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Cognitive Disorders in Chronic Kidney Disease

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Summary: *This article discusses the etiology, pathogenesis and clinical features of neurological disorders in patients with chronic kidney disease. It is emphasized that at the initial stages, changes in the central nervous system are manifested by cognitive dysfunctions, such as impaired attention, memory, psychomotor functions, and in chronic kidney disease, changes in cerebral vessels occur 10 times more often than in patients without renal pathology.*

Keywords: *chronic kidney disease, cognitive impairment, glomerular filtration, neurotoxicity.*

Relevance. According to research results, chronic kidney disease (CKD) is a strong independent predictor of short-term mortality and worse outcome in patients with acute stroke [2, 4]. Most patients with chronic kidney disease die due to cardiovascular disease (CVD), including stroke, and not from end-stage CKD [1,3]. CKD is included in the QRISK3 model for predicting the risk of CVD and stroke. Delirium, encephalopathy and dementia occur in 16-38% of patients with CKD [16]. Cognitive tests reveal moderate and severe cognitive disorders in 70% of patients with CKD, which consist in the deterioration of memory and "executive function" of patients [16,17]. Cognitive disorders occur in 30-60% of patients on hemodialysis, and in 2/3 of patients on peritoneal dialysis. In a study on patients with CKD, it was shown that the defeat of the white matter of the brain was noted in 33% of patients, and in individuals with normal renal function, this value was 6% [1,2]. Currently, the diagnosis and treatment of chronic kidney disease (CKD) is a big problem in modern medicine. The frequency of CKD is about 15% in 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, the deterioration of cognitive function occurs in parallel with a decrease in the rate of glomerular filtration and does not depend on the vascular risk factor. A rapid deterioration in cognitive function is observed with a decrease in filtration rate <30 ml / min / 1.73 m2. So it is known that in CKD, changes in the vessels of the brain occur 10 times more often than in patients without renal pathology [3,4].

Etiology of development of cognitive disorders.

The main risk factors for the occurrence of cognitive disorders include age, female sex, diabetes, hypertension, low educational status. Additional risk factors are hyperhomocysteinemia, hyperparathyroidism, oxidative stress, low levels of glomerular filtration, albuminuria, malnutrition, chronic inflammation [3, 4]. Hyperhomocysteinemia (an increase in the concentration of homocysteine in the blood of more than 15 µmol/l) is often found in CKD. A high level of homocysteine leads to the process of direct formation of blood clots on the endothelium and stimulates the endothelial inflammatory process, which increases the risk of cognitive impairment. Homocysteine has a direct neurotoxic effect by activating the receptor to N-methyl D-aspartate (NMDA) or by forming toxic homocysteinic acid from it [1,4]. Uremic intoxication causes oxidative stress by superactivation of NDMA receptors and activation of nitric oxide synthesis, which leads to the formation of peroxynitrile and protein nitration. These pathological processes can also cause

