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FEATURES OF COMPLIANCE IN THE «DOCTOR – PARENTS – PATIENT SYSTEM» IN THE TREATMENT OF CHILDREN WITH CYSTIC FIBROSIS COMMUNICATION II

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Summary: Our study shows the importance of compliance in families that have children with cystic fibrosis. The separation of questions in the questionnaire into blocks allowed us to evaluate the compliance of parents having a sick child with various aspects of prevention and treatment both at general and individual levels.

Keywords: compliance, cystic fibrosis, physiotherapy, vitamins, pancreatic enzymes.

Introduction. Cystic fibrosis (CF) is an inherited multi-organ disease that previously was attributed to early lethal illnesses, since life duration for sick children did not exceed 5 years. Over time, this pathology moved into the category of adult diseases. According to J. Dodge (2007), the estimated life expectancy of patients with CF in Great Britain for those born in 2000 is more than 50 years^{1,4}.

The successful treatment of CF requires a number of priority actions: to increase awareness of physicians for diagnosis and treatment of this disease; to provide necessary medications to patients; to improve the level of trust between patients and physicians¹. The quality of cooperation between a physician and a patient depends on the patient's life expectancy of CF, and in paediatric practice the situation is complicated by several factors: firstly, there are three participants in compliance: a doctor, parents and a patient, and, secondly, there are certain problems due to various psychological aspects of the medical approach to a child at every stage of its development³.

To assess a patient compliance a variety of methods are used but each of them has some disadvantages. The most effective, non-invasive and fastest for practical medicine is the questionnaire method⁷.

The aim of research. To find correlations between different aspects of compliance to treatment concerning parents of children with CF and to evaluate overall compliance both at general and individual levels.

Materials and methods: The study was conducted at the center of care to children suffering from CF in Western Ukrainian Specialized Children's Medical Center. 58 parents whose children suffer from CF have been surveyed. The survey was conducted by interviewing, with using of questionnaire which includes 31 questions that were divided into blocks: passport data, physiotherapy, pancreatic enzymes, vitamins and general questions about therapy.

Statistical analysis was carried out in the environment for statistical computing R 3.0.1⁶.

The level of statistical significance α in this study has been set at 0.01. In order to search for possible relationships between the answers of respondents on different questions Fisher's exact test was used, polychoric correlation coefficient (φ) was used as a measure of relationship strength between two ordinal variables and Cramer's V – in case of two nominal or nominal and ordinal attributes.

Results and discussion. Frequency of physiotherapy performance is statistically significantly associated with the percentage phy-

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siotherapy performance relative to the required level ($\varphi=0,604$, $p=0,00048$). The more a child performs physiotherapy, the higher marks are given by parents for the adequacy of these procedures.

The responses to both previous questions related to the answer on the question about physical therapy sufficiency. Polychoric correlation coefficient between the frequency and adequacy of physiotherapy is $\varphi=0,617$, $p=0,00108$;

and between the percentage of physiotherapy compared to the need and adequacy is $\varphi=0,673$, $p=0,00185$ respectively.

We have found that the frequency of physiotherapy performance correlates with a question about reasons of vitamin therapy refusal ($V=0,350$, $p=0,00378$): children of parents which forget about vitamin therapy were much more likely to miss physiotherapy (fig. 1).

