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TO STUDY IN A COMPARATIVE ASPECT THE FEATURES OF MARKERS IN PATIENTS WITH TUBULOINTERSTITIAL KIDNEY DAMAGE COMBINED WITH CHRONIC PERIODONTAL DISEASE

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ANNOTATSIYA

Patients with chronic kidney disease, namely tubulointerstitial kidney damage — 58 people were examined. In the oral fluid and urine, the content of IL-1,6,8 and TNF was determined by the enzyme immunoassay.

Key words: tubulointerstitial kidney damage, chronic generalized periodontitis, hyperoxaluria, uraturia.

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ИЗУЧЕНИЕ В СРАВНИТЕЛЬНОМ АСПЕКТЕ ОСОБЕННОСТИ МАРКЕРОВ У БОЛЬНЫХ ТУБУЛОИНТЕРСТИЦИАЛЬНЫМ ПОРАЖЕНИЕМ ПОЧЕК СОЧЕТАННОЙ ХРОНИЧЕСКОЙ ЗАБОЛЕВАНИЕМ ПАРОДОНТА

АННОТАЦИЯ

Обследованы пациенты с хронической болезнью почек, а именно тубулоинтерстициальными поражением почек — 58 человек. В ротовой жидкости и моче определяли содержание ИЛ-1,6,8 и ФНО иммуноферментным методом.

Ключивые слова: тубулоинтерстициального поражения почек, хронический генерализованный пародонтит, гипероксалурия, уратурия.

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QIYOSIY JIHATDAN O'RGANISH BUYRAKNING TUBULOINTERSTITSIAL SHIKASTLANISHI BO'LGAN BEMORLARDA MARKERLARNING XUSUSIYATLARI BIRLASHTIRILGAN SURUNKALI GENERALLASHGAN PARODONTIT KASALLIK

ANNOTATSIYA

Surunkali buyrak kasalligi bo'lgan bemorlar, ya'ni tubulointerstitsial buyrak shikastlanishi — 58 kishi tekshirildi. Og'iz suyuqligi va siydikda il-1,6,8 va TNF tarkibi ferment immunoassay usuli bilan aniqlandi.

Kalit so'zlar: tubulointerstitsial buyrak shikastlanishi, surunkali umumiy periodontit, giperoksaluriya, uraturiya.

Studies by S.I.Gazhva et al., (2013) indicate 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).

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 that increase the formation of leukotrienes, thromboxane, contributing to functional disorders of the tubulointerstitial kidney system.

It should be noted that in recent years, general clinical and paraclinical studies have been used for the diagnosis of TIPP, which allow, on the basis of a clinical and morphofunctional approach, to verify the predominance of damage to the tubules and interstitium in this pathology. In turn, 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 for 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.

Based on the above, the purpose of this study was to study in a comparative aspect the features of markers of the protective system of oral fluid and urine in patients with tubulointerstitial kidney damage with combined chronic periodontal disease, since the development of informative methods for early diagnosis and prediction of the course of TIBP is relevant and timely.

The aim of the study was to evaluate 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. The diagnosis of tubulo-interstitial kidney disease was verified on the basis of a complex of clinical and anamnestic data with an assessment of the presence of kidney pathology in the family, clinical symptoms, paraclinical examination data with an assessment of urinary syndrome (leukocyturia, bacteriuria, microproteinuria), bacteriological examination of urine samples, violations of the tubulo-interstitial structure of the kidneys according to ultrasound with Dopplerography and color Doppler mapping, as well as evaluation of the functional state of the kidneys. 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.

To study the indicator of secretory immunity of saliva, a laboratory study of oral fluid was performed in patients suffering from CKD. Saliva was taken in the morning from 9.00 to 10.00, according to the following method: the patient rinsed the oral cavity with 100 ml of a warm, pale pink solution of potassium permanganate, then for the next 10-15 minutes the patient collected saliva in a dry test tube - about 7 ml. The content of secretory immunoglobulin A (sIgA) in saliva was determined by enzyme immunoassay using Vector Best kits (Russia). Statistical processing was carried out using the program Statistica for Windows version 7.0. The difference was recognized as reliable with a reliability criterion (t) of at least 2, which corresponds to an error-free forecast of 95.5% and an error probability of no more than 0.05.

