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ASSESSMENT OF BIOMARKERS OF RENAL KIDNEY DAMAGE IN PATIENTS WITH CHRONIC GENERALIZED PERIODONTITIS

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ANNOTATSIYA

Patients with chronic kidney disease, namely tubulointerstitial kidney lesions 58 people were selected. The content of lysozyme and lipocalin-2 in the oral fluid and urine was determined by enzyme immunoassay. It was revealed that a sensitive marker of tubulointerstitial kidney damage is a study of the activity of lysozyme and lipocalin-2 in saliva, blood and urine.

Key words: lipocalin-2, chronic kidney disease, tubulointerstitial kidney damage, chronic generalized periodontitis.

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ОЦЕНКА БИОМАРКЕРОВ РЕНАЛЬНОГО ПОРАЖЕНИЯ ПОЧЕК У БОЛЬНЫХ ХРОНИЧЕСКОЙ ГЕНЕРАЛИЗОВАННОЙ ПАРОДОНТИТОМ

АННОТАЦИЯ

Были отобраны пациенты с хронической болезнью почек, а именно тубулоинтерстициальными поражением почек — 58 человек. В ротовой жидкости и моче определяли содержание лизоцима и липокалина-2 иммуноферментным методом. Выявлено, что чувствительным маркером тубулоинтерстициального поражения почек, является исследование в слюне, крови и моче активности лизоцима и липокалина-2.

Ключивые слова: липокалина-2, хронической болезнью почек, тубулоинтерстициального поражения почек, хронический генерализованный пародонтит

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SURUNKALI GENERALLASHGAN PARIODONTIT BILAN OG'RIGAN BEMORLARDA RENAL BUYRAK SHIKASTLANISHINING BIOMARKERLARINI BAHOLASH

ANNOTATSIYA

Surunkali buyrak kasalligi bo'lgan bemorlar, ya'ni tubulointerstitsial buyrak shikastlanishi 58 kishi tanlangan. Og'iz suyuqligi va siydikda Lizozim va lipokalin-2 miqdori ferment immunoassay usuli bilan aniqlandi. Tubulointerstitsial buyrak shikastlanishining sezgir belgisi tupurik, qon va siydikda Lizozim va lipokalin-2 faolligini o'rganish ekanligi aniqlandi.

Kalit so'zlar: lipokalin-2, surunkali buyrak kasalligi, tubulointerstitsial buyrak shikastlanishi, surunkali umumiy periodontit

Introduction. Studies by D.Y.Orekhov (2009) have shown that 30% of dental patients have somatic diseases. In proof of the above, the author points to the high prevalence of diseases of the oral cavity tissues in patients with chronic kidney disease, in particular with the defeat of the tubulointerstitial kidney system (TIPP). It should be noted that the pathogenesis and mechanism of development of TIPP are different; genetic, developmental abnormalities and / or kidney dysplasia, metabolic disorders (hyperoxaluria, uraturia), membranopathological processes, the development of immune damage with the deposition of tubules or interstitial epithelium (in infectious type) of immune deposits containing the pathogen antigen, a combination of these processes.hypoxia.

According to A.A.Vyalkov (2005), an unfavorable mechanism of exposure to viruses or molecules encoded by the latter may be the activation of lymphocytes and monocytes with the release of cytokines, which increase the formation of leukotrienes, thromboxane, contributing to the development of organ ischemia. With the progressive course of tubulointerstitial kidney damage, 99.2% of patients revealed inhibition of anti-infective protection, which is characterized by a decrease in the level of secretory immunoglobulins A, completion of phagocytosis by neutrophils, dysimmunoglobulinemia, combined with infection of the urinary system by viral-bacterial or bacterial pathogens capable of persistence. The basis of the diagnosis of TIPP is the generalization of the data of the general clinical examination of the patient and the results of modern paraclinical studies, which allow, on the basis of a clinical and morphofunctional approach, to verify the diagnosis, to identify the primary pathology of other organs and systems (rheumatoid arthritis, diabetes mellitus, systemic lupus erythematosus, hemorrhagic vasculitis, violation of purine metabolism, urolithiasis, essential cri- oglobulinemia, Wegener's granulomatosis, Goodpascher syndrome, solid tumors, lymphomas, monoclonal gammopathies, drug nephropathy, hypertension, chronic hepatitis, etc.) and exclude uropathies (abnormalities of the urinary system and blood vessels).

Currently, it is generally recognized that it is possible to diagnose TIPP on the basis of modern clinical and paraclinical data and functional studies confirming the predominance of damage to the tubules and interstitium. It is proved that the accuracy of the diagnosis of TIPP and timely identification of the causes of development (etiological approach) and pathogenetic features of the disease serve as the basis of rational therapeutic tactics. All this makes it extremely relevant to search for methods of early diagnosis of TIPP based on clinical analysis, the use of which allows to prevent or delay the progression of tubulointerstitial fibrosis, which often determines the outcome of renal lesions of various etiologies and different mechanisms of its development.

