

The Effectiveness of the Gastro-esophageal Reflux Disease Treatment in Persons who have Completed Successful Chronic Hepatitis C Antiviral Therapy at the Rehabilitation Stage

Skuteczność leczenia choroby refluksowej przełyku u pacjentów, którzy ukończyli z sukcesem leczenie antywirusowe przewlekłego zapalenia wątroby na etapie rehabilitacji

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SUMMARY

Aim: To assess the effectiveness of the physiopharmacological treatment of GERD in persons who successfully completed a full course of CHC therapy with direct antiviral drugs no more than 6 months ago.

Materials and Methods: 67 people with GERD who completed a course of CHC therapy with direct antiviral drugs no more than 6 months ago were under observation. The patients were divided into: 1 group (n=20) – received rabeprazole 20 mg in the morning 40 minutes before meals, 2 group (n=23) – rabeprazole 20 mg in combination with taking mineral water “Polyana Kvasova” according to the proposed scheme, group 3 (n=24 patients) – took rabeprazole 20 mg in combination with MV«Polyana Kvasova» for 24 days, and with a course of magnetic therapy procedures.

Results: Under the influence of treatment, on the 24 th day of observation, all 100% of patients in the 3rd group had positive dynamics: the elimination of heartburn ($p<0.001$), pain in the epigastrium ($p<0.001$), and manifestations of dysphagia ($p<0.001$), which were confirmed by fibrogastroscopy - disappearance of esophagitis ($p<0.001$) and gastroesophageal reflux ($p<0.001$). In 80% of the patients of the second group, positive dynamics of the clinical and endoscopic picture was also observed ($p<0.005$), and in the rest of the patients, the improvement was unreliable ($p>0.05$). After the treatment, a decrease in manifestations of asthenovegetative and dyspeptic syndromes, cholestatic syndrome was recorded in all groups of patients, with a predominance in group 3.

Conclusions: The use of complex physiopharmacological treatment has a reliable advantage over standard pharmacological treatment, as it has a positive effect not only on GERD manifestations, but also on clinical and laboratory manifestations of CHC and improves the quality of life.

Key words: GERD, CHC, mineral water, rabeprazole, magnetic therapy

Słowa kluczowe: GERD, przewlekłe zapalenie wątroby typu C, woda mineralna, rabeprazol, magnetoterapia

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INTRODUCTION

Although great success has been achieved in the study of etiopathogenesis, methods of diagnosis and treatment of chronic liver diseases, chronic hepatitis C (HCV) remains an unsolved problem of modern healthcare [1, 2]. According to the statistical data of WHO experts, about 71 million people suffer from CHC, and 350-399 thousand die annually due to liver damage and complications caused by hepatitis C virus (HCV) [3, 4]. The significant prevalence of CHC often leads

to its combined course with other gastrointestinal tract (GI) diseases [5].

Of special interest is the pathology of the gastroduodenal zone, where acid-dependent diseases, in particular gastroesophageal reflux disease (GERD), are prevalent. The World Organization of Gastroenterologists called GERD a disease of the 21st century, which is found in 20% to 50% of the world's population and has a clear tendency to grow [6-8]. The continuous relapsing course of GERD with the progressive development of complications, which

is accompanied by a significant decrease in the quality of life of patients, puts this disease among the most important medical and social problems of practical health care [9,10]. Treatment of GERD involves long-term inhibition of acid production using proton pump inhibitors (PPIs), which can interact with the cytochrome P450 system, inhibiting it [11-13].

The adverse effect of long-term drug load during the treatment of patients with GERD on the body of a patient with liver pathology necessitates the development of new rehabilitation programs based on non-drug effects with the mechanism of action of simultaneous hepatoprotection and normalization of disorders in the digestive system. An alternative to such treatment can be the appointment as part of complex mineral water (MW) therapy and magnetic therapy procedures. Hydrocarbonate waters improve carbohydrate and protein metabolism, have an anti-inflammatory effect. Taking into account that hydrocarbonates reduce the level of acid formation in the stomach, they are indicated for combined liver and gastro-duodenal system pathology [14].

MV should be drunk warm at a temperature of 40-45 degrees C in the amount of 100 to 250 ml per reception, three times a day, before eating. With increased acid formation, MW is prescribed 90-60 minutes before eating food, sometimes 40 minutes after eating food at the height of digestion. With reduced acid-forming function of the stomach, MW is prescribed 30 minutes before eating [15].

AIM

To assess the effectiveness of the physiopharmacological treatment of GERD in persons who successfully completed a full course of CHC therapy with direct antiviral drugs no more than 6 months ago, at the rehabilitation stage.

MATERIALS AND METHODS

During 2020-2021, 67 people who were being treated at the "Kvitka Polonyny" sanatorium of "Suzirya" Ltd (General Director - Honored Doctor of Ukraine P.P. Ganynets) were under observation. Among the examined patients, 58.2% were men, 41.8% were women, the average age was 47.5 ± 5.4 years. Before the start of the study, all patients were informed about the study and signed an informed consent in accordance with the methodological recommendations of the Helsinki Declaration (1975) as amended, the International Code of Medical Ethics (1983), the laws of Ukraine, the relevant provisions of the WHO and approved by the local ethics commission of the Medical Center "UzhNU" (protocol No. 7/2 dated September 30, 2020).