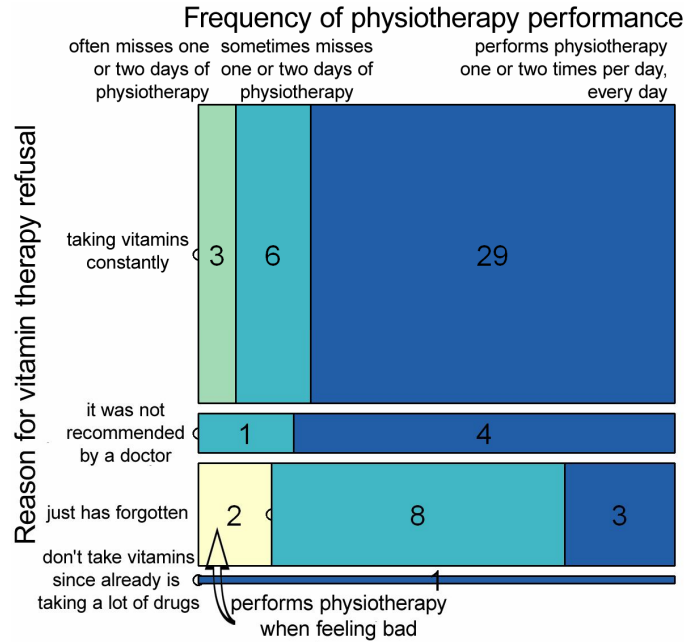


Fig. 1. The relationship between frequency of physiotherapy performance and reasons for vitamin therapy refusal

Answers to the question «Do you perform a prescription of a doctor constantly?» correlate with the responses to the questions related to the frequency ($\varphi=0,671$, $p=0,00011$) and adequacy of physiotherapy performance ($\varphi=0,789$, $p=0,00002$).

Parents of children with CF who said that they always follow a doctor's prescription, responded more often that there is sufficient amount of physiotherapy and their child performs physical therapy 1–2 times a day every day. Performance of physical therapy is also associated with frequency in skipping medication with statistical significance ($\varphi=0,579$, $p=0,00084$): 84% of children, who never miss medication, perform physical therapy sufficiently (fig. 2).

Interruption of medication course statistically significantly correlates with frequency of physiotherapy ($\varphi=-0,461$, $p=0,00673$), with the percentage of physiotherapy performance compared with the need ($\varphi=-0,668$, $p=0,00005$) and with adequacy of physiotherapy performance ($\varphi=-0,642$, $p=0,00950$). High frequency of medi-

cation interruption is associated with lower percentage and sufficiency of physiotherapy.

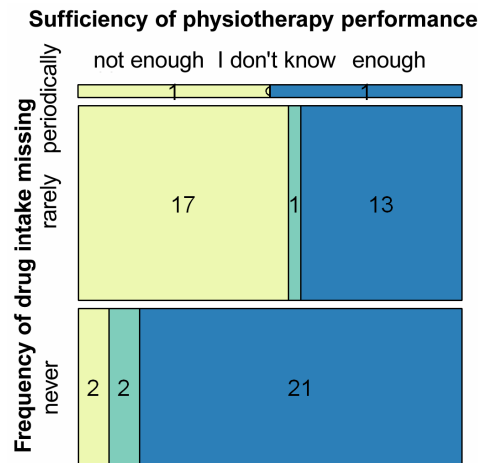


Fig. 2. The relationship between sufficiency of physiotherapy performance and the frequency of drug intake missing

It has been observed that reasons for vitamin therapy refusal correlate with the performance

of other prescriptions ($V=0,606$, $p=0,00003$). Among those patients who always follow doctor's advice, only 5% have indicated that they forget about taking vitamins, but among those who said they almost always follow the recommendations, that fraction reaches 58%. Concerning the relationship between frequency medication course violation and vitamin therapy refusal ($V=0,394$, $p=0,00048$), none of the 24 parents who never miss taking pills say that forgetting was the reason for vitamin therapy refusal. Reasons for missing vitamins are also correlated with the causes of non-compliance with recommendations for medications ($V=0,408$, $p=0,00251$) – 61% of parents that reported the large number of prescribed drugs as the reason for medication violation do not give kids vitamins due to forgetfulness).

The opinion of parents regarding sufficiency of vitamins supply correlates with assignments performance ($\varphi=0,496$, $p=0,00792$): among those parents who always execute prescriptions, only one (3%) father considers, that the intake of vitamins is insufficient, while among those parents, who answered that they almost always follow prescriptions of a doctor, the corresponding percent is equal to 32% (6 parents). The benefits of vitamin therapy (the parents' point of view) are also related to the reason for medication course violation ($V=0,399$, $p=0,00620$): from 5 parents who reported the difficulty of taking the drugs as the reason for non-compliance with the recommendations only 1 parent (20%) believes that vitamin therapy is beneficial, while among parents who cited other

reasons for non-compliance with the recommendations corresponding fraction is 85% (44 parents).

