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ASSESSMENT OF ADHESION TO TREATMENT OF PATIENTS BEING ON KIDNEY REPLACEMENT THERAPY TAKING INTO ACCOUNT THE PRESENCE OF TYPE 2 DIABETES MELLITUS

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This article presents the results of the analysis of adherence to treatment of patients on renal replacement therapy, taking into account type 2 diabetes. It was found that the adherence index to treatment is directly proportional to the patient's age and does not depend on the article and duration of treatment on programmed hemodialysis. In turn, the presence of a history of diabetes increases patient compliance, which, in turn, has a positive effect on disease control by both the doctor and the patient. Patients with stage I-II chronic kidney disease have a low level of adherence, which may be an additional risk factor for renal failure progression.

Key words: compliance, program hemodialysis, diabetes mellitus, chronic kidney disease.

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ОЦІНКА ПРИХИЛЬНОСТІ ДО ЛІКУВАННЯ ХВОРИХ, ЩО ПЕРЕБУВАЮТЬ НА НИРКОВО-ЗАМІСНІЙ ТЕРАПІЇ З УРАХУВАННЯМ НАЯВНОСТІ ЦУКРОВОГО ДІАБЕТУ 2-ГО ТИПУ

У даній статті представлені результати аналізу прихильності до лікування хворих, що перебувають на нирково-замісній терапії з урахуванням цукрового діабету 2-го типу. Виявлено, що оцінка прихильності до лікування прямо пропорційна віку пацієнта та не залежить від статті та тривалості лікування на програмному гемодіалізі. В свою чергу наявність цукрового діабету в анамнезі підвищує комплаєнс пацієнтів, що, в свою чергу, позитивно впливає на контроль захворювання як лікарем так і самим пацієнтом. У хворих з хронічною хворобою нирок I-II стадії низький рівень прихильності, що може стати додатковим фактором ризику прогресування ниркової недостатності.

Ключові слова: комплаєнс, програмний гемодіаліз, цукровий діабет, хронічна хвороба нирок.

Chronic kidney disease (CKD) is becoming an increasingly important health problem every year, due to rising morbidity, increasing disability and increasing mortality rates in Ukraine and around the world. Many large-scale studies have confirmed the high prevalence of chronic kidney disease, which is comparable to the prevalence of coronary heart disease, diabetes mellitus (DM) [4].

The high prevalence of end-stage CKD, which requires renal replacement therapy (RRT) in patients of working age, puts the problem of mental disorders and compliance in this category of patients among the socially significant [7-10]. Currently, to determine the adequacy of treatment, patients are assessed not only by somatic indices, but also by psychological status, quality of life, compliance between the doctor and the patient. Despite the rapid progress in the implementation of modern methods of treatment of the end-stage CKD, the assessment of the psycho-emotional state of dialysis patients, many issues related to rehabilitation during RRT remain open. Thus, the current problem of modern dialysis treatment is its impact not only on the manifestations of somatic pathology, but also mental health and, last but not least, on patient compliance [1, 3].

One of the negative consequences of non-compliance with the patient's medication regimen is the erroneous conclusion that the doctor may reach regarding the efficacy of the prescribed medication regimen. In such cases, the doctor may prescribe new treatment, which may worsen the patient's condition. It is important to consider comorbid diseases such as diabetes, in which dialysis patients use insulin therapy. These complex treatment regimens place a significant burden on patients and tend to make them dependent on physicians in many aspects of treatment, and can also reduce compliance between the physician and the patient. There are many factors that can cause the medication regimen violations with patient compliance.

These factors were classified by Jing Jin et al. into patient-centered factors, factors directly related to treatment, social and economic factors, health system factors, and disease factors [7]. Age, ethnicity, gender, educational and work process, marital status, smoking and/or alcohol use are among the factors that are patient-centered. Factors associated with therapy include route of administration, versatility of

treatment, duration of treatment, side effects of drugs, etc. Factors in the health care system include the lack of available programs for patients, the lack of free medicines to correct disorders in dialysis patients, the lack of proper free psychological care for this category of patients. The social and economic factors include the cost of continuous treatment, social support, the difficulty of finding the optimal job. Finally, the factors of the disease include various symptoms of the disease and the severity of its course.