Recently, dental practice has not always paid due attention to the issues of complex treatment of dental patients taking into account chronic kidney disease (CKD), since renal failure affects the condition of the periodontal, and inflammatory changes in the tissues of the oral cavity affect the condition of patients with chronic kidney disease. At the same time, changes from the oral cavity often include: excessive accumulation of bacterial plaque, gingivitis, gingival hyperplasia and enamel hypoplasia. Based on the above, in our opinion, it is important to evaluate the features of biomarkers of renal kidney damage in patients with chronic generalized periodontitis.

Material and methods of research To conduct this study, patients with chronic kidney disease, namely tubulointerstitial kidney damage — 58 people who were in the nephrological department of the TSSI clinic in Tashkent for the period in 2018-2019 were selected. To compare laboratory parameters, a control group consisting of 18 people with a healthy oral cavity and no kidney pathology was taken. At the initial stage, each patient was informed about the nature of the study. With the consent of the patient, the criteria for inclusion in a particular group were determined. Exclusion criteria from the group: patients aged 35-55 years with diseases of other organs and systems in the decompensation stage. For a comprehensive clinical assessment of the dental status of patients, the following methods were used: a patient survey, an oral examination with an assessment of the condition of periodontal tissues, using indices - the complex periodontal index (CPI), the simplified hygienic index of oral hygiene (OHI-S) according to

Green-Vermillion. X-ray diagnostics was performed by orthopantomography. In the examined patients on an empty stomach after rinsing the oral cavity and brushing teeth with toothpastes, mixed saliva was collected for 10 minutes without stimulation, by spitting into a test tube according to the method of V.K. Leontiev and Yu.A.Petrovich (1976). Oral fluid samples were collected in the morning (08.00). 1 hour before the collection of samples, patients abstained from smoking, drinking, eating and brushing their teeth. Prior to the start of the study, test tubes with samples were stored in the cold at $t = -30^{\circ}\text{C}$. The mixed saliva was centrifuged at 3000 rpm for 15 minutes and activity was determined in the supernatant. Laboratory examination of oral fluid was carried out in the Central Clinical Laboratory of TSSI. The content of lysozyme and lipocalin-2 in the oral fluid and urine was determined by enzyme immunoassay. The research was carried out in accordance with the recommendations of the manufacturer of test systems "HUMAN". Enzyme immunoassay and biochemical studies were carried out using the company's automatic analyzers. «Mindray». All the digital data obtained during the survey were subjected to statistical processing by methods of variational statistics using the Statistica 7.0 application software package. Differences at $p < 0.05$ were considered statistically significant.

Research results and their discussion. During the clinical study, the features of the clinical course and the frequency of dental diseases in patients suffering from chronic kidney disease were revealed. The condition of the hard and soft tissues of the oral cavity and dentition was assessed by the method of visual control. To assess the condition of oral tissues, the following indices were used: hygiene according to Green - Vermillion (1964) (GAMES-Y), papillary-marginal-alveolar (PMA) in the modification of Parma (1960), bleeding (SBI) according to Mühlerrmann H.R. (1971) and CPU - the sum of carious, sealed and removed teeth. The degree of tooth mobility and the depth of periodontal pockets were evaluated. For an objective assessment of the subjective feelings of patients, a questionnaire was conducted according to the questionnaires developed by us. The periodontal status of people suffering from chronic kidney disease differed from that of those in the control group. Thus, the following indicators of periodontal status were noted in patients suffering from CKD. Their incidence of gingivitis and periodontitis was 36.8% and 81.5%, respectively. The indicator of the intensity of the course of periodontal diseases (KPI index) was equal to 2.46 ± 0.17 conl. units. 95.1% of patients needed the removal of tartar deposits, and diseases of the oral mucosa were diagnosed in 9.1% of cases. The value of the indicators of the iodine number of Svrakov in persons suffering from CKD was 2.34 ± 0.14 units, the hygiene index was 1.91 ± 0.17 units. The frequency of dystrophic lesions of periodontal tissues (periodontal disease) was 4.6%. Thus, a clinical study of patients suffering from chronic kidney disease for more than three years allowed us to establish the features of the periodontal status, as well as the course of periodontal pathology. Such patients often suffered from inflammatory and dystrophic diseases of periodontal tissues, as well as diseases of the oral mucosa, lips, where complications were more pronounced relative to the indicators of the comparison group. The incidence of caries and non-carious dental lesions in persons suffering from CKD was 81.7% and 90.5%, respectively. At the same time, people with CKD were more likely to suffer from non-carious lesions of the hard tissues of the teeth (wedge-shaped defects, increased tooth erosion, dental hyperesthesia), respectively, in 31.4% and 34.5% of cases. It was also revealed that for each examined person suffering from CKD, there were, respectively, 0.67 ± 0.05 and 0.59 ± 0.04 teeth with chronic periapical foci of odontogenic infection. So, with CKD, the CPI index was 12.8 ± 1.11 (K - 3.7 ± 1.83 ; P - 5.3 ± 0.47 ; Y - 3.2 ± 1.43), and with CP - 13.1 ± 0.91 (K - 3.1 ± 0.24 ; P - 6.8 ± 0.53 ; Y - 2.7 ± 0.15). Patients suffering from CKD needed dental treatment and prosthetics, respectively, in 71.3% and 54.6% of cases and 74.5% and 57.8% of cases. The USP index index for patients suffering from CP and HCG was 51.2% and 57.6%, respectively.

