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ENDOTHELIAL DYSFUNCTION AS A PROGNOSTIC MARKER IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Abstract. *The article discusses the state of endothelial function in patients with chronic kidney disease. A group of 68 patients with stage I–III chronic kidney disease was examined. Activation of endothelial function was revealed, expressed by an increase in the level of endothelin-1, which increases with a decrease in glomerular filtration rate. In patients with the initial manifestations of renal dysfunction, changes associated with an increase in endothelin-1 levels were noted.*

Key words: *endothelial dysfunction, chronic kidney disease, endothelin-1.*

ЭНДОТЕЛИАЛЬНАЯ ДИСФУНКЦИЯ КАК ПРОГНОСТИЧЕСКИЙ МАРКЕР У ПАЦИЕНТОВ С ХРОНИЧЕСКОЙ БОЛЕЗНЬЮ ПОЧЕК

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Аннотация. *В статье рассматривается состояние эндотелиальной функции у пациентов с хронической болезнью почек. Обследована группа из 68 пациентов с хронической болезнью почек I–III стадии. Выявлена активация эндотелиальной функции, выраженная повышением уровня эндотелина-1, что усиливается при снижении скорости клубочковой фильтрации. У пациентов с начальными проявлениями почечной дисфункции отмечены изменения, связанные с повышением уровня эндотелина-1.*

Ключевые слова: *эндотелиальная дисфункция, хроническая болезнь почек, эндотелин-1.*

СУРУНКАЛИ БУЙРАК КАСАЛЛИГИ БИЛАН ОҒРИГАН БЕМОРЛАРДА ЭНДОТЕЛИАЛ ДИСФУНКЦИЯ ПРОГНОСТИК МАРКЕР СИФАТИДА

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Аннотация. *Мақолада сурункали буйрак касаллиги билан оғриган беморларда эндотелиал функция ҳолати таҳлил қилинган. Сурункали буйрак касаллигининг I-III босқичларидаги 68 нафар бемордан иборат гуруҳ текширувдан ўтказилди. Эндотелиал функциянинг фаоллашуви аниқланди, бу эндотелин-1 миқдорининг ошиши билан намоён бўлди ва гломеруляр фильтрация тезлиги пасайгани сари кучайиб борди. Буйрак дисфункциясининг дастлабки белгилари кузатилган беморларда эндотелин-1 даражасининг кўтарилиши билан боғлиқ ўзгаришлар қайд этилди.*

Калит сўзлар: *эндотелиал дисфункция, сурункали буйрак касаллиги, эндотелин-1.*

The incidence of kidney disorders is comparable to that of socially significant conditions such as hypertension, diabetes mellitus, and obesity. According to the NHANES study, kidney dysfunction affects approximately 13.1% of the general population [18,22]. Symptoms of kidney damage and/or a decline in glomerular filtration rate are detected in at least one in ten individuals [9,13]. Studies conducted in Russia have revealed that a decrease in kidney function occurs in 36% of individuals over the age of 60 [1,2]. Infections, medications, alcohol consumption, smoking, environmental factors, climate, cultural practices, dietary habits, genetic traits of the population, and other factors significantly contribute to the development and progression of chronic kidney disease (CKD) [8,10]. Cardiovascular issues are the leading cause of death among individuals with impaired kidney function, whether they are on predialysis or dialysis treatment. According to nephrological databases from various countries, cardiovascular complications account for up to 48% of the mortality rate among patients undergoing programmed hemodialysis. In the global literature on cardiovascular disorders in patients with end-stage chronic kidney disease (CKD) receiving renal replacement therapy, the primary emphasis is on cor-