In this regard, it is very important that the patient on dialysis therapy adheres to the prescribed regimens and standards of treatment, which determined the purpose of the study.

The purpose of the study was to analyze compliance with the regimen of medication by dialysis patients and to identify factors that may affect compliance.

Materials and methods. The study was performed at the Center for Nephrology and Dialysis UE "Poltava M.V. Sklifosovsky Regional Clinical Hospital of the Poltava regional council". The study involved 93 patients, of which 44 patients on programmed hemodialysis and 49 who were in the control group – patients with stage I-II CKD. Dialysis patients underwent standard bicarbonate dialysis three times a week for 4 hours. The eKt/V index in all the patients was above 1.2. In turn, the experimental group (patients on dialysis therapy) was divided into two subgroups: 20 patients (EG 1) with diabetic nephropathy (DN), 24 – with other diseases (EG 2). The mean duration of treatment with renal replacement therapy was 6.2±6.7 years.

The control group was also divided into two subgroups: 26 patients with KD (CG 1), and 23 – without KD (CG 2). The mean age of hemodialysis patients was 50.1±11.8 years, and in EG 1 the mean age was 51.9±9.5 years, in CG2 – 48.7±13.4 years. The mean age of patients in the control group was 49.3±17.1 years, and in CG 1 the mean age was 58.1±10.4 years, and in CG 2 – 39.3±17.8, respectively. By gender, all patients were distributed as follows: 62 (66.7 % women and 31 (33.3 %) men. The study group included 24 (25.8 %) women and 20 (21.5 %) men, in the control – 38 (40.9 %) women and 11 (11.8 %) men.

Compliance was determined using a specific Moriski-Green questionnaire (MMAS-8) consisting of 8 questions. The patient answered each question. "Yes" or "No". 1 point was awarded for each negative answer, except for the question of taking all drugs for yesterday (1 point for the answer "Yes"). In the 8th question with ranked answers, 1 point was awarded only for the answer "Never". Adherence to treatment was assessed by the sum of points: high adherence – 8 points, medium adherence – 6-7 points, low – below 6 points.

Statistical processing was performed using Microsoft Excel 2010. Statistically significant difference between comparison groups was determined using the parametric Student's test.
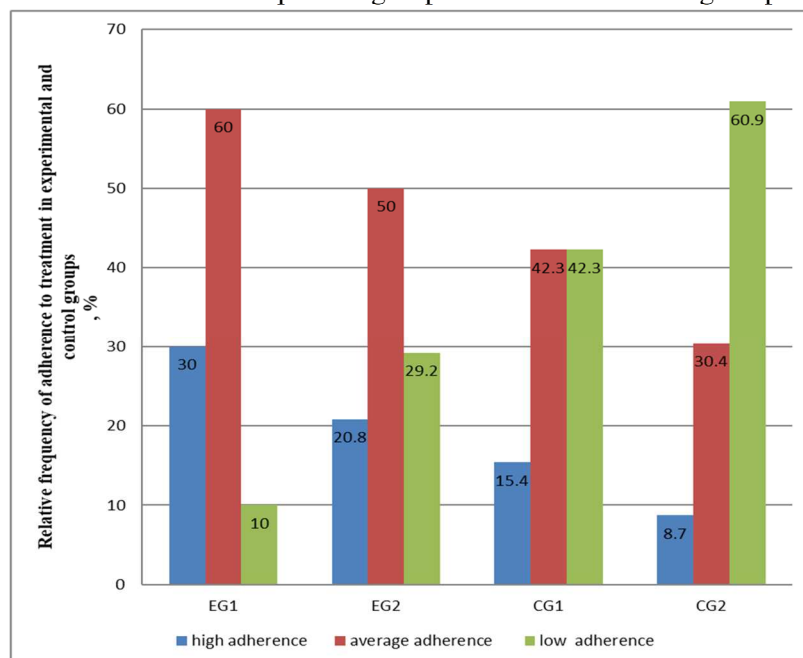

Fig. 1. Relative frequency of adherence to treatment in experimental and control groups

Results of the study and their discussion. The study was only performed after obtaining written consent to the interview in accordance with the principles of the Declaration of Human Rights in Helsinki, the Council of Europe Convention on Human Rights and Biomedicine, relevant Ukrainian laws and international instruments. Compliance results based on the MMAS-8 questionnaire were compared in experimental and control groups in the presence of type 2 diabetes. Thus, in EG 1 only 6 (30.0 %) patients showed high adherence to treatment, while in EG 2 – in 5 (20.8 %) patients. In the control groups – 4 (15.4 %) and 2 (8.7 %), respectively (fig. 1).