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. At the second stage of the study, a complete clinical and paraclinical and special examination was carried out. 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. In the oral fluid and urine, the content of IL-1,6,8 and TNF was determined by the enzyme immunoassay. The research was carried out in accordance with the recommendations of the manufacturer of test systems, CJSC "Vector-Best", Novosibirsk. 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

As is known, tubulo-interstitial kidney damage (TIPP) is a heterogeneous group of diseases of various etiologies with predominant involvement in the pathological process of tubules and interstitial tissue, which include both inflammatory (bacterial and abacterial), non-inflammatory, immuno-inflammatory, metabolic, toxic lesions.

Sh.R.Usmanova, A.A.Khadzhimotov, H.P.Komilov Assessment of local and humoral immunity in patients with chronic pyelonephritis.

Gamble J.R., Elliot M.J., Jaipargas E. proved that even asymptomatic oxaluria has a damaging effect on the tubular epithelium and initiates an inflammatory response with the development of interstitial lymphohistiocytic infiltration.

As is known, IL-1 is a mediator of acute and chronic inflammation, IL-6 induces the synthesis of acute phase proteins, provides an increase in the production of IL-2 by T-helpers that recognize the antigen, and also, acting on brain cells, promotes the release of adrenocorticotrophic hormone (ACTH). IL-8 belongs to the group of chemokines, the main property of which is to provide chemotaxis to the inflammation zone of various cell types.

Dental examination was carried out at the Tashkent State Dental Institute clinic, according to the standard scheme and included basic and additional methods (radiography of the parotid tissues). A clinical assessment of the gum condition, tooth mobility, depth of periodontal pockets, Green – Vermillion, Muhlemann, Russel indices was performed.

Clinical and laboratory examination of all patients was carried out according to the standard procedure, which included general blood and urine tests, determination of urea, creatine, total cholesterol, HDL, LDL, triglycerides, ALT, AST, LDH, CK, bilirubin, plasma glucose. The state of the hemostasis system in the blood was assessed according to the following indicators: AITV, protranbin time, inr, thrombin time, fibrinogen content, RFMC, euglobulin fibrinolysis by the method described in the classical manuals.

As an indicator of endothelial damage, the number of desquamated cells was determined by the method of J. Hladovec (1978). The amount of vascular endothelial factor was determined by the enzyme immunoassay using the Vector– Best kit. The activity of the Willebrand factor was studied using reagents from NPO Renom, the amount of soluble P – selectin using reagents from Bioscience, cytokines (TNF α , IL – 1, IL – 6, IL – 4, IL – 10) using commercial test systems “Protein Contour” (St. Petersburg).

Therefore, the study of cytokine levels in the oral fluid and urine allows us to obtain information about the functional activity of various types of immunocompetent cells, the severity of the inflammatory process and prognosis, which is very important in the differential diagnosis of a number of infectious and autoimmune diseases.

The analysis of the obtained results of the study (Table 1) showed an increase in the concentration of all studied cytokines in the oral fluid and urine in persons with TIPP.

As can be seen from the presented research results, the content of IL-1 in the oral fluid of patients with combined CGP type increases by 22% relative to healthy individuals. At the same time, the level of IL-1 in urine also increases by an average of 69% when compared with the results of the comparison group. As is known, the main source of IL-1 production are phagocytic mononuclears of various tissue localization: macrophages and monocytes of peripheral blood and peritoneal exudate, Kupfer liver cells, Langerhans cells, microglia cells of nervous tissue.

Table 1

The content of biochemical parameters of oral fluid and urine in patients with CGP combined CKD

Indicators	The object of the study is healthy	faces n=18	Patients with TIPP n=58
	oral fluid	11.71±1.07	14.35±1.21*
IL-1, pg/ml	Urine	11.88±0.25	20.13±0.23*
	oral fluid	17.48±1.71	24.53±1.69*
IL-6, pg/ml	Urine	9.54±0.11	10.52±0.09
	oral fluid	10.61±0.97	15.78±1.98*
IL-8, pg/ml	Urine	14.28±0.48	20.89±0.46*
	oral fluid	816.43±11.54	951.43±14.67
TNF-a, pg/ml	Urine	11.45± 0.32	20.92±0.35*

Note: * - the reliability of differences P 0.05 relative to the comparison groups.

It should be noted that IL-6 induces the synthesis of acute phase proteins, and therefore, as well as IL-1 and TNF-a, it can be attributed to inflammatory cytokines. The analysis of the presented research results showed that the concentration of IL-6 in the oral fluid and in the urine was also increased in the group of patients with TIPP combined CGP. The active synthesis of IL-6 begins immediately after exposure to the cells of bacteria, viruses, mitogens, and various mediators.

