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STUDY OF ORAL IMMUNITY FACTORS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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ANNOTATION

The article describes the state of factors of local immunity of the oral cavity in patients with CKD in Uzbekistan. The results of studying the contents of sIgA, IL-1ß, IL-6, IL-8, TNFa and RAIL, IL-4, IL-10 are presented.Data on the nonspecific resistance of COPD in patients with CKD are also presented.

Keywords: CAD, dentistry, chronic kidney disease, CKD, immunity, resistance, immunoglobulins, interleukins.

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ИССЛЕДОВАНИЕ ФАКТОРОВ ИММУНИТЕТА ПОЛОСТИ РТА У ПАЦИЕНТОВ С ХРОНИЧЕСКОЙ БОЛЕЗНЬЮ ПОЧЕК

АННОТАЦИЯ

В статье описано состояние факторов местного иммунитета полости рта у пациентов с ХОБЛ в Узбекистане. Представлены результаты изучения содержания sIgA, IL-1ß, IL-6, IL-8, TNFa и RAIL, IL-4, IL-10.Также представлены данные о неспецифической резистентности ХОБЛ у пациентов с ЦП.

Ключевые слова: ХОБЛ, стоматология, хроническая болезнь почек, ХБП, иммунитет, резистентность, иммуноглобулины, интерлейкины.

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SURUNKALI BUYRAK KASALLIGI BO'LGAN BEMORLARDA OG'IZ IMMUNITETI OMILLARINI O'RGANISH

ANNOTATSIYA

Maqolada O'zbekistonda SOO'K bilan kasallangan bemorlarda og'iz bo'shlig'ining mahalliy immuniteti omillarining holati tasvirlangan. SIgA, IL-1ß, IL-6, IL-8, TNFa va RAIL, IL-4, IL-10 tarkibini o'rganish natijalari keltirilgan.Shuningdek, protsessor bilan og'rigan bemorlarda o'ziga xos bo'lmagan KOAH qarshiligi haqida ma'lumotlar keltirilgan.

Kalit so'zlar: SOO'K, stomatologiya, surunkali buyrak kasalligi, KKD, immunitet, qarshilik, immunoglobulinlar, interleykinlar.

Inflammation is a biological reaction of tissue to harmful stimuli, such as pathogens or stimuli [12]. Studies have shown that inflammation is common in patients with CKD. 30-50% of dialysis patients showed signs of an increased inflammatory reaction, as evidenced by a high level of serum C-reactive protein (CRP) [4,8].

Identification of the sources of inflammation in patients with CKD is still under study.

Evidence supports the idea that deterioration of renal function is associated with increased serum cytokine levels [2,5,9], while other studies have shown that the cause is an increased concentration of glycation end products (factors contributing to vascular inflammation) due to decreased renal clearance [7], infections such as Chlamydia pneumonia [13,16,17]. Inflammatory diseases of the oral cavity [10,11] have also been suggested as possible sources of the cause of CKD. Inflammation of the epithelium of the periodontal pocket is an open door for bacteria and their products. The latter include lipopolysaccharides, peptidoglycan, cytotoxins, proteases and hemagglutinins, as well as locally produced pro-inflammatory mediators such as IL-1, IL-6, TNF- and prostaglandin E.2 (PGE2), which is produced by host cells (neutrophils, macrophages and lymphocytes) into the bloodstream [14]. These pro-inflammatory mediators can stimulate inflammation in a remote location [6, 15].

Secretory immunoglobulins (IgA and IgM) are an important factor in maintaining oral immunity. sIgA is of particular importance because it displays the state of local immunity – with a decrease in its level, the risk of pathogenic microflora increases, the possibility of developing inflammatory diseases.

In order to study the factors of local immunity of the oral cavity, data on the state of secretory immunity of the oral fluid were obtained.

The study took place in 2020-2022 on the basis of Samarkand State Medical University, Tashkent State Dental Institute.

The patients were divided into the following groups:

1. Group of persons who do not have pathology from the urinary system - 16 people (group A);

2. Patients with chronic kidney disease who are not being treated on hemodialysis - 27 people (group B);

3. Patients with chronic kidney disease who are being treated on hemodialysis - 8 people (group B).

The subject thoroughly rinsed his mouth at 8-9 in the morning, then spat 6-7 ml of saliva into a sterile tube.

The content of secretory immunoglobulin A (sIgA), pro-inflammatory cytokines - IL-1ß, IL-6, IL-8, TNFa and anti-inflammatory - RAIL, IL-4, IL-10 were studied.The collected samples were subjected to enzyme immunoassay using Vector Best reagents (Russian Federation).

