



Immunological Studies in a Group of Patients with Metal-Ceramic Prosthetics before and After

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Resume: In our Republic of Uzbekistan and a number of other foreign countries, metal crowns and bridges made of base metals are currently used; sometimes they are coated with titanium nitrate, which further aggravates the protective mechanisms of the oral cavity. The similar materials of dentures used do not meet either the aesthetic or functional requirements of modern dentistry.

Relevance. As is known, oral fluid (RS) (saliva) containing a large number of substances with antimicrobial action: lysozyme, lactoferrin, immunoglobulins, antimicrobial peptides and other active substances is important in ensuring mucosal immunity of the oral cavity. The immunoglobulins contained in RYE (saliva), especially sIgA, prevent the adhesion of microorganisms, lysozyme destroys the walls of bacteria, and lactoferrin deprives bacteria of iron [1.3.5].

Oral fluid contains components that determine its protective function – these are enzymes that make up complement systems, immunoglobulins. The composition of the oral fluid plays an important role in the functioning of not only the oral cavity, but also the body as a whole, being one of the indicators of homeostasis. Oral fluid is a substrate with colossal informative value, but its indicators are not always taken into account by clinicians [7.9.11].

The study of RV (saliva) is a valuable non-invasive method for assessing the general condition of the body and, in particular, the organs of the oral cavity. Collecting RYE (saliva) is convenient and simple, it is painless, the risk of infection of medical personnel is significantly less than when working with blood, and the content of certain substances in saliva (for example, hormones, antibodies, drugs, etc.) reflects their concentration in the blood [2.4.6.8.10]. Modern technologies for the study of proteins in biological media make it possible to determine the levels of various immune indicators and their biological activity in RYE (saliva) and other secretions containing the studied proteins in minimal concentrations [13.15.17.19].

In connection with the above, it was of interest to study the state of humoral immunity parameters, as well as cytokine status, which were determined in the oral fluid of patients.

The study of the local immune status can expand the understanding of the state of the oral cavity after prosthetics, as well as provide an opportunity to review and use the data obtained for additional correction of orthopedic treatment.

To achieve this goal, according to the tasks, men and women from 20 to 70 years old who were in the Bukhgosmi clinic in the department of dentistry with a diagnosis of prosthetics were examined and 30 practically healthy people made up a control group.

Depending on the therapeutic and preventive measures, all patients were conditionally divided into three groups:

Group 1 (control) - 30 people, only professional teeth cleaning and oral care training were carried out;

Group 2 – 87 people who underwent metal-ceramic prosthetics;

Group 3 – 93 people who underwent zirconium prosthetics

In all groups, immunological studies were conducted before the start of orthopedic treatment, as well as 7 days, 1 month after the fixation of fixed equipment. Levels of sIgA, IgM, IgG, pro-inflammatory IL-1 β , IL-6, TNF- α and anti-inflammatory IL-10 cytokines were determined in the RV.

Immunoglobulins are protective proteins of blood serum or secretions that have the function of antibodies and belong to the globulin fraction.

The leading role in the system of local immunity of the mucous membranes is assigned to secretory IgA (sIgA), the main source of which is the parotid glands. sIgA is formed by the interaction of plasma cells synthesizing IgA and the secretory component, the synthesis of which is carried out by epithelial cells of the ducts of the salivary glands. [12.14.16.18.20].

Secretory antibodies of the oral fluid are immunoglobulins of the IgA and IgM classes and are of local origin. They are produced by plasma cells located under the basement membrane in the connective tissue layer of the mucous membrane - in its own plate [21.22].

Analysis of the obtained data revealed that the content of immunoglobulins of all classes before treatment in patients in need of prosthetics were close to the indicators of control values. Thus, the sIgA level in the main group averaged 825 ± 8.80 mg/ml when in the comparison group its concentration was 780 ± 8.59 mg/ml ($P < 0.001$). The IgM concentration exceeded the values of the control group by 1.2 times (82 ± 2.71 mg/ml vs. 68 ± 1.31 , $P < 0.001$), as well as the IgG content differed from the control group by 1.5 times (56 ± 1.11 mg/ml vs. 37 ± 1.13 mg/ml, $P < 0.01$).

The data obtained by us can be interpreted as follows. According to numerous studies, the ratio of immunoglobulins in the oral cavity is different than in blood serum. If IgG is mainly present in human blood serum, and IgM is contained in small amounts, then the level of IgA in saliva can be 100 times higher than the concentration of IgG. At the same time, saliva contains much more sIgA than other immunoglobulins, so the ratio of IgA/IgG in saliva is 400 times higher than that in blood serum [23.24.25].

Therefore, in the absence of pronounced inflammatory processes in the oral cavity (periodontal disease of various degrees, gingivitis, stomatitis, etc.), the obtained indicators are absolutely appropriate.

