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CYTOKINE CHANGES IN PERIODONTITIS AND UNDER THE CONDITIONS OF USING DIFFERENT TYPES OF REMOVABLE PROSTHETIC BASES

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The study of the mechanisms of the development of inflammatory processes in periodontal tissues remains relevant due to the high prevalence of this pathology, its unfavorable prognosis, as well as the limited effectiveness of treatment and prevention.

The aim of the work – to investigate changes in cytokine status in experimental bacterial-immune periodontitis and under the conditions of using acrylic and nylon prosthetic bases.

Materials and methods. Experimental bacterial-immune periodontitis in animals was induced by injecting a mixture of microorganisms suspended in egg protein into the periodontal tissue. By the 30th day, the blood serum was then collected for subsequent analysis, and the levels of interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and interleukin-10 (IL-10) were determined using the solid-phase enzyme immunoassay method.

Results and discussion. Modelled bacterial-immune inflammation on the 30th day of the study, which was characterized by the most pronounced clinical manifestations of periodontitis, there was a reactive increase in the level of pro-inflammatory cytokines in the blood serum and a decrease in the level of the anti-inflammatory cytokine. Fixation of prosthetic bases made of different types of plastics under conditions of experimental periodontitis contributed to an increase of the inflammatory process in the periodontum. This was manifested by an increase in the level of pro-inflammatory cytokines, as well as a decrease in the concentration of anti-inflammatory interleukin-10 in blood serum.

Conclusion. An increase of IL-1β and IL-6 and a decrease of IL-10 when using acrylic bases, in comparison with nylon, indicates a smaller negative impact of nylon plastic on the development and course of inflammation in periodontal tissues.

Keywords: periodontitis, removable prosthetics, base of prosthesis, cytokines, immune system.

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ЗМІНИ ПОКАЗНИКІВ ЦИТОКІНОВОГО СТАТУСУ ПРИ ПАРОДОНТИТІ ТА ЗА УМОВ ВИКОРИСТАННЯ РІЗНИХ ТИПІВ БАЗИСІВ ЗНІМНИХ ПРОТЕЗНИХ КОНСТРУКЦІЙ

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Стаття присвячена вивченню особливостей прозапальних і протизапальних цитокінів під час розвитку експериментального бактеріально-імунного пародонтиту у білих щурів. Для цього були проведені дослідження рівнів ІЛ-1β, ІЛ-6, ІЛ-10 у сироватці крові на 30-ту добу експерименту, в процесі запалення в тканинах пародонта, й за використання різних типів базисів знімних протезів. Отримані дані дозволяють передбачити перебіг бактеріально-імунного пародонтиту й оцінити вплив знімних ортопедичних конструкцій на розвиток запального процесу. Збільшення вмісту ІЛ-1β та ІЛ-6 та зменшення вмісту ІЛ-10 у сироватці крові у разі використання акрилових базисів, порівняно з нейлоновими, свідчить про менший негативний вплив нейлонової пластмаси на розвиток і перебіг запальних процесів у пародонтальних тканинах.

Ключові слова: пародонтит, знімне протезування, базис протезу, цитокіни, імунна система.

Introduction

The study of the mechanisms of the development of inflammatory processes in periodontal tissues remains relevant due to the high prevalence of this pathology, its unfavorable prognosis, as well as the limited effectiveness of treatment and prevention [1]. The study of changes in immune processes and regulation of cytokine status when using full or partial removable dentures in periodontitis can help identify important links that lead to damage to the structures of the periodontal complex and the formation of inflammation of varying intensity and duration [2; 3]. Currently, it is recognized that the key role in the immune response is played by the innate immune system, which is not only a means of anti-infective protection, but also a universal effector that responds to signals about the

disturbance of the internal balance of the body and is a determining factor in the development of immune and inflammatory reactions [4].

