The role of immunometabolic processes in periodontal tissues for repeated endodontic treatment in patients with chronic forms of periodontitis

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Annotation. *In clinical practice, the study of the immunometabolic processes in periodontal tissues of patients with chronic forms of periodontitis makes it possible to assess the nature of the course of the process and objectively assess the effectiveness of treatment. An immunological study of 65 patients with chronic forms of periodontitis and 65 donors was carried out, which showed the maximum deviation of the immunological parameters of peripheral blood in chronic granulating periodontitis. The patients of the main groups change in the immunological parameters of the oral fluid were revealed: a decrease in the concentrations of IgG, sIgA, fibronectin, IL-4, IL-8, IL-10, IFN-γ; an increase of levels of proinflammatory cytokines IL-1β and TNF-α. The maximum deviation of the immunological parameters of peripheral blood was noted in chronic granulating periodontitis. The patients of the main groups, changes in the immunological parameters of the oral fluid were revealed: a decrease in the concentrations of IgG, sI kines IL-1β and TNF-α. In this regard, the violation of immunometabolic processes in the tissues of the root area of the tooth is the basis for repeated endodontic treatment in patients with chronic forms of periodontitis.*

Keywords: immunometabolic processes, humoral and cellular factors of the immune system, chronic forms of periodontitis, repeated endodontic treatment.

Relevance

Chronic forms of periodontitis are characterized by a protracted development of the inflammatory process in the root area of the tooth with the subsequent development of destruction of the surrounding tissues [1,2,3].

The study of the role of the immunometabolic processes in periodontal tissues is a priority in the pathogenesis of chronic periodontitis. In clinical practice, the study of the cytokine status makes it possible to assess the nature of the course of the process and objectively assess the effectiveness of treatment. Cytokines are a group of polypeptide mediators involved in the formation and regulation of the body's defense reactions [4, 5, 6, 7]. Features of the biosynthesis and regulation of cytokines are determined in the circulating blood. The diagnostic significance of assessing the level of cytokines lies in its increase or decrease in a patient with chronic forms of periodontitis, but to assess the severity and predict the course of this pathology, it is advisable to determine the concentration of pro- and anti-inflammatory cytokines in the dynamics of the process.

Chronic forms of periodontal disease are proposed to be considered as diseases in the pathogenesis of which cellular and humoral autoimmune reactions against periodontal tissues play an essential role. It has been proven that the presence of long-standing multiple foci of infection in the periodontal tissues of the teeth leads to sensitization of the body and secondary immune deficiency [8, 9]. Cytokines play an important role in maintaining normal tissue homeostasis and in inflammation. The study of the role of proinflammatory cytokines in the immune and inflammatory response is an important area of modern immunology in dentistry [10]. In this regard, impaired immunometabolic processes in patients with chronic forms of periodontitis are relevant.

The aim of the work is to evaluate the immunometabolic processes in periodontal tissues in patients with chronic forms of periodontitis

Materials and research methods

130 patients were examined, including 65 patients requiring repeated endodontic treatment based on complaints and analysis of root canal obturation by orthopantomograms (Figure 1) and 65 donors from the Samara Regional Blood Transfusion Station.

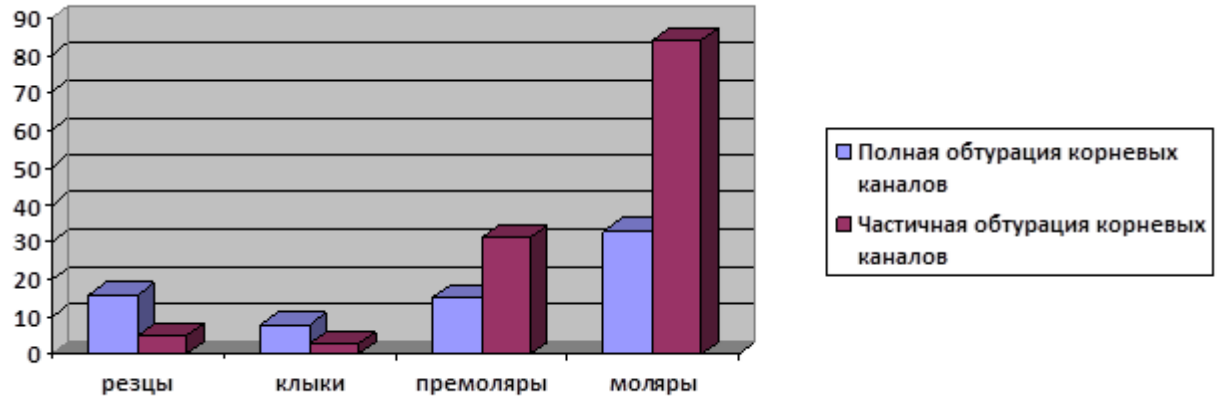

Figure 1. Analysis of obturation of root canals of teeth of different group affiliation

The age of patients who do not have a history of somatic pathology ranged from 18 to 60 years.The patients were randomized into three main groups: Group 1 - patients with a diagnosis of

chronic fibrous periodontitis - 12 people (18.5%); Group 2 - patients with the diagnosis: chronic granulating periodontitis - 26 people (40.00%); Group 3 - patients with a diagnosis of chronic granulomatous periodontitis - 27 people (41.5%). The control group (comparison group) was represented by 65 donors with immunological parameters of the cytokine profile. Donors have a sanitized oral cavity, and a history of no background pathology.