In order to assess the overall level of compliance, the numerical scores have been assigned to the responses, where 0 means the absence of compliance, 1 – moderate compliance and 2 – good compliance, and three computational approaches of increasing complexity were used. The final results are presented as a percentage compared to possible maximum. The first and the simplest way is to calculate the arithmetic mean of scores across all answers. The disadvantage of this method is that all questions in this questionnaire have the same influence on the outcome, regardless of how strongly they relate to compliance and are consistent with each other. To eliminate this drawback, it is necessary to assign appropriate weight for each question, and then to determine the weighted average. These weights should depend on the degree of consistency with all other answers. The resulting weighted average should be the best way to distinguish respondents by their level of compliance. Such problem can be solved by *Principal Components Analysis (PCA)*³, and the coefficients of the first principal component are desired weights while projections of respondents' answers to the first principal component are the scores of compliance.

Since several respondents did not answer some questions, *nonlinear iterative projection to latent structures (NIPALS)* has been used as analysis algorithm instead of traditional singular vector decomposition of studied matrix. The obtained weights are shown in table 1.

Table. 1. The weights of questions used for the estimation of general level of compliance

Questions in the questionnaire regarding:	The weight of question
1	2
Frequency of physiotherapy performance	0,559409
Adequacy of physical activity	0,333873
Adequacy of physiotherapy performance	0,268338
Frequency of assignments performance	0,265579
Regularity of examinations by physician (as recommended)	0,263067
Percent of physical therapy performance compared to the need	0,258105
The frequency of medication course violation	0,257228
Sufficient supply of vitamins	0,229639
Reason for vitamin therapy refusal	0,20014
The reasons for medication course violation	0,166616
The frequency of vitamins intake	0,155627
Frequency of satisfaction with treatment	0,117553
Parents' point of view concerning vaccination	0,09573
The frequency of «fatty» stool	0,094529
The frequency of outpatient reviews per year	0,084008
Parents' point of view concerning flu shots	0,083435
The frequency of taking drugs that are not subscribed by a doctor	0,06686
The reason for treatment failure	0,062013
The causes of exacerbations of chronic bronchitis	0,054557

Cont. table 1	
1	2
The benefits of taking vitamins	0,045377
Order of enzymes and meals intake	0,038098
Frequency of treatment regime violations	0,034996
Skipping of drug intake when feeling bad	0,026537
Frequency of pancreatic enzymes supplementation with snacks	0,01347
Frequency of pancreatic enzymes supplementation with meals	0,010891
Frequency of forgetting to take a drug	0,003113
Causes of poor weight gain	-0,02019
Falseness of the statement: «courses of treatment interfere with the development of my child»	-0,15135

In such a way, the best predictor of compliance is the answer to the question «Does your child perform physical therapy enough?». Among the most influential questions are precisely those that are directly related to compliance, namely physical therapy, performance of doctor appointments, the regularity of outpatient examinations, the frequency of medication course violation, and sufficiency of vitamins intake. At the same time, other questions have received smaller weights such as the causes of exacerbation of bronchitis, the benefits of taking vitamins, questions related to the use of enzymes, skipping of medication when feeling bad, the frequency of forgetting to take a drug.

In addition, two questions were found to be inversely related to compliance (albeit weak): about the causes of poor weight gain and whether courses of treatment interfere with the development of my child ($w=-0,02019$, $w=-0,15135$ respectively). On these questions pa-

rents, that showed low compliance with other questions, give answers that are associated with high compliance and vice versa. This may indicate either that the answers to these questions really have no connection with compliance, or their phrasing was rather difficult to understand and, thus, has been not correctly interpreted by parents.