onary heart disease (CHD), cardiac arrhythmias, heart valve damage, pericarditis, hypertension, and abnormalities in the diastolic and systolic function of the left ventricle, as well as left ventricular hypertrophy [4,7]. It has been established that endothelial dysfunction plays a significant role in the pathogenesis of cardiovascular complications among this patient group [20]. Based on current concepts, endothelial dysfunction refers to a pathological state of the endothelium characterized by impaired production of endothelial-derived factors, leading to an inability of the endothelium to maintain the hemorheological balance and resulting in impaired organ and systemic functions [3,16]. This dysfunction is the initial stage of atherosclerosis development, and its acceleration has been demonstrated in clinical studies among patients receiving renal replacement therapy [14-16]. Currently, endothelial dysfunction plays a significant role among the mechanisms leading to glomerular kidney damage [19,21]. According to experimental data obtained by A.V. Smirnov et al., one of the factors contributing to the progression of chronic kidney disease is a disruption in endothelium-dependent vasodilatation [11,12]. Endothelium-dependent vascular constriction is primarily associated with the production of endothelin-1 (ED-1). The synthesis of ED-1 is stimulated by various factors, including a reduction in shear stress on the vascular wall, stretching of the vessel, norepinephrine, thrombin, severe tissue hypoxia, angiotensin II, arginine, vasopressin, bradykinin, insulin, glucocorticoids, thromboxane A2, elevated extracellular potassium levels, growth factors such as endotoxin or interleukin-1 and transforming growth factor β1, and others. A limited number of factors inhibit the production of ED-1, including cyclic guanosine monophosphate (cGMP), nitric oxide (NO), atrial and cerebral natriuretic peptides. Under normal conditions, ED-1 is only produced when the endothelium is activated [12,21]. The association between endothelial dysfunction and impaired renal function appears to be logical, although it is not well understood. Of specific interest is the relationship between the reduction in glomerular filtration rate and endothelial dysfunction.

Objective: To investigate the severity of endothelial dysfunction in patients with stage I–III chronic kidney disease.

To tackle this problem, a prospective study was conducted in a single phase. The study involved 20 healthy individuals (average age 28.9±3.7years) and 68 patients with chronic kidney disease (CKD) who were undergoing inpatient evaluation and treatment at the nephrology department of the TMA Clinic. The diagnosis of CKD was confirmed based on patient data, laboratory results, and imaging findings. The exclusion criteria included individuals under the age of 18 or over 65, individuals with type I or type II diabetes mellitus, individuals with a glomerular filtration rate of less than 30 ml/min, and individuals with an active oncological process.

All participants were divided into three groups based on their glomerular filtration rate (GFR), calculated using the CKD-EPI formula. The comparative characteristics of the groups in terms of gender and age are presented in Table 1.

Table 1.

Distribution of examined patients with stage I–III chronic kidney disease and the control group by gender and age (M ± m)

Indicator	Healthy (n=20)	CKD I (n=20)	CKD II (n=25)	CKD III (n=23)
Men	13 (65%)	9 (45%)	8 (32%)	16 (69,57%)
Women	7 (35%)	11(55%)	17 (68%)	7 (30,43%)
Age, years	35,6±3,41	38,1±2,37	42,7±3,58	45,5±2,93

The disparity in the gender ratio among individuals with stage I and II CKD can be attributed to the fact that the primary cause of the condition was chronic inflammatory interstitial kidney disease, such as chronic pyelonephritis and chronic glomerulonephritis. From a public health perspective, women are more susceptible to these diseases in their youth and middle age, owing to anatomical, physiological, and hormonal differences. In addition to the standard clinical evaluation conducted in the nephrology clinic, all patients underwent a blood test to measure the level of endothelin-1 using the Biomedical ENDOTELIN (1-21) test kit manufactured by Biochim-Mak. The statistical analysis of numerical data was conducted using the software «STATISTICA 6.0» for Windows, employing both parametric and nonparametric techniques. The mean (M), standard deviation (σ), and standard error of the mean (m) were calculated. The significance level was set at $p<0.05$.