Immunological research methods included the determination of lymphocyte subpopulations using monoclonal antibodies of the LT series. The percentage of the total population of cells expressing CD3 +, CD4 +, CD8 +, CD19 +, CD16 +, CD25 +, CD95 +, CD4 / CD8 was calculated. At the same time, a clinical blood test was performed to determine the absolute number of cells.

The levels of cytokines IL-1α, IL-1β, IL-4, IL-8, TNF-α, IFN-γ, total IgE and fibronectin in blood serum and oral fluid were determined using enzyme-linked immunosorbent assay. The concentration of total IgE in blood serum in patients was determined using DIA-plus kits (Switzerland) and NPF Hema Medica (Russia).

The content of immunoglobulins of classes A, G, M in blood serum was determined by the method of radial immunodiffusion according to Mancini (1965). To assess the state of peripheral blood neutrophils, latex produced by the Institute of Biological Instrumentation (Russia) was used. Hemolytic units CH50 were calculated from the standard hemolysis curve and correction factors. The level of myeloperoxidase was determined using a medium consisting of 50 ml of water, 60 mg of ortomedin.

For statistical analysis, we used the PSIMAGO 4.0, IBMSPSS Statistics 24 software package (license No. 5725-A54). The arithmetic mean (M) and its standard error (m) or the median with quartiles are given as descriptive statistics.

To analyze the characteristics of the quality of treatment in dynamics, the paired Wilcoxon test was used.

Results and discussion

In all forms of periodontitis, the content of leukocytes and lymphocytes is significantly higher than in the control group. Their maximum number was found in patients with chronic granulating periodontitis.

The results of the study of the characteristics of systemic immunity revealed in chronic forms of periodontitis a decrease in the phagocytic activity of neutrophils, the level (relative and absolute) of the main populations and subpopulations of lymphocytes - T-lymphocytes, T-helpers, B-lymphocytes, NK (natural killer cells).

Studying the state of cellular immunity factors by the ratio of lymphocyte subpopulations CD3, CD4, CD8, CD16, CD19, CD25 +, CD95 +, CD4 / CD8, depending on the form of chronic periodontitis, the following was found. The absolute content of CD3 + cells tended to decrease more significantly in chronic granulating periodontitis (0.2 ± 0.1 cells / ml) than in other forms of periodontitis and in the control group. The level of cells with helper functions (CD4 + lymphocytes) is significantly reduced in all forms of periodontitis, but especially significantly in granulating

periodontitis (0.1 ± 0.05). A decrease in the level of these indicators, reflecting the cellular link of immunity, indicates the presence of a defect in cellular immunity.

At the same time, the absolute level of cells with suppressor activity (CD8 + lymphocytes) in patients with granulating periodontitis is significantly higher than in patients with other forms of periodontitis and in the control group. The number of CD19 + cells is higher in patients with chronic fibrous and chronic granulomatous periodontitis compared with the control group. In the group of patients with chronic granulating periodontitis, their content is minimal - 0.09 ± 0.04. The same picture was observed in relation to CD16 + lymphocytes: the minimum content was found in granulating periodontitis (3.1 ± 1.2). Immunoregulatory index, i.e. the ratio of the number of cells expressing markers CD4 + and CD8 + on their surface has significant differences. The CD4 + / CD8 + ratio is minimal in patients with chronic granulating periodontitis (0.2 ± 0.08). The maximum was found in the control group - 2.6 ± 0.4.

There were no statistically significant differences in the quantitative content of CD95 + in the studied groups of patients and in the control. The level of CD25 + lymphocytes was slightly increased in all patients with periodontitis. The content of HLA-DR + cells was significantly higher in all patients with periodontitis. There were no differences in this indicator among groups of patients with various forms of the studied pathology.

The study of humoral immunity factors showed that the level of myeloperoxidase was significantly increased in all patients with periodontitis in comparison with the control group. The maximum indicator was found in patients with granulomatous periodontitis - 60.9 ± 1.0% and fibrous periodontitis - 59.4 ± 1.4%. The level of fibronectin, which is a marker of inflammation, was increased in all patients with periodontitis: the maximum level was observed in patients with fibrous (579.4 ± 11.4 ng / ml) and in patients with granulomatous forms (504.7 ± 6.5 ng / ml).

