIA

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Observation of the patient Sh., 49 y.e., first applied in 2009, the clinic urgently arisen portal hypertension (ascites, esophageal and gastric varices 2 grade, swelling of the lower limbs, hepatosplenomegaly, portal gastropathy). As for laboratory data there was an increase in transaminases to 2 upper normal border, hyperfibrinogenemia (7.8 g / l), increased D-dimer (1780 ng / ml). Viral hepatitis markers and tumor markers (AFP, CEA, CA 19-9) were not identified. Alcoholic liver disease was excluded also. By ultrasound and spiral CT in the vascular mode, found occlusive thrombosis of portal and splenic vein, patency of the superior mesenteric and inferior vena cava, under liver portal hypertension without structural changes in the liver. Hereditary thrombotic history is not burdened. Standard laboratory criteria for antiphospholipid syndrome were not found. In molecular genetic testing revealed a combined thrombophilia: homozygous factor V Leiden mutation, heterozygous mutation in the prothrombin gene (FII 20210 A / G), fibrinogen (FI 455 A / G), plasminogen activator inhibitor type 1 (PAI-1 5G/4G), folate cycle genes (MTHFR 677 C / T and MTRR 66 A / G), homocysteine levels - 17.8 mmol / L (normal 5 - 15 mmol / l). Under the antithrombotic therapy with LMWH with switching to warfarin (INR 2.0 - 3.0 supports more than 80% of the measurements on record in 2010 - 2012.), a courses of treatment with folic acid, vitamins B6, B12 there was regression of clinical manifestations of portal hypertension with normalization of laboratory markers of thrombinemia, homocysteine level and signs of complete portal and splenic veins recanalization on CT. To sum up, making a diagnosis of portal hypertension the hereditary thrombophilia should be taking into account as a cause of idiopathic thrombosis.

STUDYING OF THE TYPE OF RELATION TO AN ILLNESS IN YOUNG PATIENTS WITH GALLSTONE DISEASE.

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Purposes: Studying of the type of relation to an illness in patients with gallstone disease depending on its clinical course.

Materials and methods: The type of the relation to an illness is studied at 44 patients with a gallstone disease (GSD) in comparison with group of control - 28 healthy individuals of age of 18-35 years. The diagnosis was verified by means of clinical and laboratory methods. Psychological research was carried out with according psychological diagnostic method.

Results: The obtained data shows, in patients with GSD most common types of the relation to an illness are diffusion (a combination of three and more types) and mixed (a combination of two types). In group of patients with an asymptomatic stones in gallbladder or a latent form of GFD pure types predominated (adaptive types of the relation to an illness in most cases, anozognostic in particular). Harmonious and ergopathic types were most common in control group. Psychological reactions to an illness depended on habitus, as was shown. The tendency to a choice of disadaptive types of response to an illness ($p < 0.01$) is noted, and greatest incidence was registered in patients with the painful (symptomatic) form of GSD.

Results: Psychological reaction of patients with GSD has essential impact on an illness on formation of psychoemotional shifts. Satisfactory psychosocial adaptation is characteristic in patients with latent form of GSD, while the dyspeptic and painful form of GSD was associated with the expressed psychosocial disadaptation caused by psychoemotional disturbances in introversive habitus.

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