Note that in EG 1–2 (10.0 %) and 7 (29.2 %) in EG 2 patients were not committed to treatment. As in CG 1 and CG 2 11 (42.3 %) and 14 (60.9 %) patients, respectively, were not committed to treatment, which could potentially lead to negative consequences in the further treatment of chronic disease, if such indices are not taken into account as medical staff and patients themselves. In the study by Ghimire S. et al, more than half of the patients studied, namely 56.7 %, had low adherence to treatment, whereas in our

study only 9 (18.3 %) patients out of the total number of subjects who were on replacement therapy did not have adherence to treatment [6]. Another study, namely Alkatheri AM et al, showed that of the 89 patients who underwent regular hemodialysis sessions, 71.9 % had low and moderate adherence to treatment, equivalent to poor health control and deteriorating patient-medical compliance staff [2]. 6 (30 %) patients with diabetes mellitus had a high adherence to treatment in the experimental groups, while it was EG 2–5 (20.8 %) in dialysis patients without diabetes. The similar picture is seen in the control groups: 4 (15.4 %) patients with CKD stage–II with diabetes had a high adherence to treatment, while patients with stage CKD–II without diabetes had only 2 (8.7 %). As it can be seen from the results of the study, the percentage of adherence to treatment is higher in patients with diabetes. In our study, the mean adherence to treatment in EG 1 was 12 (60 %) patients as in EG 2 also 12 (50 %) patients. In the control groups also: in CG1 the average adherence to treatment was observed in 11 (42.3%) patients, while in EG 2 there were only 7 (30.4 %) patients with initial changes in the renal system. The low level of compliance of a patient with chronic kidney disease largely determines his further prognosis, which is the cause of poor replacement therapy, as well as work ability and death.

Drug failure is quite common in chronic disease, and can occur in more than 50 % of patients. The main goal of CKD treatment is to slow the progression of the disease along with the control of comorbidities and complications. Non-compliance with medications is potentially harmful and can increase the cost of treatment. Failure by a patient to take medication creates a number of problems for both the patient and the health care system as a whole. Let's take the example of a dialysis patient who takes an average of 6-8 drugs daily in combination with constant dietary restrictions: usually 2-3 drugs to correct blood pressure, phosphate binder – correction of blood phosphorus, necessarily antiplatelet therapy in interdialysis days, antianemic drugs, statin therapy. These drugs are universal for every dialysis patient. Acceptance of the disease, full compliance between the patient and medical staff is an indicator of a high level of adherence to treatment. Not only the compliance between the patient and the doctor, but also the compliance between the patient and the nurses play an important role in the success of the treatment. Thus, in a study by Ghimire S et al. was performed a survey of nurses on adherence to treating patients in the hemodialysis center. And it was found that most nurses pay attention to the high result of low compliance and agreed that the presence of specialists who perform a survey of compliance and monitor the compliance process can lead to quality care and successful monitoring of hemodialysis patients [5].

Peculiarities of adherence to treatment in patients of different age groups were analyzed. All patients of the experimental and control groups were divided into 3 age subgroups: up to 40 years, 41 Peculiarities of adherence to treatment in patients of different age groups are analyzed. All patients of the experimental and control groups were divided into 3 age subgroups: up to 40 years, 41–55 years and older than 56 years, respectively (table 1).