Before the start of sanatorium-resort treatment, all patients were diagnosed with a refractory form of GERD at their place of residence, and all patients completed a full course of CHC therapy with direct antiviral drugs (DAV) sofosbuvir 400 mg + daclatasvir 60 mg no more than 6 months ago, which served as a criterion for inclusion in the study.

Exclusion criteria were infection with hepatitis B and D viruses, alcoholic, autoimmune, toxic liver damage, liver cirrhosis, concomitant diseases of the respiratory system, diseases of the nervous system, psycho-emotional sphere, mental disorders that prevent the conduct of this study and the patient's decision to stop participating in the study.

General clinical, biochemical, serological tests were carried out in certified Uzhgorod and commercial laboratories ("Dila" and «Sinevo»). Indicators of biochemical blood analysis - total bilirubin and its fractions, total protein and protein fractions, activity of serum cytolytic enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST), activity of cholestatic enzymes alkaline phosphatase (ALP) and γ -glutamyl transpeptidase (GGT) were determined using an automatic biochemical analyzer and original ChemWell reagents, Awareness Technology INC (USA). All patients underwent FEGDS using endoscopy equipment with a "Pentax" EPM-3300 video processor, during which any pathological changes in the esophagus and/or stomach and the degree of varicose veins of the esophagus were detected. Hp infection was diagnosed using a rapid urease test (CLO-test) or a stool test (CITO TEST, manufactured by Farmasco LLC, USA). The examined patients underwent an ultrasound examination of the abdominal organs (HDI-1500 device, USA).

Depending on the tasks and options of pharmacotherapy, all patients are divided into three groups. The groups were representative by age and sex. The first group (n=20) received only PPI rabeprazole 20 mg (PPI) in the morning 40 minutes before meals. The second group of patients (n=23) took rabeprazole 20 mg (PPI) in the morning 40 minutes before a meal in combination with a course of internal administration of "Polyana Kvasova" MW according to our proposed scheme. The third group (main, n=24 patients) patients took rabeprazole 20 mg (PPI) in the morning 40 minutes before meals in combination with internal reception of MW "Polyana Kvasova" according to the scheme: reception of warm MW at a temperature of 40-45 degrees C in quantities of 200 ml per reception, three times a day, 90-60 minutes before eating, for 24 days in combination with a simultaneous course of magnetotherapy procedures, which included a low-frequency pulse variable magnetic field on the area of the lower esophageal sphincter with a pulse frequency of 0.1-10.0 Hz, with induction of 128 μ T, procedure duration 40 minutes, treatment course 8-10 procedures, every other day. The dynamics of treatment were evaluated according to generally accepted standard research methods on the 24th day of stay in the sanatorium. The criteria for the effectiveness of therapy were the reduction or disappearance of patients' complaints, disappearance of esophagitis, gastroesophageal reflux, and improvement in quality of life. Quality of life (QoL) was assessed in patients according to the scale of the SF-36 questionnaire. The analysis and processing of the results of the examination of patients was carried out using the Statistics for Windows v.7.0 computer program (StatSoft Inc, USA) using parametric and non-parametric methods of evaluating the obtained results. The difference was considered to be significant at $p < 0.05$.

RESULTS

Under the influence of treatment, on the 24th day of observation, all 100% of patients in the main group had positive dynamics: elimination of heartburn ($p < 0.001$), pain in the epigastrium ($p < 0.001$) and manifestations of dysphagia ($p < 0.001$), which were confirmed by fibrogastroscopy - disappearance of esophagitis ($p < 0.001$) and gastroesophageal reflux ($p < 0.001$). In 80% of the patients of the second group, positive dynamics of the clinical and

endoscopic picture was also observed ($p<0.005$), in the remaining patients the improvement was unreliable ($p>0.05$). In patients of the third group, positive dynamics of GERD clinical symptoms were registered only in 67.5% of patients. After the treatment, a decrease in manifestations of asthenovegetative and dyspeptic syndromes, cholestatic syndrome was recorded in all groups of patients, with a predominance in group 3. Dyspeptic complaints decreased or disappeared in 91.7% (22 out of 24) of patients in group 3 versus 65.0% (13/20) and 73.9% (17/23) of patients in groups 1 and 2. Disappearance of heaviness in the right hypochondrium was also significantly more frequent in patients of group 3 than in patients of groups 1 and 2 (95.8% (23/24) versus 60.0% (12/20) and 69.6% (16/23), respectively; $p<0.05$).

Under the influence of the physiopharmacological therapy proposed by us, positive changes were registered not only in the well-being of the patients, but also in the biochemical indicators of the blood, which characterized the cholestatic syndrome – alkaline phosphatase, gammalutamyltransferase (GGT) and total bilirubin (TB). After 24 days of treatment, group 3 patients showed a decrease in the levels of TB from normally high to normal, normalization of ALP and GGT, which were increased before treatment by 1.5 and 1.9 times, respectively. No significant changes in these indicators were registered in the patients of the other two groups.