The properties of IL-8 to cause cell migration and promote their adhesion define it as an active participant in an acute inflammatory reaction at the sites of pathogen penetration. As can be seen from the presented research results, an increased level of IL - 8 in the oral fluid and urine of patients with combined CGP is associated with chronic and acute inflammatory conditions and correlates with tissue infiltration of neutrophils in kidney diseases.

Inflammatory cytokines also include TNF-a. TNF-a in the oral fluid of patients with TIPP combined CGP increased by 17%, respectively, compared with healthy individuals, which was of unfavorable significance, since TNF-a activates osteoresorption processes by stimulating osteoclasts. A prolonged and pronounced increase in TNF-a introduces an imbalance between the osteoforming function of osteoblasts and the osteorestructive function of osteoclasts in the direction of hyperactivation of the latter. An increase in the level of TNF in urine by 1.9 times indicated an inflammatory process in the kidneys of the subjects.

Dental examination of middle-aged men included in the control group of the study showed that their incidence of gingivitis and periodontitis was, respectively, 19.8% and 64.9%, with an indicator of the intensity of the course of periodontal diseases (KPI index) of 1.98 ± 0.14 cont. units. In the control group of men, 76.1% of patients needed removal of tartar deposits, and diseases of the mucous membrane of the oral cavity, lips and tongue (SOPRG) they met in 6.4% of cases. The value of the indicators of the Svrakov iodine number was 2.29 ± 0.16 units, the hygiene index was 1.88 ± 0.15 units.

The periodontal status of people suffering from chronic pyelonephritis and chronic glomerulonephritis differed from that of those in the control group. Thus, a dental examination of middle-aged men suffering from chronic pyelonephritis (CP) showed that their incidence of gingivitis and periodontitis was, respectively, 31.3 and 79.5%, with an indicator of the intensity of the course of periodontal diseases (KPI index) of 2.34 ± 0.15 cont. units. In this group of patients, 92.7% of patients needed removal of tartar deposits, and diseases of the mucous membrane of the oral cavity, lips and tongue (SOPRGiA) were

diagnosed in 7.8% of cases. The value of the indicators of the iodine number of Svrakov in persons suffering from CP was 2.28 ± 0.17 units, the hygiene index was 1.94 ± 0.14 units. The frequency of dystrophic lesions of periodontal tissues (periodontal disease) was 4.2%.

People suffering from chronic glomerulonephritis (HCG) have the following indicators of periodontal status. 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 concl. units. In the group of patients suffering from HCG, 95.1% of patients needed to remove tartar deposits, and diseases of the joint were diagnosed in 9.1% of cases.

The value of the indicators of the iodine number of Svrakov in persons suffering from HCG was 2.34 ± 0.14 concl. units, the hygiene index was 1.91 ± 0.17 concl. units. The frequency of dystrophic lesions of periodontal tissues (periodontal disease) was 4.6%.

Thus, a clinical study of patients suffering from various chronic kidney diseases for more than three years allowed us to establish the features of the periodontal status, as well as the course of periodontal pathology, depending on the nosological form of chronic kidney disease. Thus, in individuals suffering from chronic pyelonephritis and chronic glomerulonephritis, there were differences in the condition of periodontal tissues, compared with practically healthy individuals of the same age group. Such patients equally often suffered from inflammatory and dystrophic diseases of periodontal tissues, as well as diseases of the oral mucosa, lips, where complications were more pronounced in patients.

Thus, the features of the cytokine status in the oral fluid and urine allow us to expand the understanding of the pathogenesis of pyelonephritic changes at the stage of acute interstitial inflammation and tissue destruction involving IL-1, IL-6, IL-8, TNF, as well as with the likelihood of immune aggression or immunosuppression.

Conclusions

On the basis of the obtained research results, the question arises what is primary; renal insufficiency that affects the condition of the periodontal or inflammatory changes in the tissues of the oral cavity affect the functional state of the kidneys. This problem requires further research.

In chronic generalized periodontitis, patients with CHEM develop hypercoagulation in the blood, procoagulant activity increases in saliva and fibrinolytic activity decreases, which indicates the involvement of hemostasis, antihemostasis and fibrinolysis factors in the processes of proliferation, inflammation or immuno-regulatory reaction.

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ЖУРНАЛ РЕПРОДУКТИВНОГО ЗДОРОВЬЯ И УРО-НЕФРОЛОГИЧЕСКИХ ИССЛЕДОВАНИЙ

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