Table 1

Mean values of adherence assessment for different age groups in the experimental and control groups

Age of patients	EG 1, n (%), M±m	EG 1, n (%), M±m	CG 1, n (%), M±m	CG 2, n (%), M±m
Total number	20 (100.0). 6.9±0.9	24 (100.0), 6.2±1.3	26 (100.0), 5.8±1.7	23 (100.0), 4.3±2.3
<40 years	2 (10.0)*. 5.5±0.7	9 (37.5)**, 4.8±0.7	2 (7.6)***, 3.5±0.7	13 (56.6)****, 2.5±1.4
41–55 years	10 (50.0), 6.8±1.0	6 (25.0), 6.6±0.8	20 (76.9), 5.8±1.6	5 (21.7), 5.8±0.4
>56 years	8 (40.0)*, 7.3±0.5	9 (37.5)**, 7.3±0.7	4 (15.4)***, 7.5±0.5	5 (21.7)****, 7.4±0.5

Note: p> 0.05 significance of differences between EG 1 and EG 2, as well as CG 1 and CG 2, * level of significance of differences p <0.05 in EG 1, ** level of significance of differences p = 0.01 in EG 2, *** level of significance differences p = 0.05 in CG 1, **** level of significance of differences p = 0.001 in CG 2

Although there was no statistically significant difference between EG 1 and EG 2 and CG 1 and CG 2, respectively, in the same age ranges, but in the internal structure of the groups themselves in different age ranges there was a statistically significant difference. Thus, comparing patients in EG 1, but in different ranges, up to 40 years and older than 56 years, there is a statistically significant difference p <0.05. In EG 2 in these age ranges, the statistically significant difference is already at p=0.01. The similar picture is observed in the control groups in the appropriate age ranges (up to 40 years and after 56 years): in CG 1 the statistically significant difference is at p=0.05, in CG 2 – at p = 0.001. Such data in both the experimental and control groups indicate a significant gap in adherence to treatment in different age ranges. Elderly patients are more likely to monitor their health and follow their doctor's recommendations. The results showed that older age is associated with better compliance – adherence to

the medication regimen as in another study by Alkatheri et al [2]. In addition, this study also reported that adherence to diet therapy in dialysis patients improved with age. Absence from dialysis at least once a month was higher in patients <55 years of age. If we compare EG 1 and CG 1 and EG 2 and CG 2, the probability of differences between these groups will be $p \geq 0.05$. Arithmetic mean and standard deviations indicate that patients in the control groups have a lower adherence to treatment than patients in the experimental groups. This may indicate a frivolous attitude of the patients themselves to their disease, which in turn may lead to the progression of renal failure. In combination with other studies, it can be assumed that low and medium compliance rates may be an additional risk factor for CKD progression [11]. If we compare EG 1 with EG 2 and CG 1 and CG 2, the probability of differences will be $p > 0.05$. But, if we assess the arithmetic mean, then in groups with diabetes compliance rates will be higher. This may indicate that these patients, for a long time taking regular antihyperglycemic drugs or insulin therapy, have adapted to a fixed regimen and for them to follow the doctor's recommendations on hourly medication, diet, work and rest regimen are mandatory.

Analyzing the relationship between the dialysis age of patients in the experimental groups and indices of adherence to treatment, it was found that dialysis age does not affect the indices of patient compliance ($p > 0.05$). Similar studies also found that the duration of the CKD terminal stage and the duration of dialysis did not significantly affect adherence to the drug regimen [7]. Similar results were also found in the analysis of the questionnaire data in our study – no statistically significant difference was found in the experimental group, regardless of the presence of diabetes mellitus ($p > 0.05$). The duration of CKD stage I–II in the control group also did not affect adherence to drug treatment, as indicated by no statistically significant difference ($p > 0.05$).

Currently, CKD is an extremely important situation not only in this country. The number of patients in need of dialysis therapy is constantly growing. Compliance between medical staff and patients played an important role in the success of treatment in this category of patients. In our study, it was found that out of all 49 patients on RRT, 9 (18.3 %) patients had no adherence to treatment at all. In 2009, the Institute of Public Health of England (NEHI) estimated that poor adherence to medication cost the US health care system $ 289 billion annually.