The CH50 level was significantly lower in all patients with periodontitis, especially in patients with granulating forms (37.6 ± 0.8). The indicators of phagocytic activity of neutrophils were significantly reduced in all patients with periodontitis, especially in patients with granulating periodontitis (42.4 ± 2.0%). Apparently, the decrease in phagocytic activity indicates the dominant place of phagocytosis disorders along with T-system defects in the pathogenesis of chronic periodontitis.

The levels of serum IgA, IgM, IgG were the highest in patients with granulating periodontitis - 3.2 ± 0.2 g / l, 1.8 ± 0.1 g / l, 18.1 ± 0.9 g / l, respectively ... The maximum level of total IgE was found in patients with granulomatous form (142.3 ng / L) and fibrous form of periodontitis (139.6 ± 7.5 ng / L). The increase in the levels of total IgE in the blood serum in all examined groups of patients is characteristic of allergic sensitization.

The levels of IL-8, IL-1α, IL-1β are significantly higher in all forms of periodontitis in comparison with the control group. Thus, IL-8 in patients with chronic granulating periodontitis was found at a concentration of up to 84.6 ± 2.0 ng / ml. The level of IL-1α in this group of patients reached 30.6 ± 1.0 ng / ml, while this interleukin was not detected in the control group. The concentration of

IL-1β was maximal in patients with granulating and granulomatous periodontitis - 64.9 ± 1.0 ng / ml and 54.5 ± 1.1 ng / ml, respectively. IFN-γ was significantly reduced in all patients with periodontitis. The most significant decrease in this indicator was observed in patients with granulating (46.4 ± 1.0 ng / ml). The level of TNF-α was most elevated in patients with granulating and granulomatous periodontitis - 128.0 ± 2.8 ng / ml and 71.2 ± 1.0 ng / ml, respectively. The level of IL-4 was significantly reduced in all patients with periodontitis, especially in patients with granulating periodontitis - 6.8 ± 0.6 ng / ml.

As you know, there is a close relationship between oral fluid and blood. The blood-salivary barrier, by changing the permeability and activity, provides a balanced redistribution of biologically active substances between blood and saliva.

A comparative analysis of the concentration of cytokines in the blood serum in patients with chronic forms of periodontitis revealed a dependence on the form of the disease. In chronic granulating periodontitis, the production of pro-inflammatory cytokines (IL-1, TNF-α, IL-8) is significantly increased, and anti-inflammatory cytokines (IFN-γ) are reduced.

Determination of cytokines in blood serum and oral fluid in healthy people showed that there is a balance of pro- and anti-inflammatory cytokines. In inflammatory processes in the periapical region, an increase of 2.5-3 times in the indices of pro-inflammatory cytokines (IL-1, TNF-α, IL-8) was noted in comparison with healthy individuals.

According to the results of the studies, it can be assumed that the sharply increased concentration of IL-1, TNF-α, IL-8 is the result of the attraction and activation of macrophages in the inflammation focus, which are the main producers of these cytokines.

In chronic forms of periodontitis, immune mechanisms are suppressed at the level of the oral mucosa - the phagocytic activity of neutrophils is reduced, there is an imbalance in the cytokine system in blood serum and saliva, the production of pro-inflammatory cytokines - IL-1, TNF-α, IL-8 is increased and the level of anti-inflammatory cytokine IFN-γ.

From the analysis of indicators of proinflammatory cytokines, it follows that in patients with chronic granulating periodontitis, compared with the control group, there is an increase in the concentration of IL-lα, TNF-α and IFN-γ both in the blood serum and in the oral fluid. The content of pro-inflammatory cytokines and the nature of the inflammatory process are interrelated. There is a direct relationship between the level of proinflammatory cytokines and the type of chronic periodontitis.

The revealed disorders in patients with chronic fibrous, granulating, granulomatous periodontitis indicate a significant cytokine imbalance in all forms of chronic periodontitis. Based on the studies carried out, the severity and individual prognosis of a patient with chronic periodontitis are determined by the severity of immunological disorders - a defect in cellular immunity factors and an imbalance in the cytokine profile. Consequently, when examining a patient, it is necessary to establish which link of the immune response suffers in certain forms of chronic periodontitis.

Conclusion

According to the results of the immunological studies in patients of the main groups with chronic forms of periodontitis and in the control group (indicators of cellular, humoral immunity factors, cytokine profile), it can be concluded that there is an imbalance of the cellular immune response and cytokines in this pathology, as well as a low level of local immune response.

In fibrous and granulomatosis forms of periodontitis, humoral immunity factors (myeloperoxidase activity, fibronectin, immunoglobulins) and phagocytic activity of neutrophils play a leading role in immunopathogenesis; in chronic granulating periodontitis, the most significant is a defect in cellular immunity factors (lymphocytes and their associated subpopulations) , impaired immune regulation of the inflammatory process.

Thus, the violation of the immunometabolic processes in the tissues of the root region of the tooth is the basis for the justified conduct of repeated endodontic treatment in patients with chronic forms of periodontitis.

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