The development of inflammatory diseases is determined by the state of cytokine regulation. Most of both pro- and anti-inflammatory cytokines are present not only in peripheral blood, but also in other body fluids [22]. The sources of their production are both lymphocytes and macrophages embedded in the epithelium of the mucous membranes, as well as epithelial cells of the mucous membranes and the salivary glands themselves. Another source of cytokines in RV (saliva) may be their transudation from blood serum. However, many researchers have noted that the content of cytokines in RYE (saliva) does not correlate with their level in the blood, which indirectly indicates their local synthesis [13.15.17.19].

As a result of the analysis, significant differences in the content of the studied pro-inflammatory IL-1 β , IL-6, and TNF- α and anti-inflammatory IL-10 cytokines were revealed in the RV of patients and conditionally healthy individuals.

IL-1 (α and β) (IL-1) Producing cells are monocytes, macrophages, dendritic cells, endothelial cells, etc. Its active production is observed in inflammatory processes, tissue lesions []. IL-1 participates in almost all stages of the immune response, promotes the activation of cells in the focus of inflammation, enhances the production of other cytokines, as well as prostaglandins, collagen and fibronectin synthesis, stimulates phagocytosis, generation of superoxide radicals, causes degranulation of mast cells. [22.23.24.25].

The immunological role of IL-1 β is to trigger the first stages of the immune response, involving certain T-lymphocytes – T-helpers in the process. It stimulates the transformation of B-lymphocytes into plasma cells, accelerates the formation of antibodies. The inflammatory role of IL-1 β is

manifested by an increase in neutrophil motility, stimulation of cell activity in the focus of inflammation, and increased activity of other cytokines [24.25].

Analysis of the obtained data revealed that the content of IL-1 β before treatment in patients was relatively close to the control data. Thus, the level of IL-1 β in the main group averaged 7.5 \pm 0.20 pg/ml when in the comparison group its concentration was 4.2 \pm 0.26 pg/ml (P<0.001).

It is known that the role of IL-6 in inflammation is closely related to IL-1 β and TNF- α . Cytokine producing cells are monocytes, macrophages, Th2 cells, bone marrow stromal cells, fibroblasts, hepatocytes, etc. IL-6 is an inducer of maturation of B cells into plasma cells, their production of antibodies. Cytokine is a powerful stimulator of the production of proteins of the acute phase of inflammation by liver cells. This proinflammatory cytokine is able to enhance the proliferation of endothelial cells []. After meeting with the antigen, specialized cells initially secrete IL-1 β and TNF- α , and only then IL-6 [22.24].

The data obtained indicate that the concentration of IL-6 in the general group of patients before the start of orthopedic treatment exceeded the values of the control group by more than 1.3 times (14.7 \pm 0.46 pg/ml versus 11.8 \pm 0.55, pg/ml, P<0.001), which indicates an already formed inflammatory focus in the oral cavity (Fig.4.2).

The next stage was the study of the synthesis of tumor necrosis factor - α (TNF- α), which is a product of monocytes, macrophages, endothelial basophils, mast and myeloid cells, neuroglia cells and has a wide spectrum of biological action. This cytokine plays a role in the development of an inflammatory response: it initiates the synthesis of interleukin-1, interleukin-6, and also stimulates the proliferation of T- and B-lymphocytes [12.14.16.18].

As a rule, the content of TNF- α is not determined, or is at a low level in the blood serum of healthy donors, whereas with the development of the pathological process, its amount increases several times.

Thus, the synthesis of TNF- α in patients in the general group before prosthetics averaged 12.3 pg/ml, when in the control group these values were equal to 9.4 pg/ml, which is 1.3 times more (P<0.001).

In this study, the level of the important anti-inflammatory cytokine IL-10 in rye was studied. The main effect of IL-10 is anti-inflammatory. It is realized through the suppression of the activity of macrophages and T-lymphocytes, and also suppresses the production of all pro-inflammatory cytokines, interferon, and the proliferative response of T cells to antigens and mitogens [13.15.17]. Acting as a Th2-cytokine and due to the ability to suppress cytokine production in monocytes and Th1-lymphocytes and inhibit the antigen presenting ability of monocytes, IL-10 inhibits the cellular immune response, stimulating at the same time the proliferation of B-lymphocytes and humoral immune response [17.19.21].

When analyzing the data obtained as a result of the study, a significant increase in the level of IL-10 in the main observation group before orthopedic treatment was found to be 1.2 times (10.6 pg/ml versus 8.5 pg/ml) (P<0.01).

Thus, the data obtained by us on the humoral link of local immunity and the cytokine status of the oral cavity indicate a weakening of the local immune protection of the oral cavity associated with the need for prosthetics.

Orthopedic dentistry uses prostheses made of a wide variety of materials. The most popular option for many years now is cermet. Metal–ceramic prostheses are structures that represent a frame, the base of which is made of metal. The upper coating is made of ceramic. Such constructions make it possible to solve the problem of adentia in patients of any age. They perfectly restore the chewing function, and also have an excellent appearance.

