ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

The Local Immunity of Dental Patients with Oral Galvanosis.

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ABSTRACT

The purpose of this study was to evaluate the role of immune inflammation in the development of clinical symptoms of oral galvanosis. For evaluating local immunity in the oral cavity, an oral liquid of the patients was measured for levels of immunoglobulins M, G, secretory immunoglobulin A, interleukins 2 and 4, interleukin-1β, γ-interferon. A comparative analysis of local immunity and clinical manifestations of oral galvanosis in patients with metal dentures was carried out. Patients with galvanosis have an increased content of cytokine TNF-alfa in mixed saliva, which indicates the presence of inflammation of the oral mucosa. The stimulation of the chronic inflammation with the electrochemical potential activates innate immune mechanisms, resulting in increased levels of salivary immunoglobulin M. The increase of the content of immunoglobulins M and TNF-alfa in patients with oral galvanosis indicates activation of the immune inflammation in the mucosa of the oral cavity and is the basis for development of clinical symptoms.

Keywords: galvanosis, immunoglobulins, cytokines, interferon.

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ISSN: 0975-8585

INTRODUCTION

Oral mucosa has its own immune system that operates independently from the general immunity. Many immunological reactions occur in oral cavity, providing natural protection, preventing oncological diseases and preserving homeostasis [1, 5, 6]. The epithelium of the mucosa itself is full of immune cells - neutrophils that migrate from the vessels of the lamina propria and retain up to 90% of the functional activity of the epithelial surface [7-13]. Cytokines play leading role in the local immunity of the oral cavity. They influence on biochemical messengers regulating stimulation and inhibition of inflammatory reactions, which initiate an immune response. Source of cytokines in the saliva is serum transudate and salivary glands. The mucosal epithelial cells themselves produce cytokines in contact with the microbes [2]. The intolerance of dentures shows significant growth of IFN-y and IL-8 indicators in the oral fluid, which is contributed to the maintenance of the inflammatory process and the development of destructive changes in the oral mucosa. Other authors also point at a high level of IL-8 in the oral fluid in case of intolerance of dental materials [4].

Several authors explain the influence of increased galvanic currents on the development of allergic reactions by the proximity of the mast cells and nerves of the oral mucosa, which ensures their interaction. Irritation of the nerve cells with electric current causes an increase in the neuropeptides, which stimulate their degranulation and the release of cytokines by acting on mast cells. As a result of autocrine and paracrine effects, cytokines ensure maintenance of the allergic reaction by supporting mast cell degranulation [14].

Study of the influence of metals on the viability of cells in cell culture (fibroblasts, keratinocytes) has shown that the cell viability was greatly reduced after incubation with samples of copper, a significant decrease in viability was also observed after incubation with nickel, chromium, cobalt, and zinc, iron, palladium, gold, indium showed the smallest effect on cell viability [1, 2].

Corrosion products come in various biochemical reactions with molecules present in the oral and tissue fluids, resulting in new chemical substances. Binding to proteins, they may serve as a hapten, forming an antigen molecule, which an immune response can develop to [2].

Patients with pathologic galvanic currents have low content of a secretory IgA, lysozyme, and increased levels of cytokines in the oral cavity [4].

In vitro studies demonstrated that the influence of non-toxic doses of metals (titanium, cobalt, chromium, etc.) on lymphocytes, macrophages, keratinocytes, fibroblasts was resulting in increased production of cytokines by these cells [12]. Most of these cytokines are anti-inflammatory. Increase of their levels indicates the development of inflammatory reactions.

Therefore, the presence of metals in oral cavity and their corrosion leads to a large amount of ions or particles of these metals, which react with the organic constituents of

tissues and body fluids; they come into contact with the cells of the organism and its microflora. These processes depend on the acidity of the medium, which reflects the extent of the pH value. Accumulating in the body, metal ions may have toxic effects on its cells [3, 12].

Currents induced, irrespective of the force, have impact on both the oral cavity and the whole organism. They start and strengthen corrosive processes associated with corrosion of orthopedic materials. This results in both the destruction of denture materials and accumulation of metal ions with their intensive transfer to the tissues. Here they interact with biochemical substances and form new substances, which can serve as allergens.