The most objective assessment of the treatment effectiveness is the evaluation of the quality of life of patients with GERD. After the course of treatment of patients with GERD, a tendency to improve all quality of life indicators was found, but a statistically significant difference between the signs before and after treatment was established only in patients of the first group.

After treatment, scores on the entire scale of SF-36 increased the most in patients of group 1, namely quality of life improved most significantly in this group.

Analyzing the integrated indicators of the physical and mental components of health in GERD patients by group, the following dynamics were revealed: the average values of the integrated indicator of the physical component of health (PH)

in patients of groups 1 and 2 increased by 5 ± 1.5 and 6 ± 0.2 points, and in patients of 3 groups, the maximum improvement was observed – by 8 ± 1.7 points compared to the indicators before treatment. The same dynamics were observed in the characteristics of the integrated mental component of health (MH), namely: in patients of groups 1 and 2, the indicator increased by 7 ± 1.8 points and 7 ± 4.1 points, and in patients of group 3 – by 11 ± 0.5 points (Table 1).

DISCUSSION

As the observations showed, in the majority of patients of all groups, after the treatment, the general well-being improved, the severity of subjective and objective symptoms of GERD significantly decreased, and the functional state of the liver normalized. The most expressive positive dynamics of complaints was in patients who received mineral water on the background of rabeprazole intake according to the proposed scheme and magnetic therapy procedures. Obviously, this is due to the mechanism of the therapeutic and preventive effect of MW, the hydrocarbons of which neutralize increased acid formation in the stomach [14]. The obtained data coincide with numerous experimental and clinical studies by scientists of the Ukrainian Research Institute of Medical Rehabilitation and Spa, which demonstrated the multifaceted therapeutic effect of MW [15, 16]. Mineral waters are able to influence the regulation of the work of the central brain structures, tissue respiration, stimulate the work of the enteroinsular axis and the release of gastrointestinal hormones, strengthen the function of the gastric glands, the processes of regeneration of the gastric mucosa, normalize its motor and evacuation functions. The ability to restore the metabolism of hepatocytes, exert an immunoregulatory effect, stimulate the processes of bile formation, bile secretion and pancreatic secretion, were confirmed by the normalization of cholestasis markers, namely ALP, GGP and total bilirubin. Similar data on the effect of MW on the indicators of pigment metabolism ($p<0.001$) and cholestasis ($p<0.05$) in patients with steatohepatitis were obtained by other scientists [15, 16]. The improvement in the quality of life, which we registered in people

Table 1. Quality of life indicators before and after treatment

Index	Control group (n=25)		Group 1		Group 2		Group 3	
			Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
PF	78±1.6	81±2.2	77±2.1	81±1.7	72±1.2	79±1.8	77±2.5	86±1.4
RP	56±3.3	59±1.6	51±3.3	58±1.2	41±3.6	49±2.5	39±2.2	45±1.5
BP	52±1.1	56±2.7	53±1.1	62±2.2	42±4.2	45±3.1	35±4.1	42±1.7*
GH	52±1.6	58±2.1	52±2.0	59±2.4	43±3.1	49±2.1	36±3.5	45±4.4*
VT	56±2.4	60±1.3	54±2.3	61±3.2	46±2.0	51±2.5	37±4.2	46±5.4*
SF	57±1.4	61±2.1	59±2.0	69±4.4	52±2.5	58±2.7	45±1.2	50±2.5
RE	38±4.2	42±3.1	41±2.1	45±2.6	33±2.5	39±2.1	27±1.7	33±2.1*
MH	51±1.9	55±3.1	51±1.9	60±1.7	44±3.3	48±2.0	41±3.5	48±1.1*
PH	54±1.2	58±1.4	55±2.2	60±1.7	50±1.2	56±1.4	44±1.8	52±3.5
MH1	50±2.4	53±2.7	48±3.3	55±1.5	44±1.1	51±5.2	40±1.7	51±1.2

Notes: * – the difference is significant ($p<0.05$); a – before treatment; b – after treatment

who received complex treatment, is probably due to an increase in the level of serotonin [17]. Our data coincide with experimental data obtained by other scientists, who showed that after a course of taking MW together with other hormones, the basal level of serotonin increases by almost 75%. At the same time, similar to insulin, there is stimulation of the early phase of serotonin secretion [17, 18]. Therefore, the use of complex physiopharmacological treatment has a reliable advantage over standard pharmacological treatment, as it has a positive effect not only on the manifestations of GERD, but also on the clinical and laboratory manifestations of CHC and improves the quality of life.

CONCLUSIONS

The proposed complex therapy with the use of natural physical factors (magnetotherapy) and the internal intake of «Polyana Kvasova» bicarbonate-sodium mineral water against the background of rabeprazole administration contributes not only to the rapid normalization of the acid-forming function of the stomach, but also to the restoration of the functional state of the hepatobiliary system, and improves the quality of life of patients.

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