A possible drawback of principal components analysis is that compliance is considered as a single indivisible entity, when in fact the problem of compliance is multilateral so different aspects can be identified, such as compliance with physical therapy, enzyme therapy, vitamin therapy, and compliance concerning general questions. For evaluation of each part separately, we have conducted multiple factor analysis (MFA) as implemented in additional statistical package FactoMineR⁷. The computed weights for each group are listed in table. 2.

Table 2. The weights of questions for the assessment of various aspects of compliance

Questions	The weight of questions
1	2
Compliance with physiotherapy	
Frequency of physiotherapy performance	0,743352
Percent of physical therapy performance compared to the need	0,745909
Adequacy of physiotherapy performance	0,839785
Adequacy of physical activity	0,456779
Compliance with enzyme therapy	
Frequency of pancreatic enzymes supplementation with meals	0,658841
Order of enzymes and meals intake	-0,36487
Frequency of pancreatic enzymes supplementation with snacks	0,341224
Causes of poor weight gain	0,701617
The frequency of «fatty» stool	-0,40572
Compliance with vitamin therapy	
The frequency of vitamins intake	0,680644
Reason for vitamin therapy refusal	0,814193
Sufficient supply of vitamins	0,649149
The benefits of taking vitamins	0,426611
Compliance concerning general questions	
The frequency of taking drugs that are not subscribed by a doctor	0,362097
Frequency of assignments performance	0,7236
The reason for treatment failure	0,462716
The causes of exacerbations of chronic bronchitis	0,440085

Cont. tabl. 2

1	2
The frequency of medication course violation	0,801225
The reasons for medication course violation	0,700265
Frequency of forgetting to take a drug	0,481886
Frequency of treatment regime violations	0,064012
Skipping of drug intake when feeling bad	0,546312
Falseness of the statement: «courses of treatment interfere with the development of my child»	-0,19745
Frequency of satisfaction with treatment	0,208755
Parents' point of view concerning vaccination	0,327522
Parents' point of view concerning flu shots	0,217079
Regularity of examinations by physician (as recommended)	0,504158
The frequency of outpatient reviews per year	0,191056

As it can be seen in table 2, the parents' score of adequacy of physiotherapy performance is the best indicator of compliance in the group of questions about physiotherapy. In the group of questions regarding the admission of enzyme preparations the response to the question about the reasons for the slow weight gain helps to distinguish parents with strong and weak compliance the most efficiently. While the questions about order of enzymes and meals intake and the presence of fatty stool give only a little information. As for vitamin therapy, the most informative question relates to the reasons for vitamin therapy refusal ($w=0,814$).

Among general questions, the best predictors of compliance are the questionnaire points regarding the frequency of medication course violation and the frequency of assignments performance.

Using multiple factor analysis the overall level of compliance can be obtained as the simple average of groups (assuming that all sides

of compliance have equal importance's, as well as the generalized output of the algorithm (assuming that those sides of compliance that are in better agreement with each other are more important). While calculating the compliance scores, those questions that have received negative weights were not taken into account, because there is no reason to believe that a favorable to compliance response may actually reduce it. All scores were converted to percentages relative to the maximum value that can be obtained with the most favourable responses to all questions. The analysis of scores, which have been obtained by different methods (table 3) shows that there are no patients with a complete absence of compliance (actually, there is only one parent that has compliance with physiotherapy equal to 0%). However, rather difficult question is still unclear: what percentage of compliance is sufficient for successful therapy?

Table 3. Scores of compliance of the respondents obtained through different methods

№	Arithmetic mean, %	Projection on the first principal component, %	MFA, compliance with physiotherapy, %	MFA, compliance with enzyme therapy, %	MFA, compliance with vitamin therapy, %	MFA, compliance with general questions, %	MFA, arithmetic mean of groups, %	MFA, generalized results, %
1	2	3	4	5	6	7	8	9
1	2	3	4	5	6	7	8	9
1	95	99	100	100	87	98	96	94
2	96	100	100	90	100	100	98	98
3	80	77	53	94	100	76	81	75
1	2	3	4	5	6	7	8	9
4	91	94	73	90	100	87	88	85
5	75	76	30	90	75	80	69	63
6	59	64	0	100	58	57	54	44
7	91	96	100	90	87	86	91	88
8	79	81	63	69	75	90	74	79
9	90	96	100	83	71	85	85	85
10	55	65	16	90	46	49	50	38
11	68	81	92	90	58	56	74	62
12	86	95	100	90	100	81	93	89
13	88	91	70	90	100	87	87	84