Another factor of local immunity of the oral cavity is nonspecific resistance - the ability of epithelial cells to adhere to microorganisms. The degree of activity of epithelial cells was determined by the method of Danilevsky N.F., Belenchuk T.A. in the modification of Vasilyeva E.S. [1]. To do this, scraping is performed from the cheek with a sterile metal spatula and transferred to a slide. The glasses are dried at a temperature of 20- 25C and a relative humidity of 58-60% and painted with methylene blue. The preparations are studied with a light microscope, using a liquid immersion system (magnification 90x7); 100 cells are evaluated (integrity, structure, size, staining). The studied cells are divided into five categories depending on the number of microorganisms adsorbed on their surface. Group 1 – 0-5 adsorbed bacteria; group 2 – 5-25 bacteria; group 3 – 26-50; group 4 – 50-200; group 5 – more than 200 adsorbed microorganisms [1].

Results.

Table 1. The concentration of secretory immunoglobulin A in the saliva of patients with CKD before and after dental treatment

Groups of patients	sIgA (g/l)		
	Before treatment	After 6 months	After 1 year
Group A, n=16	1,10±0,12	1,12±0,10	1,12±0,11
Group B, n=27	0,66±0,17	0,64±0,12	0,65±0,14
Group C, n=8	0,59±0,18	0,61±0,14	0,60±0,12

The concentration of sIgA in the oral fluid in persons with group A was higher than in patients with CKD by almost 70%. And in group B individuals, the concentration of this secretory immunoglobulin practically did not differ from the results of group B patients.

The concentration of IL-1β and TNFa in the oral fluid in persons with group B was higher than in persons receiving hemodialysis treatment.And in group B individuals, the concentration of these pro-inflammatory cytokines almost did not differ from patients in the control group.

The content of pro-inflammatory and anti-inflammatory cytokines in the oral fluid.

Table 2. The content of proinflammatory cytokines in the oral fluid with time dynamics

The group of patients	IL-1ß (pg/ml)			IL-6 (pg/ml)			IL-8 (pg/ml)			TNFa (pg/ml)		
	Before treatment	After 6 months.	After 12 months.	Before treatment	In 6 months.	After 12 months.	Before treatment	After 6 months.	After 12 months.	Before treatment	After 6 months.	After 12 months.
Gr.A	14,6±2,9	13,4±1,4	12,9±3,0	13,2±1,7	13,6±1,2	13,5±2,3	511±39	509±37	524±41	12,1±2,6	11,4±1,2	11,3±2,7
Gr. B	12,93±2,06	13,53±3,26	14,38±3,47	19,4±4,2	22,1±1,4	25,3±1,7	813±33	815±27	818±35	11,4±1,5	13,7±1,3	14,0±2,1
Gr.C	13,83±2,2	14,61±3,52	15,67±3,78	24,5±3,5	25,5±1,8	25,7±1,7	845±32	874±23	878±27	13,1±2,3	14,5±2,1	14,9±1,7

P<0,001												

After 6 months, patients with CKD had a significant increase in the concentration of IL-6 and IL-8 compared to group A – by almost 2 times - 22.1±1.4 and 25.5±1.8. After 12 months, this dynamics continued – these indicators were 25.3±1.7 and 25.7±1.7 in groups B and C, accordingly. Thus, it can be argued that patients with CKD require oral sanitation at least 1 time in six months.

The content of anti-inflammatory cytokines (RAIL, IL-4, IL-10) in the examined patients, all three groups are shown in Table 3.

There was no significant difference between both groups of patients with CKD in the content of the IL-1 receptor antagonist (RAIL), as well as IL-4 and the main anti—inflammatory cytokine - IL-10 (p>0.05) in saliva, however, there was a difference with people without diseases of the urinary system (p>0.05).

Table 3. Concentration of anti-inflammatory cytokines in saliva of patients with CKD before and after dental treatment, pg/ml

The group of patients	RAIL (pg/ml)			IL-4 (pg/ml)			IL-10 (pg/ml)		
	Before treatment	After 6 months.	After 12 months.	Before treatment	In 6 months.	After 12 months.	Before treatment	After 6 months.	After 12 months.
Gr.A	2,46±1,08	1,86±0,98	1,92±1,0	8,9±2,8	8,7±2,9	8,8±2,4	12,2±1,3	12,5±1,6	12,7±1,7
Gr. B	2,14±1,1	2,3±0,67	2,4±0,8	9,7±2,8	10,1±1,8	9,9±1,7	12,7±1,9	15,8±1,6	17,3±1,4
Gr.C	2,21±1,2	2,31±0,7	2,6±1,2	10,2±1,9	10,8±2,3	11,2±1,8	14,1±1,6	16,4±1,4	18,7±1,8
P<0,01									

In the salivary fluid of patients with CKD, an increase in the concentration of pro-inflammatory cytokines IL-6 and IL-8 with an increase in the content of anti-inflammatory cytokines was noted.