Cytokines play a key role in the development and maintenance of the inflammatory process. Thanks to pro-inflammatory cytokines and chemokines, intact monocytes, granulocytes and lymphocytes are attracted to the site of inflammation [5]. The cytokine network is a complex self-regulating mechanism in which the activity of some components is controlled and balanced by others [6]. Some cytokines have effector properties capable of causing destructive changes in tissues [7]. It is known that any imbalance in the cytokine network, caused by various factors, can complicate the course of the disease, change its character, and introduce new features into its pathogenesis [8]. Prognostically significant cytokines have been determined, the levels of which allow predicting the course of bacterial-immune periodontitis and assessing the impact of removable prosthetics on the inflammatory process in the tissues of the periodontal complex [9].

To date, the cytokine system includes more than 300 polypeptide substances. The best studied cytokines of the immune system, which are secreted during the implementation of mechanisms of general and local immunity, showing activity even at very low concentrations. These molecules can be considered as mediators of inflammatory reactions, which also perform endocrine, paracrine and autocrine regulatory functions [10].

Interleukins are of greatest clinical and immunological interest. According to their mechanism of action, these polypeptides can be conditionally divided into several groups: inflammatory (inducing an inflammatory response), anti-inflammatory (limiting the development of an inflammatory response), and regulators that have their own effector functions, such as cytotoxic and antiviral effects [11].

The aim of the work – to investigate changes in cytokine status in experimental bacterial-immune periodontitis and under the conditions of using acrylic and nylon prosthetic bases.

Material and methods

The study was carried out on clinically healthy white rats weighing 150–200 g, kept under vivarium conditions in compliance with sanitary standards and Good Laboratory Practice (GLP). All procedures adhered to the guidelines of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986), as well as the "General Ethical Principles of Animal Experimentation" (Kyiv, 2001).

The experimental animals were randomly selected and divided into four groups: Group I consisted of intact control animals (n = 10); Group II included animals with experimental periodontitis on the 30th day of the study (n = 8); Group III included animals with experimental periodontitis on the 30th day of the study and with acrylic bases (n = 8); Group IV included animals with experimental periodontitis on the 30th day of the study and with nylon bases (n = 8).

Dental prostheses were made according to established methods: acrylic bases by thermal polymerization from polymethacrylate material "Villacryl H Plus" (Zhermack, Poland) [12], and nylon bases – from thermoplastic material "Vertex ThermoSens" (Vertex, Netherlands) by pressing method under pressure [13]. Orthopedic structures were designed so as not to cover the occlusal surfaces of the teeth and were simultaneously fixed on both central incisors of the lower jaw.

Experimental bacterial-immune periodontitis in the test animals was induced by injecting a mixture of microorganisms suspended in egg protein into the periodontal tissue. To boost the immune response, a simultaneous injection of complete Freund's adjuvant was administered into the rat's paw. This procedure was repeated on the 14th day of the experiment to reinforce the efficiency of inducing and chronicling periodontitis of bacterial-immune origin [14]. By the 30th day, the experimental animals were euthanized via exsanguination under thiopental anesthesia. Blood serum was then collected for subsequent analysis, and the levels of interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and interleukin-10 (IL-10) were determined using the solid-phase enzyme immunoassay method, employing a RayBio Rat Cytokine Antibody Array reagent kit (RayBiotech, Norcross, USA). The concentrations of IL-1β, IL-6, and IL-10 were expressed in ng/l.

The Commission on Bioethics of I. Horbachevsky Ternopil National Medical University confirmed that no violations of moral and ethical standards were found during the research (Protocol No. 76 dated January 15, 2024).

The results were analyzed using non-parametric statistical methods in the STATISTICA 10.0 software (StatSoft, USA). The significance of the differences between independent quantitative variables with a normal distribution was assessed using the Mann-Whitney U test [15].

Results and discussion

As a result of the research, it was established that the formation of the inflammatory process in the periodontal complex, which included the period from the 1st to the 30th day of experimental observation, was accompanied by a significant increase in blood serum (1.96 folds; $p<0.001$) of interleukin-1β relative to the intact group of rats (Table 1).