Cont. tabl. 3

1	2	3	4	5	6	7	8	9
14	82	80	56	90	100	88	84	79
15	80	87	58	69	100	93	80	84
16	82	88	78	90	87	83	85	84
17	64	72	27	85	58	70	60	55
18	82	85	56	100	100	71	82	73
19	89	96	87	100	100	90	94	91
20	89	96	87	92	100	90	92	91
21	66	79	58	69	50	67	61	60
22	73	76	40	69	100	72	70	69
23	79	84	73	69	92	78	78	82
24	82	86	73	90	100	75	85	79
25	69	69	27	90	46	73	59	53
26	94	97	100	90	87	95	93	94
27	73	84	70	69	100	69	77	78
28	70	72	40	90	84	65	70	58
29	66	66	43	90	58	64	64	53
30	89	96	100	69	100	95	91	97
31	68	74	43	90	46	70	62	55
32	78	81	84	83	100	62	82	76
33	89	92	100	100	87	84	93	88
34	96	98	100	79	100	98	94	99
35	70	79	100	90	59	50	75	63
36	71	76	30	69	71	68	60	61
37	84	89	84	69	100	92	86	90
38	77	78	27	90	87	78	71	66
39	84	88	87	100	74	80	85	81
40	91	97	100	79	87	95	90	94
41	79	86	87	90	87	73	84	79
42	73	77	70	69	39	88	67	74
43	93	91	73	100	100	95	92	92
44	89	93	100	80	87	91	90	92
45	82	81	27	100	100	93	80	79
46	64	64	27	79	66	58	58	54
47	80	72	40	71	92	89	73	81
48	73	82	87	100	58	73	80	74
49	69	66	43	65	92	67	67	66
50	82	83	84	100	71	91	87	85
51	83	81	57	100	97	86	85	82
52	82	85	100	90	100	71	90	84
53	89	95	100	90	87	85	91	90
54	68	84	87	79	53	65	71	69
55	93	97	100	90	100	92	96	96
1	2	3	4	5	6	7	8	9
56	78	82	87	29	100	75	73	82
57	87	94	73	90	100	89	88	89
58	79	73	27	100	63	90	70	69

In fact, the border between a good, medium and low compliance are conventional. Therefore, without introducing strict limits in table 3, we have identified 10 most adherent to treatment parents (green colour) and 10 parents with the lowest compliance for each indicator (red colour).

To investigate the relationships between the obtained scores and to choose the best one correlation matrix was computed. The subjective rating of compliance given by a physician (in three categories: low, medium, high) has been

also included to the matrix. Polyserial correlation coefficient has been used to evaluate the correlation between physician's rating and all other scores, while Pearson correlation coefficient has been computed for the remaining pair wise combinations (table 4.).

It was found that the calculated estimates correlate with subjective rating of physician weakly or moderately, with the strongest relationship observed with score of compliance with general questions ($\rho=0,407$).

Table 4. Correlation coefficients between the estimated compliance obtained by different methods

	Subjective rating from physician		Projection on the first principal component, %		MFA, compliance with enzyme therapy, %		MFA, compliance with general questions, %		MFA, generalized results, %	
	Arithmetic mean, %		MFA, compliance with physiotherapy, %		MFA, compliance with enzyme therapy, %		MFA, compliance with general questions, %		MFA, compliance with enzyme therapy, %	MFA, arithmetic mean of groups, %
The assessment of physician	1	0,371	0,238	0,108	0,353	0,407	0,299	0,282		
Mean arithmetic, %		1	0,905	0,176	0,686	0,855	0,938	0,946		
The projection on the first principal component, %			1	0,115	0,562	0,705	0,917	0,905		
MFA, compliance of physiotherapy, %				1	0,351	0,412	0,815	0,781		
MFA, compliance of enzyme therapy, %					1	0,072	0,253	0,000		
MFA, compliance of vitamin therapy, %						1	0,707	0,710		
MFA, compliance of general questions, %							1	0,832		
MFA, mean arithmetic of groups, %								1		0,944
MFA, general results, %										1