cognitive impairment, as they lead to pronounced metabolic and structural changes in the brain [2,3]. A clear relationship has been established between cognitive impairment and glomerular filtration rate [11,12]. It was revealed both with a slight decrease in filtration characteristics, and with an average degree of CKD [3]. It has been shown that in elderly patients, regardless of the presence of small vessel disease, albuminuria is associated with cognitive dysfunction [4]. Apparently, this is due to the fact that albuminuria better characterizes the presence of CKD and generally reflects vascular endothelial dysfunction [2]. The defeat of the white matter of the brain in CKD is characterized by the accumulation of degenerative cells in it, the presence of which is a prognostic factor for the onset of stroke, dementia and death [11]. Recently, in case of impaired cognitive function in CKD, much attention has been paid to studying the role of the transmembrane protein Klotho. This protein is expressed in many tissues, but especially in large quantities in the kidneys and brain. It exists in a soluble form and in a form associated with cell membranes. The soluble variety of this substance is secreted directly from the membrane or is formed by the Klotho gene by alternative splicing. In the kidneys, the form associated with the membrane forms a bond with fibroblast growth factor 23 (FGF-23) and is involved in the regulation of calcium phosphate homeostasis. In CKD, a decrease in Klotho expression is observed. This is due to a decrease in kidney mass, hyperphosphatemia, vitamin D deficiency, activation of the renin-aldosterone system, dyslipidemia, an increase in the content of such substances as tumor necrosis factor-a, interferon, indoxyl sulfate. It is believed that in CKD, not only renal, but also systemic deficiency of the Klotho protein is observed. It has been established that the soluble form of this protein has an endocrine function and inhibits the aging process by blocking the signals of growth factors and oxidative stress [3,4]. In experiments on mice and when examining people, it was shown that with an increase in the content of the Klotho protein, there is an improvement in cognitive tests. In experiments on mice, it was found that this effect is realized through the a-glutamate receptor [2,3]. The authors showed that vascular nephropathy was an independent prognostic risk factor for the onset of damage to the white matter of the brain. As a result of examination of patients with CKD (subject to the exclusion of persons with diabetes mellitus and hypertension), a clear relationship was revealed between damage to the white matter of the brain, albuminuria and glomerular filtration rate [1, 3]. More recently, it has been found that high concentrations of cystatin-C, regardless of age, race, education and concomitant diseases, are accompanied by a decrease in cognitive function [5,6]. It is believed that the neurotoxic effect of cystatin-C is associated with the formation of amyloid plaques in the CNS under its influence [6].

Pathogenetic mechanisms of development of neurological disorders in CKD. It is believed that the pathophysiological mechanisms that underlie neurological disorders in CKD include morphological changes in the vascular wall, disturbances in the regulation of vascular function and changes in bilateral humoral pathways. actions between the kidneys and the brain. All this leads to the onset of degenerative changes not only in the kidneys, but also in the brain [3]. The brain and kidneys are organs with a high degree of perfusion blood flow and low vascular resistance, which allows large volumes of blood to flow through these organs. In this case, any metabolic disorders can lead to a change in the walls of blood vessels and disruption of their function due to constant contact with high concentrations of various compounds in the blood. In patients suffering from CKD, there are such traditional risk factors for CNS damage as hypertension, diabetes, hypercholesterolemia, advanced age. Although these factors are considered the main cause of vascular damage, in CKD their action is enhanced and accelerated by such non-traditional factors that are characteristic of renal failure, such as metabolic disorders, inflammation, the state of hypercoagulability and oxidative stress. All this leads to increased endothelial dysfunction and accelerates the processes of atherosclerotic vascular changes. Thus, a decrease in the excretion of phosphates in CKD causes an increase in their concentration in the blood serum and leads to the formation of calcium phosphates and an increase in the concentration of parathyroid hormone, which causes an acceleration of the process of vascular calcification of the wall [4, 6]. A weighty confirmation of the vascular etiology of CNS lesions in CKD is the fact that in patients with various stages of CKD, strokes, micro bleeds, atrophic changes in the brain, and a disease of the white matter of the brain are more common. o brain, cognitive disorders, compared with patients without kidney damage. Moreover, in CKD, there is a low cellular concentration of thiamine and folic acid and impaired nitric oxide metabolism,

which increases the likelihood of stroke and destruction of the white matter of the brain. brain [11,12]. So far, it has not been possible to fully understand the pathophysiological mechanisms of the onset of cognitive impairment in CKD. It has been established that homocysteinemia and the process of age-related neurodegeneration play a major role in the occurrence of cognitive impairment. For a long time, it was believed that vascular damage is the determining factor in the occurrence of these disorders. However, it was shown that this process does not affect all areas of the CNS, but is associated exclusively with subcortical lacunar lesions of the brain [12]. Although it is commonly believed that the white matter disease of the brain also leads to the occurrence of cognitive disorders, one study was able to demonstrate that CKD itself, even without correction the presence of small vessel disease and white matter damage is an independent risk factor for dementia and cognitive disorders [11]. The defeat of the vascular bed in CKD is called small vessel disease (SVD). BMS is a pathological process that, due to the great similarity of the vascular system of the kidneys and the central nervous system, simultaneously affects the arterioles, venules and capillaries of both the kidneys and the brain. This leads to the occurrence of thromboses and hemorrhages in these organs.

