COGNITIVE CHANGES IN PATIENTS WITH CHRONIC KIDNEY DISEASE DEPENDING ON THE DEGREE OF THE DISEASE.

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Summary

51 patients with CKD were examined, 20 of them with CKD stage I-II (glomerular filtration rate - GFR ≥60 ml/min/1.73 m2, signs of kidney damage), 20 with CKD stage III (GFR 60-30 ml/min/ 1.73 m2), 11 with CKD stage IV (GFR 30-15 ml/min/1.73 m2). A questionnaire was conducted to identify limitations in daily activity, neuropsychological testing was performed using the MMSE scale, a test battery for frontal lobe dysfunction (FAB), and a test to assess regulatory functions. To clarify the etiology of CI, magnetic resonance imaging (MRI) was performed. In patients with chronic renal failure (CKD stages III-IV), cognitive impairment was detected more often than in patients without chronic kidney disease (CKD stages I-II).

Key words: chronic kidney disease, cognitive impairment, glomerular filtration.

Relevance. Chronic kidney disease (CKD) is a global problem, and currently, diagnosis and treatment of CKD is a big problem in modern medicine. The incidence of CKD is about 15% of the total incidence in developed countries. It is believed that these complications arise for many reasons. It has been established that at stages 3-5 of CKD, deterioration in cognitive function occurs in parallel with a decrease in glomerular filtration rate and does not depend on the vascular risk factor [1, 2]. Thus, the medical and socio-economic significance of CKD is determined both by its progressive course with the development of end-stage chronic kidney disease (CKD), requiring the use of expensive methods of therapy that replaces kidney function, and by the high risk of cardiovascular complications and death from them in the population working age. Damage to the cardiovascular system in CKD is based on remodeling of the vascular wall, which occurs under the influence of risk factors for the development of CKD, both traditional and caused by renal failure (anemia, impaired phosphorus-calcium metabolism, hyperhomocysteinemia, uremic toxins, oxidative stress) [3]. Remodeling of cerebral vessels in CKD leads to the development of cerebrovascular insufficiency (CVI) and the emergence of cognitive impairment (CI), reaching the stage of dementia in the later stages. Cerebrovascular complications largely determine the fate of patients with CKD, causing permanent disability and death [4]. In kidney diseases, CI not only leads to disability of patients, a decrease in the quality of life of patients and their relatives, but also makes it difficult, in particular, to obtain informed consent from the patient if hemodialysis or kidney transplantation is necessary [5—7]. In addition, in contrast to the early stages of CI, the treatment options for severe CI (dementia) are limited and obviously do not allow achieving sufficient social rehabilitation of patients [8]. In this regard, identifying cognitive dysfunction (CD) in the early stages is of particular importance: it is known that approximately 50% of patients with chronic CVI and mild or moderate CI (MCI) develop dementia within the first 5

years [9]. The study of cognitive functions is carried out using a number of neuropsychological tests, which allow not only to assess the severity of changes, but also to determine disorders in certain areas of higher brain functions. However, the nature of CI in patients with CKD needs further study, since the currently available data are scattered and extremely contradictory [10—13]. To determine the severity of CD, it is necessary to study the patient's functional status using a questionnaire that assesses the impact of cognitive defect on daily activities. Due to impairment of the most complex cognitive operations, the professional competence of a patient with MCI may be limited, but unlike dementia, the performance of a set of everyday activities that determine the patient's ability to live independently is not affected [14]. To clarify the etiology of CIs, as well as assess the risk of their progression to the degree of dementia, the use of neuroimaging examination methods, such as computed tomography (CT) and magnetic resonance imaging (MRI) of the brain, is also considered indicated. Signs of CVI are at least one lacunar infarction or leukoaraiosis exceeding the age norm. At the same time, cerebral infarctions, which manifest themselves as cysts of varying diameters ("completed infarcts") or focal changes in white and gray matter without cyst formation ("incomplete infarcts"), are considered the most reliable diagnostic sign [15].

The purpose of this study was to assess the frequency, severity and nature of CI in patients with CKD at pre-dialysis stages, as well as to study clinical and neuroimaging relationships in CKD patients with CI.

Materials and methods. The study included 51 patients with CKD (21 men and 30 women) aged from 30 to 74 years, average age 52±10 years. CKD was defined as kidney damage of any etiology, accompanied by impairment of their structure and/or function for 3 months or more. CKD stages were determined according to the US National Kidney Foundation classification (NKF K/DOQI, 2002). GFR was calculated using the abbreviated MDRD (Modification of Diet in Renal Disease Study) formula. All patients were divided into 2 groups: group 1 - 20 patients with CKD stages I-II (GFR ≥60 ml/min/1.73 m2, signs of kidney damage); Group 2 - 31 patients with CKD stages III and IV (GFR 60-15 ml/min/1.73 m2).

To assess the severity of CI depending on the stage of CKD, patients were divided into 3 groups: The 1st group included 20 patients with CKD stages I and II, the 2nd group included 20 patients with CKD stage III (GFR 60-30 ml/min/1.73 m2), the 3rd group included 11 patients with CKD stage IV (GFR 30-15 ml/min/1.73 m2). All patients underwent a questionnaire to identify limitations in daily activity (basic and instrumental activities of daily living scale, ADL and IADL), as well as to assess emotional status (Beck Depression Scale). Neuropsychological testing was performed to identify and assess the severity of CI using the following tests: 1) brief mental status scale (Mini-mental state examination — MMSE), including the study of the functions of gnosis, praxis, speech, auditory-verbal memory, attention, counting, visual-spatial functions; 2) Frontal Lobe Dysfunction Test Batteries (Frontal assessment battery — FAB), batteries of tests for dysfunction of the frontal lobes of the brain, with the help of which they examine thinking, speech, dynamic praxis, semantic memory, and regulatory functions; 3) test for memorizing 10 words according to the method of A.R. Luria for short-term memory (immediate reproduction of 10 words, immediately after their presentation); 4) delayed memory (reproduction of words 30 minutes after their presentation); 5) a test to assess regulatory functions (sequential combination of letters and numbers, Trail-making test B), reflecting the processes of planning, goal formation, step-by-

step implementation of actions, the ability to switch and control the achievement of the planned result.