To date, dental prosthetics using cermet is the most popular among patients. This is due to the many advantages that metal-ceramic structures have. Complications may occur after installation. This is a consequence of the direct impact of prostheses or the materials from which they are made.

In the present study, patients using metal-ceramic bridges had a different clinical picture. Among the examined 72 patients (83%) had gingivitis. These patients have been using metal-ceramic bridges for more than 5 years. Periodontitis of moderate severity was observed in 51 patients (58.6%). We have not observed severe periodontitis in the acute stage. After applying the dentures, the 1st dental examination was carried out the next day, at the stage of correction of the denture.

Patients complained of painful sensations on the mucous membrane of the oral cavity when closing teeth, as well as when applying a denture. The examination revealed inflammatory changes on the mucous membrane of the prosthetic bed, which were represented by hyperemia and erosion localized in the area of the border of the denture, as well as in areas of increased pressure of the base on the mucous membrane.

Thus, inflammatory changes on the mucous membrane of the prosthetic bed were caused by the traumatic effect of the denture.

It is known that the role of immunoglobulins of various classes in the immune response and protective functions of the immune system is different. And depending on this role, their synthesis occurs, and the concentration depends on the switching of C-genes, as a result of which immunoglobulins appear on the surface of macrophages [22.23].

It should also be noted that the sIgA level after fixation of orthodontic equipment after 1 month significantly decreased below the baseline data (after 30 days 751 ± 8.84 mg/ml versus control 825 ± 8.80 mg/ml) ($P < 0.001$), which may contradict some studies. However, in the work of Lee Y. (2009) it was proved that acute and chronic inflammatory processes in the tissues of the oral cavity are characterized by a decrease in sIgA in saliva. sIgA deficiency in secretions causes a tendency to frequently recurring inflammatory processes, therefore, determining the concentration of sIgA in saliva is an important test characterizing the state of local immunity of the oral cavity [12.16]. The reduction of sIgA allows not only to assume the pathology of periodontal tissues, but also to serve as a tool to assess the effectiveness of the therapy, on which the optimal course of regeneration processes depends.

The next stage of our research was to study the concentrations of unclassified IgM and IgG in the rye.

Non-secretory immunoglobulins enter the oral cavity with blood flow, but they can also be synthesized directly in it by plasmocytes after specific stimulation. Then they enter the place of the immune conflict – in the submucosal or mucous layer. Factors that enhance the flow of serum immunoglobulins into the secrets are inflammatory processes of the oral mucosa, its trauma, local allergic reactions.

In the process of humoral immune response, IgMs are formed first in the initial collision with the antigen, they appear also in repeated collisions, but in smaller quantities [21.23.25]. Analysis of the results of the study on the level of IDM showed that patients had an average of 174 ± 5.22 mg/ml 2 times for 7 days, which indicates the beginning of maximum expression ($P < 0.001$).

The above data of our study indicate the receipt of a large amount of serum antibodies to the site of inflammation, which in this case is a biologically appropriate mechanism for enhancing local immunity. However, due to the fact that IgM normally practically does not enter saliva, in particular RV, in the case of an increase in the level of IdM in patients with metal-ceramic fixed prostheses, there appears to be ulceration of the oral mucosa and massive transudation of immunoglobulins of this class from the blood, which is confirmed by examination the very next day. Ulceration after a week of establishing the structure was represented by defects of the mucous membrane within the epithelium with smooth edges. The bottom of the traumatic lesions was moist, located just below the surrounding mucosal tissues. Patients complained of painful sensations in the area of the lesion, which increased when the denture was applied and the teeth were closed.

On the 30th day, after the correction of the denture, inflammatory changes on the oral mucosa manifested in moderate forms. So after 1 month, the level began to decrease before the initial values, while amounting to 96 ± 2.44 mg/ml versus 82 ± 2.71 mg/ml ($P < 0.001$).

Completely opposite dynamics was recorded by the IgG indicator.

This immunoglobulin is produced in both primary and secondary immune responses. IgG has the maximum ability to penetrate into tissues, so it binds and removes antigens most effectively. [22.24.25]. Thus, the level of IL-1 β decreased to 16.4 \pm 0.74 pg/ml (P<0.001), IL-6 to 28.7 \pm 0.72 pg/ml (before treatment 14.7 \pm 0.46 pg/ml) (P<0.001), TNF- α -24.5 \pm 1.03 pg/ml (before treatment 12.3 \pm 0.32 pg/ml) (P<0.001), IL-10 - 15.3 \pm 0.65 pg/ml (before treatment 10.6 \pm 0.32 pg/ml) (P<0.001).

Thus, based on the conducted studies, it can be stated that the established cytokine imbalance in the RV indicates an increase in the antigenic load and increased permeability of the oral mucosa as a result of the traumatic genesis of the prosthetic bed and as a consequence of the developed inflammatory process.

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