Dynamics of cognitive function in CKD. The occurrence of neurological disorders is largely determined not by the degree of impairment of biochemical parameters that reflect kidney function, but by the rate of growth of these biochemical disorders [10]. At the initial stages, with encephalopathy caused by CKD, patients may show increased fatigue, mental retardation, daytime drowsiness and night sleep disturbances, as well as others, all ma nonspecific signs (in particular, tremor), in some cases accompanied by nausea and vomiting. This condition is characterized by a fluctuating course, when the condition of patients changes not only within days, but even hours [3, 11]. In the early stages, patients show general weakness, attention disturbances, apathy, and decreased libido. As CKD progresses, behavioral disorders become more and more pronounced, mnestic disorders increase, sleep is inverted. With CKD, neurological disorders can be compensated for quite a long time (months and even years) and do not manifest themselves clinically. In CKD, there are memory impairments, even in the absence of neurological disorders, psychometric tests can detect cognitive impairment in patients with CKD [2,4]. «Mini Mental Status Examination» (MMSE) is a standard psychometric screening method for detecting impaired cognitive function with a sensitivity and specificity of more than 80%. This test has one drawback: it does not allow you to evaluate the "executive function" of the patient. Scale "Monreal Cognitive Assesment" (MOCA) specificity and proceeded to pay an this way, that and entry, accommodation of decision -making, venerates in the adherence, venients in the premium, veneen in the arrangement. Rubilant to put on and speech. These two tests are widely used to assess cognitive impairment in CKD [1, 2].

Cognitive disorders in the terminal stage of renal failure depend on the various risk factors indicated earlier - these are the main ones (age, gender, diabetes, hypertension, cardiovascular diseases, low educational level) and additional (hyperparathyroidism, increased concentration of FGF-23, decreased vitamin D, anemia, malnutrition, inflammation and oxidative stress) [3,4]. In addition, it has been established that there are factors specific only for dialysis: adequacy, modality, hemodynamic instability and osmotic shifts [4]. With a deficiency of vitamin D in patients on hemodialysis, there is deterioration in cognitive indicators according to the test for detecting violations of "executive function" with negative indicators according to tests for determining memory impairment [4]. Fibroblast growth factor (FGF-23 (Fibroblast growth factor-23)) is a phosphaturic hormone and its high concentrations are determined in the bones and brain in CKD. In patients on hemodialysis, a high level of this substance is associated with deterioration in cognitive performance, especially with a total assessment of memory [1, 3]. It was shown that after the end of the hemodialysis session, there is an improvement in cognitive performance. It is believed that this is due to a decrease in the concentration of uremic toxins [17].

An acute disorder of cognitive function, such as delirium, also occurs during hemodialysis and may be associated with changes in blood pressure, the occurrence of hypoperfusion syndrome, metabolic races structures and hyponatremia [12]. It has been established that the optimum indicators of cognitive function are observed 24 hours after dialysis, then its deterioration is observed by the beginning of the next dialysis session. The development of hemodialysis technology has led to the

widespread use of succinate-containing dialysis solutions, which improve cognitive function in patients on hemodialysis [3,4].

Thus, neurological complications are common in CKD. It turned out that the rate of glomerular filtration and protenuria are closely related to the development of vascular diseases of the brain. An increase in the first indicator and a decrease in the second one leads to a decrease in the likelihood of a stroke, “silent” cerebral infarctions, and damage to the white matter of the brain. A number of new risk factors for the occurrence of cognitive disorders have been identified, such as changes in the content of 25-OH, vitamin D, FGF-23, the trans-membrane protein Klotho, as well as hyperhomocysteinemia, oxidative stress, and others requiring further o study.