Determination of nonspecific resistance of the oral mucosa

Table 4. Nonspecific resistance of the oral cavity in patients with CKD

Patient Groups	Content RAM-positive cells (M+m,%)	
	Primary study	Study in a year
Group A	85.23±2.57	88.24±3.41
Group B	64.3±3.21	65.45±2.29
Group C	62.2±4.32	60.3±3.87
P<0,001		

The results of the study indicate that in patients of group A, who underwent therapeutic and preventive measures, were taught the rules of oral care, the number of RAM-positive cells (cells of category 3 and 4) increased by 3.53% in 1 year, in group B - only by 1.78%, and in group B - their number it fell by 3.05%. Compared with healthy individuals, the adsorption properties of epithelial cells in patients with CKD are worse by 32.55%, and in hemodialysis treatment - by 37.0%. The results obtained indicate that the adhesion properties of the epithelium of the SOPR are worse than in healthy individuals.

Discussion of the results obtained.

The concentration of sIgA in the oral fluid in patients without urological diseases is almost 70% higher than in patients with CKD. And in groups of patients with CKD, the concentration of secretory immunoglobulin A practically does not differ. The concentration of IL-1β and TNFa in the oral fluid in persons with group B was higher than in persons receiving hemodialysis treatment. And in group B individuals, the concentration of these pro-inflammatory cytokines almost did not differ from patients in the control group. A decrease in the synthesis of secretory immunoglobulin A leads to a decrease in the activity of local immunity. And this is due to the low activity of the course of inflammatory diseases in the oral cavity. At the same time, the clinical symptoms often do not correspond to the radiological picture of the disease.

The main role of IgA class antibodies is to prevent the attachment of bacteria and microbial toxins to the epithelium, the absorption of harmful xenobiotics. sIgA are an important element of the first line of defense against pathogens. As is known, the sIgA level reflects the status of local immunity, aimed at the formation of protective mechanisms to changes in external conditions, adaptation to stress. An increase in the level of sIgA leads to a decrease in the probability of the appearance of pathogenic and conditionally pathogenic microflora and the displacement of protective groups of microflora in the oral cavity and, thus, leads to a decrease in the activity of inflammatory processes [10].

In the salivary fluid of patients suffering from CKD, there was an increase in the concentration of pro-inflammatory cytokines IL-6 and IL-8 with an increase in the content of anti-inflammatory cytokines. The level of IL-8, the main chemotactic factor of neutrophils, on the one hand affects the level of local immunity, but on the other hand affects the production of oxygen radicals by neutrophils that damage the SOPR, contributing to the activation of repair processes [2].

Proinflammatory cytokines ensure the attraction of neutrophils, macrophages to the focus of inflammation, stimulate bactericidal, phagocytic activity, start the launch of the antigen-specific immune response of the latter. Excessive production of proinflammatory cytokines leads to the development of dysfunctions in organs [2].

A significant increase in the concentration of IL-6 and IL-8 to 22.1±1.4 and 25.5±1.8 in patients with CKD after six months and to 25.3 ± 1.7 and 25.7±1.7 after a year indicate that these patients require oral sanitation at least once in six months.

There was no significant difference between both groups of patients with CKD in the content of the IL-1 receptor antagonist (RAIL), as well as IL-4 and the main anti—inflammatory cytokine - IL-10 (p>0.05) in

saliva, however, there was a difference with people without diseases of the urinary system (p>0.05).

As with any infectious and inflammatory diseases, the pathogenesis of CKD is based on the launch of cytokine cascade reactions, which includes the production of both pro- (IL-1β, TNFa, IL-6) and anti-inflammatory cytokines (IL-10, RAIL, TGFß).

Changes in the concentration of saliva cytokines in various diseases can be considered an important diagnostic criterion for the presence of inflammation [3]. The predominance of pro- or anti-inflammatory cytokines leads to a decrease in the effectiveness of inflammation, the development of purulent complications or autoimmune pathology [2].

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