



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.1069435>Available online at: <http://www.iajps.com>

Research Article

**IMMUNOLOGICAL PECULIARITIES OF ADAPTATION OF
PATIENTS WITH CARDIOVASCULAR DISEASES TO THE
NON-REMOVABLE DENTURES ON THE BACKGROUND OF
BALNEOLOGICAL IMMUNOCORRECTION****A.T. Iakovlev^{1*}, T.F. Danilina¹, V.N. Naumova¹, V.A. Virabian¹,
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Moscow, Trubetskaya street, 8-2), Russia**Abstract**

In order to study the immunological aspects of adaptation to the non-removable bridged dentures on the background of cardiovascular pathology, 115 patients of the dental polyclinic VolgSMI were examined. The cytokine profile and concentration of immunoglobulins in the gingival fluid were studied at the stages of odontopreparation and prosthetics using the traditional technique and against the background of balneological immunocorrection with Elton.

It was established that the patients without immunocorrection during orthopedic treatment have increase in the concentrations of proinflammatory cytokines in their gingival fluid, which indicates active inflammatory processes in the tissues. The use of Elton helps to reduce the inflammatory process in marginal periodontium and shorten the period of adaptation to bridged solid dentures, which is manifested by a decrease in the concentrations of proinflammatory cytokines in the gingival fluid against the background of activation of local secretory immunity of the mucous membranes.

Keywords: cardiovascular diseases, dental diseases, fixed prosthetics, cytokines, immunocorrection.

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Please cite this article in press as A.T. Iakovlev et al., *Immunological Peculiarities of Adaptation of Patients with Cardiovascular Diseases to the Non-Removable Dentures on the Background of Balneological Immunocorrection*, Indo Am. J. P. Sci, 2017; 4(11).

INTRODUCTION:

Aspects of the relationship between cardiovascular and dental diseases have been fairly well studied [2,5,6]. People suffering from coronary heart disease (CHD), are typically susceptible to impaired microcirculation and oxygenation in the tissues of periodontal and oral mucosa [1]. Patients with atherosclerosis, essential arterial hypertension on the background of vascular disorders, predominantly have dystrophic periodontal diseases, caused by violations of central and regional hemodynamics [4,7]; the course of inflammatory processes in the maxillofacial area (MFA) is aggravated.

Mutual complication of cardiovascular and dental diseases is associated with the processes of systemic inflammation in the body. In inflammatory periodontal diseases in peripheral blood, there is an increased level of C-reactive protein and fibrinogen, which increases the risk of atherosclerotic changes in blood vessels. By activating monocytes or directly affecting the vascular endothelium, lipopolysaccharides of the cell wall of the parodontopathogenic microflora trigger a cascade of immunological reactions accompanied by the synthesis of pro-inflammatory cytokines such as interleukin 6 (IL-6), interleukin 8 (IL-8), tumor necrosis factor alpha (TNF α) and acute phase proteins [8,9,10,11]. C-reactive protein and fibrinogen, being acute phase proteins, enhance platelet activation and aggregation, aggravating thereby atherosclerotic changes in blood vessels, which are a pathogenetic component of IHD and hypertension. Thus, somatic pathology has a significant effect on the immune response formed by the body.

Odontopreparation for non-removable orthopedic structures often leads to trauma of the gingival margin, disruption of epithelial attachment, development of inflammation in the marginal periodontal [3]. Disturbance of the integrity of periodontal tissues and inflammatory response of the immune system are also possible at the stages of gum retraction, removal of impressions, fit and fixation of dentures, which initiates microcirculatory and immunological disorders similar to changes in inflammatory periodontal diseases of a microbial nature. These aspects can influence the success of prosthetics in patients with cardiovascular diseases (CVD).

Special literature contains not enough data on the immunological features of adaptation of CVD patients with with non-removable bridged dentures. It is known that the use of immunocorrection in

prosthetics with removable dentures significantly facilitates the period of adaptation to the manufactured structures, but this aspect has been little studied in patients who suffer from cardiovascular pathology and are at the stages of the prosthetic treatment with non-removable solid bridges.

MATERIALS AND METHODS:

Total 115 patients (59 men and 56 women) underwent orthopedic treatment with solid bridges with a differentiated approach to the application of the balneological agent "Elton" on the marginal periodontal area. The first group consisted of 45 patients suffering from CVD, who got solid bridges in the course of immunocorrection with the balneological agent "Elton". The second group consisted of 40 patients with CVD, who got solid bridges manufactured by the traditional method of prosthetics. The third group included patients receiving treatment in the orthopedic unit of the dental polyclinic of VolgSMI and did not have a history of CVD (30 people). As a control, gingival fluid parameters were used for 30 healthy volunteer donors.