List of references:

1. Дамулин И.В., Воскресенская О.Н., Неврологические нарушения при хронической болезни почек// Неврологический вестник2017
2. Юсупов Ф.А. и соав. Неврологические нарушения при хронической болезни почек // The scientific heritage №84. – 2022
3. Никитина А. А., Хрулёв А. Е. Цереброваскулярные расстройства додиализного периода хронической болезни почек и механизмы их развития// Медицинский альманах №5 (56) - 2018
4. Синюхин В.Н., Рабинович Э.З. Неврологические нарушения при хронической болезни почек// Экспериментальная и клиническая урология №2 – 2017
5. Ахорова, Ш. Б. (2017). Возрастные и гендерные клинико-патогенетические особенности острой невропатии лицевого нерва. Международный неврологический журнал, (4 (90)), 52-56.
6. Ахорова, Ш. Б. (2021). Prevalence and neurological features of diabetic polyneuropathy in type 1 diabetes. Журнал неврологии и нейрохирургических исследований, 2(2).
7. Гаффарова В.Ф., .Ходжиева Д.Т. Особенности течения фебрильных
8. судорог у детей.// Тиббиётда янги кун. – Ташкент, 2021. - №1 – С. 170- 173. (14.00.00, №22).
9. Давронова, Х. З. (2022). Роль сахарного диабета ii типа на развитие когнитивных нарушений при ищемическом инсульте. Журнал неврологии и нейрохирургических исследований, 3(2).
10. Давронова, Х. З. (2022). Снижение коеффициента фракционного анизотропии как фактор развития когнитивных нарушений у постинсультных больных. In Actual Issues and Solution of Development of Economic Sectors of the Republic of Uzbekistan in Modern Conditions Proceedings of the international conference.–Jizzakh (Vol. 1, pp. 764-770).
11. Саломова, Н. К. (2022). Факторы риска цереброваскулярных заболевание и полезное свойство унаби при профилактики. Oriental renaissance: Innovative, educational, natural and social sciences, 2(2), 811-817.
12. Саломова, Н. К. (2021). Особенности течения и клинико-патогенетическая характеристика первичных и повторных инсультов. Central Asian Journal of Medical and Natural Science, 249-253.
13. Саломова, Н. Қ. (2023). Кайта ишемик инсультларнинг клиник потогенитик хусусиятларини аниқлаш. Innovations in Technology and Science Education, 2(8), 1255-1264.
14. Akhmedova, D. B. (2021). Tension headache-treated with amitriptyline-A. In International Multidisciplinary Scientific Conference on the Dialogue between sciences & arts, religion/march-april-91-92.

15. Akhmedova, D. B., & Xodjieva, D. T. (2021). Analysis of the prevalence of headaches among the population in bukhara region. ACADEMICIA: An International Multidisciplinary Research Journal, 11(3), 431-433.
16. Watanabe K, Watanabe T, Nakayama M. Cerebrorenal interactions: impact of uremic toxins on cognitive function. Neurotoxicology 2014; 44: 184-193. DOI:10.1016/j.neuro.2014.06.014
17. Yaffe K, Kurella-Tamura M, Ackerson L, Hoang TD, Anderson AH, Duckworth M, et al. Higher levels of cystatin C are associated with worse cognitive function in older adults with chronic kidney disease: the chronic renal insufficiency cohort cognitive study. J Am Geriatr Soc 2014;62(9):1623-1629. DOI: 10.1111/jgs.12986
18. Zavkiddinovna, D. H. (2023). Features of the Course of Cognitive Dysfunction in Patients with Type II Diabetes Mellitus. American journal of science and learning for development, 2(3), 53-55
19. Gaffarova V.F. , Khodjieva D.T. Features of the course of febrile seizures in children. // Asian Journal of Pharmaceutical and Biological Research. 2021. -P. 4-6.
20. Gaffarova V.F. Clinic-eeg correlation somatogenous of conditioned febrile seizures in children. // International Journal of Human Computing Studies.2021. –P.114-116.