Study of local and general nonspecific body resistance have shown a sharp decline of all indicators in patients with galvanosis. Normalization of the electrical conductivity of the oral fluid is directly depends on both the magnitude of the potential difference and the severity of clinical symptoms of galvanosis. Corrosion processes in turn initiate the increase in amperage and difference in potentials. Ff patients with metal orthopedic structures in the oral cavity have potential difference more than 150 mV, and there is a clinical manifestation of intolerance of denture materials, this indicates the development of galvanosis. Nevertheless, the majority of patients, using metal dentures for a long time, have no galvanosis, which should be explaind by good adaptation of the organism to pathological factors (galvanic currents induced, increase in the concentration of metal ions, reduction of pH of saliva, etc.) [5, 6].

Thus, the analysis of the literature available suggests an absence of a single integrated approach to diagnosis and prevention of galvanosis and the need in further study of the effects of this disease on the local immunity of the oral cavity of dental patients.

The purpose of this study was to evaluate the role of immune inflammation in the development of clinical symptoms of oral galvanosis.

Technique

In accordance with the tasks set 120 patients with metal orthopedic structures aged 45 to 74, applying to dental clinic of VolgSMU were examined and treated. Total 39 males (67,5 %) and 81 females (32,5%) were examined. Persons with metal orthopedic structures involved patients with crowns, console, bridge and clasp dentures, which were made of stainless steel, chromium-cobalt, chromium-nickel alloys, and other metals, as well as dentures with metal protective coating (MPC).

The examination did not include patients with acute and chronic diseases in the acute stage, epilepsy, diseases of the immune system (HIV), hepatitis B and C, sexually transmitted diseases, malignant tumors, those with obvious signs of mental illness, individuals taking medications that could affect the immune status.

Measurement of the electrochemical potential difference of the oral cavity in patients with metal dentures was carried out due to the standard procedure using the

biopotential meter unit "BPM - 03" [3]. Measuring electrodes have a small, stable potential asymmetry, their design ensures operation at any position without contaminating with the electrolyte an object measured. Electrodes are equipped with bulky electrolytic disposable keys, which provide contact of measuring electrodes with the oral mucosa. To determine the electrochemical potential of metal constructions in the oral cavity, one silver chloride reference electrode and a metal nickel-based electrode are used. he electrodes are connected to the input of the recording unit in accordance with the markings on the electrode housing.

Due to the value of electrochemical potentials, patients with metal dentures were divided into 3 groups: Group 1 - 40 patients, with the difference of electrochemical potentials less than 80 mV (reference group); Group 2 - 43 patients, with the difference of electrochemical potentials from 80 mV to 100 mV; Group 3 - 37 patients, with the difference of electrochemical potentials more than 100 mV.

For evaluating local immunity in the oral cavity, an oral liquid of the patients was measured for levels of immunoglobulins M (IgM), G (IgG), secretory immunoglobulin A (sIgA), interleukins 2 and 4 (IL-2 и IL-4), interleukin-1β (IL-1β), γ-interferon(TNF-alfa), with the help of immunoenzyme method using "Vector-BEST" reagents [3].

Main Body

Study of cytokine level in the oral fluid of the patients from Group 3 compared to Group 1 has shown that IL-8 level in oral fluid was not significantly different (323 ± 45 μg/ml versus 290 ± 34 μg/ml, respectively). IL-8 level in oral fluid of the patients from Group 2 compared to Group 1 was not changed (326±37 μg/ml versus 290±34 μg/ml, respectively) (Table 1).

Table 1: Levels of cytokines and immunoglobulins in oral fluid of the patients [M(25% - 75%)].

Cytokines	Control group (up to 80 mv)	Group 2 (80 to 100 mv)	Group 3 (more than 100 mv)
IL-8 (pg/ml)	290 (221-413)	326 (294-399)	323 (354-413)
IL-4 (pg/ml)	1.95 (0-17)	(33) (6.9-40)	2.6 (0-18)
IL-1β (pg/ml)	218 (42-269)	78.5 (53-98)	205 (53-228)
TNF α (pg/ml)	5.3 (2.6-7.3)	24.3* (14-27)	17.5* (5-26)
Proinflam. Potential	1.59 (1.17-1.78)	6.6* (5.6-14)	2.95* (1.8-3.8)

* - Significant differences from the control group (p <0,05)

IL-4 level in the oral fluid of the patients from Group 3 compared to Group 1 was significantly higher (p <0,05) (2.65 ± 2 μg/ml vs. 1.95 ± 1 μg/ml, respectively). IL-4 level in the oral fluid of the patients from Group 2 was also significantly higher than in patients from the control group (33 ± 14 μg/ml vs. 1.95 ± 1 μg/ml, respectively).