In general, the study of the dental status of patients suffering from chronic kidney disease showed that somatic pathology affects both the incidence of pathology of hard tissues of teeth and the clinical picture of the course of major dental diseases. This version coincides with the studies conducted (B. And Shulutko 2015).

Lysozyme (muramidase)- is a low molecular weight enzyme. As is known, lysozyme not only cleaves the glycoside bonds of polyaminosaccharides of bacterial peptidoglycans, but also participates in the processes of regulating the permeability of tissue barriers, regeneration and healing of oral cavity wounds. Lysozyme enters saliva as a result of active secretion by mononuclear phagocytes, as well as the destruction of polymorphonuclear leukocytes, which contain it in large quantities. As can be seen from the presented research results (Table 1), the content of lysozyme in the oral fluid in patients with TIPP exceeded the baseline level by 1.6 times, which indicates the strengthening of the local protective system of the oral cavity in the examined persons.

The kidneys are the organ with the highest lysozyme content. As is known, serum lysozyme is formed from decaying granulocytes and monocytes. As these cells are destroyed, it passes into the plasma, where it is in a free state, easily filtered in the glomeruli, reabsorbed in the

proximal tubules. As for the origin of urine lysozyme, there is a theory about its synthesis in the epithelial cells of the renal tubules.

When determining lysozymuria in patients with TIPP, compared with the indicators of healthy individuals, a significant increase in its level was found on average by 8 times. As is known, lysozyme is produced up to 500 mg per day, and the period of stay in plasma is short - 75% of the protein is removed within 1 hour mainly by the kidneys. A decrease in the level of lysozyme in the blood and an increase in its concentration in the urine, i.e., increased urinary excretion, observed in our studies indicates a violation of the functional activity of the proximal tubules in this group of patients. The observed change in the level of lysozyme in saliva, according to some researchers (Khusnutdinova L.M., 2004; Artyushkin S.A., 2017), is due to an increase in mucus formation, which leads to a decrease in the antibacterial, antiviral activity of the mucous membrane and activation of inflammatory processes in the mucous membrane of the oral cavity and periodontal.

1. Table

The content of biochemical parameters of mixed saliva and urine in patients with CGP combined CKD

Indicators	The object of the study	Unit measurement	Healthy Faces n=18	Patients with TIPP n=58
Lysozyme	blood	mg/l	12,81±0,82	2,43±0,17*
	spittle	g/l	0,022±0,001	0,013±0,001*
	urine	mg/l	2,47± 0,19	19,76±1,43*
Lipocalin-2	Blood	mg/l	1,58±0,11	8,43±0,61*
	urine	ng/ mg	5,47±0,43	39,68±2,43*

Note: *- the reliability of the differences is $P < 0.05$ when comparing the indicators of a group of healthy individuals.

Lipocalins are proteins secreted into the blood and other biological fluids that are able to bind siderophores - small hydrophobic iron-carrying proteins. The important role of lipocalin in the processes of apoptosis and adaptation of degraded tissues is evidenced by the facts of increased synthesis of this lipocalin in damaged tissues. It is involved in stimulating the proliferation process in damaged cells, primarily epithelial cells and protection from bacterial infection, since this protein has a bacteriostatic effect. Haase-Fielitz A. In 2009, co-authors discovered a sharp increase in the concentration of this protein in the cells of the proximal tubules during reperfusion of an ischemic kidney. A 5-fold increase in lipocalin in the blood is apparently due to endogenous intoxication and the release of reactive protein into the blood in patients with TIPP. An increase in lipocalin synthesis in the cells of the proximal

tubules and its release into the urine by an average of 7 times is caused by disorders associated with ischemia of the renal parenchyma and its lesions with nephrotoxic compounds in the examined individuals.

Thus, the study of dental diseases in patients with TIPP and the obtained results of markers of proximal renal tubules in this contingent of patients allow us to offer therapeutic and preventive measures for patients with TIPP aimed at improving the quality of their treatment and life.

Conclusions. It was revealed that a sensitive marker of tubulointerstitial kidney damage is a study of the activity of lysozyme and lipocalin-2 in saliva, blood and urine, which makes it possible to offer therapeutic and preventive measures for patients with TIPP.

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ЖУРНАЛ РЕПРОДУКТИВНОГО ЗДОРОВЬЯ И УРО-НЕФРОЛОГИЧЕСКИХ ИССЛЕДОВАНИЙ

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