In order to study the immunological features of adaptation of patients with CVD to solid bridges, the state of local immunity of the oral cavity was evaluated before the odontopreparation, on day 3 after odontopreparation and day 7 after fixation of non-removable orthopedic structures. The study included evaluation of the level of cytokines: interleukin 6 (IL-6), interleukin 8 (IL-8), tumor necrosis factor alpha (TNF α) in pg/ml, and immunoglobulin concentrations: secretory A (sIgA), IgM, IgG in mg/l. The material of the study was gingival fluid. The obtained data were processed using Stat Soft Statistica v6.0 statistical software package.

RESULTS AND DISCUSSION:

IgA is a component of secretory immunity of the oral cavity, synthesized primarily by lymphocytes in response to local damage; it protects mucous membranes from pathogenic microorganisms and allergens. A decrease in IgA concentration indicates a lack of humoral and local immunity, a violation of synthesis and an increase in IgA catabolism and its adsorption on immune complexes. The kinetics of synthesis of immunoglobulins of different classes is different. If the antigen is administered for the first time, then a primary immune response arises and IgM-producing cells are detected, the number of which is further reduced. IgG synthesis reaches its maximum values after a longer period of time.

The patient of group 3 had approximately a 4-fold increase in their secretory IgA after odontopreparation as compared to the control indices (2.20 ± 0.55 mg/l and 0.59 ± 0.12 mg/l, respectively) and only slight decrease after fixation of orthopedic structures: 1.90 ± 0.65 mg/l, which indicates the active participation of immunoglobulins of this class in protecting the mucous membranes from invasion and inhibiting the inflammatory process in marginal periodontitis of the supporting teeth in patients without somatic pathology. The level of IgM and IgG at the different stages of orthopedic treatment of patients without a history of CVD differed slightly and was within 0.03-0.05 mg/ml, without demonstrating significant differences with the control group.

Thus, acute inflammation, which develops in response to traumatic injury, is a classic protective reaction of innate immunity in a healthy body. In inflammation, T-helpers stimulate B-lymphocytes to produce IgA, in turn, T-suppressors suppress the formation of IgM and IgG by B-cells, limiting thereby the process of inflammation.

The increase in the level of the proinflammatory cytokine TNF- α , which is typical for all inflammatory processes, is associated with its regulatory effect on general and local inflammatory responses and indicates the activation of macrophage function in response to damage or antigenic stimulation. This cytokine has a powerful pro-inflammatory activity and plays an important role in the damage and regeneration of tissues, acts as an immunostimulant and mediator of the immune response. It is the first synthesized in the focus of inflammation.

The content of tumor necrosis factor alpha (TNF α) in the gingival fluid in non-CVD patients was within the range of 1.86-2.04 pg/l at different observation time and did not have significant differences between their values and those of healthy donors.

The synthesis of IL-6 in the focus of inflammation occurs later than the synthesis of TNF α . The increase in the formation of IL-6 in tissues is often associated with their damage caused by various effects, including mechanical, thermal, ischemic, which occur during odontopreparation and application of a denture. Among the biological effects of this cytokine, activation of the maturation of megakaryocytes and an increase in the number of platelets, as well as the induction of the synthesis of acute phase proteins by hepatocytes, can affect the state of patients with CVD.

The level of IL-6 in patients without CVD has significant changes both after odontopreparation (10.1 ± 3.45 pg/l) and after prosthetics (14.9 ± 0.85 pg/ml), as compared with the control group (2.70 ± 0.60 pg/l). Probably, this is due to the fact that inflammation in the marginal zone is caused precisely by a traumatic, rather than by a microbial or antigenic factor.

IL-8 refers to chemokines, i.e. it is a chemoattractant for neutrophils and an important component of nonspecific innate immunity. Significant differences were observed in concentrations of IL-8 (pg/ml) before and after prosthetics, as well as with the parameters of the control group (Table 1).

Table 1: Indicators of local immunity of gingival fluid in non-removable prosthetics in patients without CVD, in comparison with the control.

No.	Indicator	Group 3 (30 people)		Healthy donors (control) (30 people)
		After odontopreparation (day 3)	After prosthetics (day 7)	
1.	S-IgA, mg/l	$2.20 \pm 0.55\#$	$1.90 \pm 0.65\#$	0.59 ± 0.12
2.	IgM, mg/ml	0.03 ± 0.02	0.03 ± 0.01	0.02 ± 0.01
3.	IgG mg/ml	0.04 ± 0.01	0.05 ± 0.01	0.05 ± 0.01
4.	TNF α , pg/ml	1.86 ± 0.55	2.04 ± 0.39	2.00 ± 0.50
5.	IL-6, pg/ml	$10.10 \pm 3.45^{*}\#$	$14.90 \pm 0.85\#$	2.70 ± 0.60
6.	IL-8, pg/ml	$341.70 \pm 63.10^{*}\#$	$397.50 \pm 85.15\#$	73.30 ± 19.95

Note: *- Significant difference according to the Wilcoxon test between groups of patients before and after prosthetics, $p < 0.05$;

#- Significant difference according to the Mann-Whitney test between a group of patients and the control, $p < 0.05$.