ISSN: 0975-8585

The analysis of the content of IL-1β in the oral fluid of the patients from Group 3 compared to the Group 1 has shown no significant differences (205 ± 60 μg/ml vs 218 ± 66 μg/ml, respectively). Patients from Group 2 had much lower average IL-1β value than those from the control group, however, high index variation in the group made impossible to establish significant differences (78 ± 14 μg/ml vs 218 ± 66 μg/ml, respectively).

Study of TNF-αlfa level in oral fluid of patients from the groups examined allowed to establish significant excess of cytokine content in the oral fluid of patients from Groups 2 and 3 (17 ± 6 μg/ml vs 24 ± 7 μg/ml, respectively) above the TNF-αlfa level in the oral fluid of patients from the control group (5 ± 1 μg/ml).

The proinflammatory potential of oral fluid, calculated as the sum of the proinflammatory cytokines normalized by average value of their level was almost the same in patients from Group 3 and 2 (6.6% and 2.95%, respectively) and significantly ($p < 0,05$) exceeded in the patients from the control group (1.59%).

The increase in TNF-αlfa level in the oral fluid of patients from Groups 3 and 2 indicates the activation of Th2-dependent immune response to the oral mucosa, which may be the basis for the development of allergic reactions to dental materials and other antigens. Furthermore, the increase of the proinflammatory potential of oral fluid in these patients suggests that galvanosis is coupled with active immune inflammation that also affects local place where a source of potential difference is. The development of immune reactions involves all mucosa as an immune organ, which may result in the development of symptoms of inflammation: rubor, tumor, color, dolor. In addition, it may start an immune mechanism of transplant rejection or the development of an autoimmune process.

The assessment of the content of immunoglobulins G in oral fluid of patients from the groups examined has revealed that the level of antibodies in all groups was about the same and not significantly different. Patients from Group 3 had IgG level of 0.67±0.65 μg/ml, Group 2 and the control group (0.51±0.11 μg/ml and 0.59±0.44 μg/ml, respectively) (Table 2).

Table 2: Levels of immunoglobulins in oral fluid [M(25% -75%)].

Immunoglobulins	Group 1 (up to 80 mv)	Group 2 (80 to 100 mv)	Group 3 (more than 100 mv)
Ig G (μg/ml)	0.59 (0.54-0.71)	0.51 (0.4-0.65)	0.67 (0.66-0.8)
Ig M (μg/ml)	0.15 (0.11-0.18)	0.40* (0.17-0.55)	0.43* (0.14-0.92)
Ig A (μg/ml)	15.4 (8.5-19.3)	10.7 (5.7-11.2)	12 (8.3-14.6)

* - Significant difference from the patients from the control group ($p<0,05$)

However, the IgM content in the oral fluid of the patients from Group 3 (0.43 ± 0.14 μg/ml) was significantly higher ($p < 0,05$) than in patients from Group 2 and the control group (0.40 ± 0.13 μg/ml and 0.15 ± 0.01 μg/ml, respectively).

The average sIgA level in the oral fluid of the patients from Group 3 (12 ± 1.4 μg/ml) compared to Group 2 and the control group (10.7 ± 4.1 μg/ml and 15.4 ± 2.2 μg/ml respectively) were a bit lower, however, the differences were not statistically significant.

CONCLUSION

The features of the immunoglobulin profile of oral fluid revealed, associated with a significant increase in immunoglobulin M in patients from Group 3, may be associated with the activation of local immunity. Moreover, this activation is associated only with an increase in the synthesis of primary immune antibodies that may occur during stimulation of mechanisms of innate immunity without triggering the formation of antigen-specific resistance by switching synthesis to the immunoglobulin G. This may be due to chronic inflammation, the focus of which can be an orthopedic structure and its difference of potentials may be a driving force.

SUMMARY

Patients with galvanosis have an increased content of cytokine TNF-alfa in mixed saliva, which indicates the presence of immune-mediated inflammation of the oral mucosa. The stimulation of the chronic inflammation with the electrochemical potential activates innate immune mechanisms, resulting in increased levels of salivary IgM ($p<0.05$). Conjugacy of the galvanosis and the immune-mediated inflammation of the oral mucosa is the basis for the development of clinical symptoms of galvanosis.

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