Results. Among all examined patients with CKD, CN was detected in 35 (68.6%). All patients with CI complained mainly of difficulties in remembering new information, forgetfulness of names, names of objects, inability to retain a plan of action in memory, remember where one or another object was placed, difficulty concentrating, finding words when speaking, and sleep disturbances. At the same time, none of the patients had significant limitations in daily activity based on the results of filling out a questionnaire by them and their relatives to assess social, instrumental activity, and the ability to self-care.

In the group of patients without chronic renal failure (n=20), CI was noted in 7 (35%), in the group with chronic renal failure (n=31) - in 28 (90.3%). The frequency of detection of CI in patients with chronic renal failure was statistically significantly higher than in the group without chronic renal failure. When comparing the severity of CI in 3 groups of patients with different stages of CKD, a deterioration in the results of the MMSE test, tests for the function of the frontal lobes of the brain and regulatory functions was noted as the stage of CKD increased. Depression was detected in 26 (51%) patients, of which 21 (41.2%) were mild and 5 (9.8%) were severe. Among patients with depression, CI was observed in 18 (69.2%), of which 15 (83.3%) had mild depression, and 3 (16.7%) had severe depression. Among 25 (49%) patients without depression, CIs were detected in 17 (68%). The incidence of CI in patients with depression was practically no different from that in patients without depression. We also did not reveal statistically significant differences in the severity of CI in the group of patients with and without depression. MRI of the brain was performed in 38 patients (8 with CKD I-II, 30 with CKD III-IV), among them CI was noted in 30. Focal changes in the brain were detected in 11 (28.9%) patients, of which 10 (26.3%) with localization in the carotid region, in 1 (2.6%) in the vertebrobasilar region; diffuse changes in the white matter (leukoaraiosis) were noted in 9 (23.7%) patients; in 17 (44.7%) dilation of the lateral ventricles was detected and in 3 (7.9%) there was a pronounced dilation of the sulci of the cerebral hemispheres. Among patients with CI, focal changes were noted in 9 (30%), leukoaraiosis - in 7 (23.3%), dilatation of the lateral ventricles - in 15 (50%), pronounced dilation of the sulci of the cerebral hemispheres - in 3 (10%). Our study showed a statistically significant increase in the frequency and severity of CI with the progression of CKD according to the results of the Mini-Mental Status Assessment, the study of frontal lobe function and regulatory functions, but not short-term and delayed memory. These data are consistent with the results of a number of large studies in which, with increasing stage of CKD, an increase in the frequency and severity of cognitive function impairments was revealed on a brief scale for assessing mental status, attention, regulatory functions, gnosis, but not semantic, short-term or delayed memory, intelligence. At the same time, a number of other studies have shown deterioration in performance on tests of semantic and auditory-verbal memory in the absence of differences in the Mini-Mental Status Rating Scale and the results of a study of visuospatial functions. Despite the contradictory data obtained, a common disorder associated with CKD and confirmed by all studies is a defect in regulatory functions. That is why the test for regulatory functions can be proposed as the most reliable method for the early diagnosis of CI in patients with CKD. In our study, patients with higher stages of CKD showed statistically significantly lower scores on neuropsychological testing, reflecting worsening cognitive function. However, the indicators of cognitive defect in none of the patients reached the level

of dementia. It should be taken into account that the selection of patients for the study was carried out in a therapeutic hospital, where patients with dementia are rarely admitted. These data, along with the absence of restrictions on daily activity in the examined patients with CI, allow us to state the development of MCI. CIs are often combined with emotional and behavioral disorders or are secondary to emotional disorders. The presence of severe depression suggests a secondary nature of CI [15]. In cerebrovascular diseases, depression and CI represent a single clinical symptom complex, while depression and cognitive defect reinforce each other. The main objective of brain MRI in the study was to confirm the vascular origin of MCI in patients with CKD. According to several studies, in patients with end-stage renal failure on dialysis and with CI, leukoaraiosis is the most common neuroimaging finding and is closely associated with the severity of renal damage. In patients with CKD at pre-dialysis stages, there is virtually no data on the relationship between brain changes and the nature and severity of CI. It has been proven that, along with CKD, the number of lacunar cerebral infarctions is an independent risk factor for dysfunction of the frontal lobes of the brain. As the study showed, the development of CI in patients with CKD is based on vascular changes in the brain, visualized using MRI. It is important to keep in mind that in patients with CKD with mnestic type MCI, a mixed vascular-degenerative nature of CI cannot be excluded, which contributes to a more rapid development of dementia.

Conclusion. In patients with chronic renal failure, a statistically significant increase in the frequency of developmental renal failure was revealed according to the results of the brief mental status assessment scale, a study of regulatory functions and the function of the frontal cortex compared to patients with kidney damage without chronic renal failure. The progression of CKD is associated with an increase in the severity of CI in the same cognitive areas. The main substrate of CD in CKD is chronic CVN, which is confirmed by the results of MRI of the brain.

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