Thus, the patients of group 3, in response to a traumatic effect, showed a tendency to increase in the concentrations of pro-inflammatory cytokines in the gingival fluid.

The second group of patients with CVD, who got non-removable dentures without immunocorrection, showed the following results. The IgA level was 1.85 ± 0.073 mg/l before the prosthetics; after the preparation it increased to 2.05 ± 0.43 mg/l and continued to increase: after the prosthesis its level was 2.20 ± 0.12 mg/l. The concentrations of IgM and IgG on day 3 and 7 were in the range of 0.03-0.05 mg/ml. Thus, the content of IgM and IgG in the gingival fluid of patients of group 2 did not change reliably at different observation time. Just as in group 3, there was activation of local humoral immunity, manifested in increased IgA synthesis as compared to the control group.

The concentration of proinflammatory interleukins increased dynamically on days 3 and 7, with significant difference in values at different observation time, which indicated the initiation and maintenance of the inflammatory process in the tissues (Table 2).

The general dynamics of the content of gingival fluid immunoglobulins in the first group of patients with CVD, who got solid bridges in the course of immunocorrection with the balneological agent "Elton", during different periods of observation was similar to the dynamics of the same parameters in the 2nd and 3rd groups: an increase in the secretory IgA, IgM and IgG concentration did not differ significantly both at different observation times and on the parameters of the 2nd and 3rd groups (Table 3).

Table 2: Indicators of local immunity of gingival fluid in non-removable prosthetics in non-CVD patients without immunocorrection.

No.	Indicator	Patients without immunocorrection (40 people)		
		Before prosthetics	After odontopreparation (day 3)	After prosthetics (day 7)
1.	S-IgA, mg/l	1.85 ± 0.73	$2.05 \pm 0.43^*$	$2.20 \pm 0.12^{*#}$
2.	IgM, mg/ml	0.03 ± 0.01	$0.03 \pm 0.01^*$	$0.04 \pm 0.01^{*#}$
3.	IgG mg/ml	0.05 ± 0.01	$0.05 \pm 0.01^*$	$0.05 \pm 0.01^*$
4.	TNF α , pg/ml	1.89 ± 0.25	$1.99 \pm 0.22^*$	$2.13 \pm 0.16^{*#}$
5.	IL-6, pg/ml	15.75 ± 3.15	$18.00 \pm 2.93^*$	$19.20 \pm 2.75^{*#}$
6.	IL-8, pg/ml	396.4 ± 28.40	$399.20 \pm 19.43^*$	$401.55 \pm 19.03^{*#}$

Note:

*- Significant difference according to the Wilcoxon test from the values before prosthetics, $p < 0.05$;

#- Significant difference according to the Wilcoxon test from the values after odontopreparation, $p < 0.05$;

Table 3: Indicators of local immunity in patients with CVD at the stages of prosthetics with immunocorrection with the balneological agent "Elton".

No.	Indicator	Patients with immunocorrection (40 patients)		
		Before treatment	day 3 post treatment	day 7 post treatment
1.	S-IgA, mg/l	1.70 ± 0.80	$2.20 \pm 0.65^*$	$2.50 \pm 0.60^{*#}$
2.	IgM, mg/ml	0.03 ± 0.01	$0.03 \pm 0.01^*$	$0.03 \pm 0.01^{*#}$
3.	IgG mg/ml	0.04 ± 0.01	$0.04 \pm 0.01^*$	$0.03 \pm 0.01^{*#}$
4.	TNF α , pg/ml	1.89 ± 0.21	1.88 ± 0.16	$1.74 \pm 0.11^{*#}$
5.	IL-6, pg/ml	15.40 ± 1.55	$14.20 \pm 1.35^*$	$13.4 \pm 1.70^{*#}$
6.	IL-8, pg/ml	399.50 ± 14.65	$389.30 \pm 19.05^*$	$377.20 \pm 21.50^{*#}$

Note:

*- Significant difference according to the Wilcoxon test from the group of patients before prosthetics, $p < 0.05$;

#- Significant difference according to the Wilcoxon test from the group of patients on day 3 post treatment, $p < 0.05$;

The cytokine profile of the gingival fluid in patients with CVD, whose prosthetics were performed on the background of immunocorrection with the use of the balneological agent "Elton", showed a positive progress, which was absent in patients of groups 2 and 3 without immunocorrection: the concentration of all investigated pro-inflammatory cytokines was dynamically reduced by day 3 and 7 of observation, which indicated the arrest of the inflammatory process. However, these indicators still differed significantly from the control values.

CONCLUSION:

The obtained results substantiate the expediency of using immunocorrection at the stages of prosthetics with non-removable bridged dentures in patients with cardiovascular diseases.

SUMMARY:

The use of balneological agent "Elton" promotes the reduction of the inflammatory process in the marginal periodontium and shortens the period of adaptation to the bridged dentures. A harmonizing effect of Elton on local immunity of the oral cavity is manifested in a significant decrease in the concentrations of proinflammatory cytokines in the gingival fluid, which also have a systemic effect on the body.

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