General questions mainly relate to the thoughts and attitudes of respondents that a doctor can reveal when communicating with the patient, while other groups of questions describe real behaviour and life situation in respondents that are less available for observation. All other compliance scores correlate well with each other, except the compliance with enzyme therapy. That is, parents may exhibit good compliance with most aspects of treatment, and at the same time a low compliance related to enzyme therapy and vice versa. Looking at the values of Table 4, the highest levels of correlation with all parameters are demonstrated by MFA scores, obtained as the arithmetic mean of four individual aspects of

compliance. Though the answers to questions about enzyme therapy are not consistent with other aspects of compliance, the significant role of enzyme therapy should be taken into account while calculating the overall level compliance in the treatment of patients with CF. Therefore, the arithmetic mean of the four groups of MFA is recommended to determine the level of compliance further.

If we assume that the values of the compliance score <70% indicate a low level of compliance, the values from 70 to 90% – medium level and above 90% – high level, then 24% of respondents will have a low level of compliance, 50% – medium, and 26% – high.

Conclusions:

1. The answers of the questions in blocks (physiotherapy, vitamin therapy and general questions) were positively correlated with statistical significance. However, this trend was not observed for the results of questions about enzyme therapy. In practice this means that the importance of taking pancreatic enzymes for complex treatment should be emphasized by doctors during consultations
2. We have found that the best predictor of compliance with physiotherapy is the answer to the question «Is it enough your child performs physiotherapy?»; as for vitamin therapy, the most informative question is a point concerning the reasons for refusal of taking vitamins; regarding common questions the best compliance indicators are items in the questionnaire regarding the frequency of drug intake skipping and performance of prescriptions.
3. The calculated compliance estimates correlate with subjective rating of physician weakly or moderately with the strongest relationship observed with score of compliance with general questions.

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ОСОБЕННОСТИ КОМПЛАЕНСА В СИСТЕМЕ ВРАЧ – РОДИТЕЛИ – ПАЦИЕНТ В ЛЕЧЕНИИ ДЕТЕЙ, БОЛЬНЫХ МУКОВИСЦИДОЗОМ. СООБЩЕНИЕ II.

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Резюме: Проведенное нами исследование показывает, насколько актуальным является проблема комплаенса в семьях, где есть дети больные муковисцидозом. Вопросы в анкете по уходу за такими пациентами были распределены на блоки, ответы на которые позволили нам установить уровень комплаенса родителей больного ребенка относительно различных аспектов профилактики и лечения в целом и в каждом отдельном случае.

Ключевые слова: комплаенс, муковисцидоз, физиотерапия, витамины, панкреатические ферменты.

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ОСОБЛИВОСТІ КОМПЛАЄНСУ В СИСТЕМІ ЛІКАР – БАТЬКИ – ПАЦІЄНТ У ЛІКУВАННІ ДІТЕЙ, ХВОРИХ НА МУКОВІСЦИДОЗ. ПОВІДОМЛЕННЯ II.

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Резюме: Проведене нами дослідження показує наскільки актуальним є проблема комплаєнсу у сім'ях, де є діти хворі на муковісцидоз. Запитання у анкеті по догляду за пацієнтами на цю недугу були розподілені на блоки, відповіді на які дозволили нам виявити рівень комплаєнсу батьків хворої дитини щодо різноманітних аспектів профілактики і лікування загалом та у кожному окремому випадку.

Ключові слова: комплаєнс, муковісцидоз, фізіотерапія, вітаміни, панкреатичні ферменти.

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