In general, for many chronic diseases, non-compliance with medication regimens and other aspects of non-compliance with treatment regimens can adversely affect the outcome of treatment, leading to additional and unnecessary tests, dosage adjustments, changes in treatment plan, additional consultations, which ultimately increases the cost of medical care [2, 3]. Quality medical care, control by the doctor of the patient's compliance with recommendation, social support are the components of successful treatment.

Conclusions

1. The results of the study showed a commitment to the treatment of dialysis patients in comorbid conditions. Thus, in EG 1–2 (10.0 %) and 7 (29.2 %) in EG 2 patients had no adherence to treatment at all. The average adherence in EG 1 was 60 % of patients, while in EG 2 only 50 %. Only 30 % of patients had a high adherence to treatment in EG 1, while in EG 2–20.8 %.

2. It was found that the index of adherence to treatment is directly proportional to the age of the patient. In EG 1, but in different ranges, up to 40 years and older than 56 years, there is a statistically significant difference $p < 0.05$. In EG 2 in these age ranges, the difference is statistically significant already at $p = 0.01$.

3. In turn, the presence of a history of diabetes increases patient compliance, which has a positive effect on disease control by both the doctor and the patient.

4. In patients with stage I–II CKD (CG 1 and CG 2) 11 (42.3%) and 14 (60.9%) patients, respectively, were not committed to treatment, which may be an additional risk factor for CKD progression.

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CHANGES IN THE INTESTINAL MICROBIOTA IN PATIENTS WITH ULCERATIVE COLITIS AND IRRITABLE BOWEL SYNDROME COMBINED WITH UROLITHIASIS

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The paper is devoted to the study of changes in the intestinal microbiome in patients with urolithiasis that occurred against the background of ulcerative colitis and irritable bowel syndrome. It was found that about 20 % of patients with urolithiasis have symptoms of irritable bowel syndrome, with more than half of the stones consisting of oxalates. In the study of fecal microflora in patients with the method of sequencing of the 16S gene of ribosomal RNA, compared with healthy, a significant decrease in Firmicutes, Faecalibacterium prausnitzii, Akkermansia muciniphila and the Firmicutes/Bacteroidetes ratio was revealed. The detected changes in the microflora can be associated both with direct changes in the intestine, inherent in nonspecific ulcerative colitis and irritable bowel syndrome, and with more frequent use of uroseptics/antibiotics in this category of patients.

Key words: urolithiasis, fecal microflora, phylotypes, intestinal diseases

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ЗМІНИ КИШКОВОЇ МІКРОБІОТИ У ПАЦІЄНТІВ ІЗ НЕСПЕЦИФІЧНИМ ВИРАЗКОВИМ КОЛІТОМ ТА СИНДРОМОМ ПОДРАЗНЕНОГО КИШЕЧНИКА І СЕЧОКАМ'ЯНОЮ ХВОРОБОЮ

Робота присвячена вивченню змін кишкового мікробіома у пацієнтів із сечокам'яною хворобою, що виникла на тлі неспецифічного виразкового коліту та синдрому подразненого кишечника. Виявлено, що близько 20 % хворих із сечокам'яною хворобою мають симптоми синдрому подразненого кишечника, причому більше половини каменів складалися з оксалатів. При вивченні фекальної мікрофлори у хворих методом секвенування гена 16S рибосомальної РНК, порівнюючи із здоровими, виявлено достовірне зменшення Firmicutes, Faecalibacterium prausnitzii, Akkermansia muciniphila і співвідношення Firmicutes/Bacteroidetes. Виявлені зміни мікрофлори можуть бути пов'язані як з безпосередніми змінами в кишці, властивими неспецифічному виразкового коліту і синдрому подразненого кишечника, так і з більш частим використанням уросептиків/антибіотиків у даної категорії хворих.

Ключові слова: уролітіаз, фекальна мікрофлора, філотипи, захворювання кишечника

Intestinal microbiota changes are one of the leading links in the pathogenesis of both inflammatory and functional intestinal diseases. The intestinal microbiome has a direct effect on the development of inflammation, disruption of the permeability of the intestinal mucosal barrier and, as a consequence, the appearance of extraintestinal manifestations and complications. In addition, the combined pathology of internal organs and systems largely depends on the condition and permeability of the intestinal mucosal