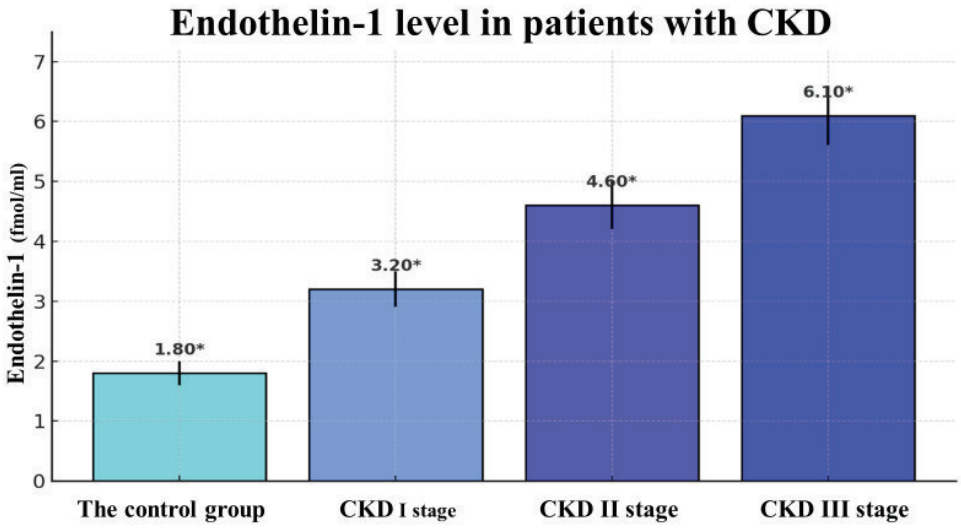

Figure 1. Endothelin-1 level in patients with CKD

The level of endothelin-1 significantly increased in patients with CKD compared with healthy individuals. In the control group, the concentration of endothelin-1 was 1.8 ± 0.2 fmol/ml. In patients with stage I CKD, this indicator increased to 3.2 ± 0.3 fmol/ml ($p<0.05$), in stage II CKD — to 4.6 ± 0.4 fmol/ml ($p<0.05$), and in stage III it reached 6.1 ± 0.5 fmol/ml ($p<0.05$) (Fig.1). Thus, there is a clear trend towards a progressive increase in endothelin-1 levels as kidney function decreases, which indicates an increase in endothelial dysfunction already in the early stages of CKD.

Conclusions. The data obtained indicate that already in the early stages of chronic kidney disease, signs of endothelial dysfunction are formed, manifested by increased levels of endothelin-1. The increasing content of endothelin-1 is associated with a decrease in glomerular filtration rate, an increase in proteinuria and a violation of intrarenal hemodynamics, which confirms its pathogenetic role in the progression of CKD. These results emphasize the expediency of early diagnosis of vascular homeostasis disorders in order to predict the course of the disease and optimize therapeutic strategies.

Literature.

1. Агранович, Н.В. Особенности течения хрони- ческого пиелонефрита у лиц пожилого и старческого возраста / Н.В. Агранович, С.А. Кнышова // Медицинский вестник Северного Кавказа. 2011. № 4. С. 85-87.

2. Бикбов, Б.Т. Состояние заместительной терапии больных с хронической почечной недостаточ- ностью в Российской Федерации в 1998-2007 гг. (Аналитический отчёт по данным Российского регистра заместительной почечной терапии) / Б.Т. Бикбов, Н.А. Томилина // Нефрология и диализ. 2009. №3. С. 144-223.

3. Давыдкин, И.Л. Основы клинической гемоста- зиологии. Монография / И.Л. Давыдкин, В.А. Кондурцев, Т.Ю. Степанова, С.А. Бобылев. – Самара, 2009. 436 с.

4. Жаббаров О. О., Турсунова Л. Д., Хужаниязова Н. К. ВНУТРИПОЧЕЧНАЯ ГЕМОДИНАМИКА ПРИ ДИАБЕТИЧЕСКОЙ НЕФРОПАТИИ //Академические исследования в современной науке. – 2024. – Т. 3. – №. 44. – С. 114-115.

5. Крупаткин, А.И. Лазерная допплеровская фло- уметрия микроциркуляции крови. Руководство для врачей / А.И. Крупаткин, В.В. Сидоров. – М., 2005. 125 с.

6. Мирзаева Ш. Х. и др. Сурункали буйрак касаллиги бўлган беморларда кардиоренал синдромни даволаш. – 2022.

7. Мухин, Н.А. Кардиоренальные соотношения и риск сердечнососудистых заболеваний / Н.А. Мухин, В.С. Моисеев // Вестник Российской Академии медицинских наук. 2003. № 11. С. 50-55.

8. Мухин, Н.А. Хронические прогрессирующие нефропатии и образ жизни современного человека / Н.А Мухин, И.М. Балкаров, С.В. Моисеев и др.// Терапевтический архив. 2004. №76 (9). С. 5-10.

9. Нефрология: ил. (Серия «Библиотека врача-специалиста»). / под ред. Е.М Шилова. 2-е изд., испр. и доп.–М: «ГЭОТАР-Медиа», 2010. 696 с.

10. Смирнов, А.В. Превентивный подход в современной нефрологии / А.В Смирнов, И.Г. Каюков, А.М Есаян. и др. // Нефрология. 2004. №8 (3). С. 7-14.

11. Смирнов, А.В. Уровень эндотелина -1 и реактивность сосудов микроциркуляторного русла кожи у больных на ранних стадиях хронической болезни почек / А.В. Смирнов, Н.Н. Петрищев, И.Ю.Панина и др. // Терапевтичекий архив. 2011. №6. С. 13-15.

12. Смирнов, А.В. Хроническая болезнь почек: на пути к единству представлений / А.В Смирнов, А.М. Есаян, И.Г. Каюков // Нефрология. 2002. № 6 (4). С. 11-17.

13. Турсунова Л. Д. и др. Кардиоренал синдромда ангиотензин-неприлизин рецепторлари ингибиторларининг буйрак функционал холатига таъсири. – 2022.

14. Foley, R.N. The prognostic importance of left ventricu-lar geometry in the uremic cardiomyopathy / R. N. Foley, P. S. Parfrey, I. D. Harnett // J. Am. Soc. Nephrol. 1995. Vol. 5. P. 2024-2031.

15. Ho-dac-Pannekeet, M.M. Analysis of non enzymatic glycosylation in vivo: impact of different dialysis solu-tions / M.M. Ho-dac-Pannekeet, M.F. Weiss, D.R. Waart et al. // Perit. Dial. Int. 1999. Vol. 19, №2. P. 68- 74.

16. Jabbarov O. O. Disorders Function of the Heart and Kidney in Diabetes Mellitus. – 2023.

17. Jones, C.A. Serum creatinine levels in the US popula-tion: Third National Health and Nutrition Examination Survey / C.A Jones., G.M. McQuillan Kusek et al. // Am. J. Kidney Dis. 1998. №32. P. 992-999.

18. Kang, D.H. Role of microvascular endothelium in progressive renal disease / D.H. Kang, J. Kanellis, C. Hu-go et al. // J. Am. Soc. Nephrol. 2002. № 13. P. 806- 816.

19. Levey, A.S. Cardiovascular disease in chronic renal disease / A.S. Levey, G. Eknoyan // Nephrol. Dial Transplant. 1999. Vol. 14. P. 828-833.

20. O'Riordan, E. Endothelial cell dysfunction: the syn-drome in mankind / E. O'Riordan, J. Chen, S. Brodsky et al. // Kidney Int. 2005. №67. P.1654-1657.

21. Tursunova L., Jabbarov O. O. THE ROLE OF RENAL VASCULAR DOPPLEROGRAPHY IN THE DIAGNOSIS OF CHRONIC KIDNEY DISEASE // Медицинский журнал молодых ученых. – 2024. – №. 12 (12). – С. 52-57.