In studies using acrylic bases of removable prostheses in experimental periodontitis on the 30th day, there was also an increase in the content of interleukin-1β in blood serum compared to the intact group of animals – 3.39 folds ($p<0.001$). It is worth noting that when compared with a group of rats with bacterial-immune periodontitis in the same period without prosthetics, it was established that the above indicators increased 1.73 folds ($p<0.001$), this indicates that their use contributed to the increase of inflammatory process in periodontal tissues (Fig. 1).

Fixation of the bases of prostheses made of nylon plastic in the experiment led to an increase in pro-inflammatory IL-1β in the blood serum of animals 2.57 folds ($p<0.001$), compared to the group of control rats. Compared to animals with bacterial-immune inflammation of the periodontium on the 30th day of the experiment without prosthetics, the studied indicator was 1.32 folds higher ($p<0.01$). It should be noted that the level of this interleukin in the serum was 1.32 folds lower ($p<0.01$) compared to the group of animals with acrylic prosthetic bases.

Table 1

Changes in cytokine indicators in blood serum of white rats with bacterial-immune periodontitis and under the condition of fixation of prosthetic bases (M±m)

Research conditions and indicators		Study duration (days)	Number of rats	IL-1β, ng/l	IL-6, ng/l	IL-10, ng/l
Control (intact) group		–	10	6.63±0.47	10.81±0.63	20.93±0.64
Animals with experimental bacterial-immune periodontitis	No prosthetics	30	8	12.97±0.51 p_1<0.001	14.34±0.58 p_1<0.01	12.52±0.43 p_1<0.001
	Acrylic base	30	8	22.47±0.69 p_1<0.001; p_2<0.001	20.80±0.62 p_1<0.001; p_2<0.001	6.67±0.28 p_1<0.001; p_2<0.001
	Nylon base	30	8	17.05±0.80 p_1<0.001; p_2<0.01; p_3<0.01	16.99±0.31 p_1<0.001; p_2<0.01; p_3<0.001	9.64±0.50 p_1<0.001; p_2<0.01; p_3<0.01

Note. p_1 – statistical significance of differences with an intact group of animals; p_2 – statistical significance of differences with the group of animals with bacterial-immune periodontitis on the 30th day without prosthetics; p_3 – statistical significance of differences with a group of animals with bacterial-immune periodontitis on the 30th day with acrylic bases.

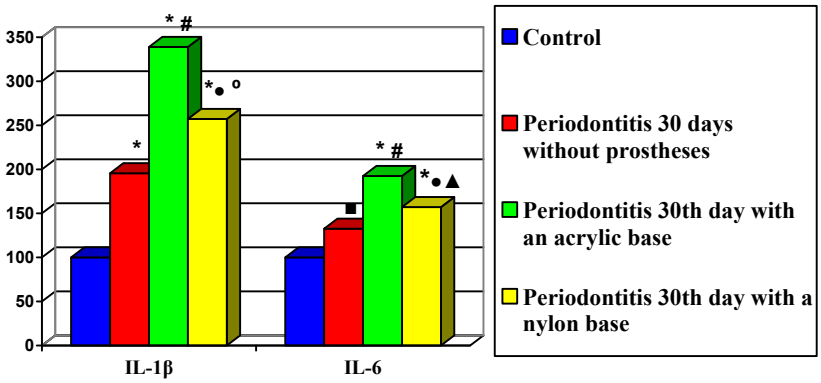

Fig. 1. Changes in the content of pro-inflammatory cytokines in the blood of animals under the conditions of the development of bacterial-immune periodontitis and the use of prosthetic bases (in % of control)

Note. * – statistical significance of differences with the intact group of animals (p<0.001); ■ – statistical significance of differences with the intact group of animals (p<0.01); # – statistical significance of differences with the group of animals with bacterial-immune periodontitis on the 30th day without prosthetics (p<0.001); ● – statistical significance of differences with the group of animals with bacterial-immune periodontitis on the 30th day without using bases (p<0.01); º – statistical significance of differences with the group of animals with bacterial-immune periodontitis on the 30th day using acrylic bases (p<0.01); ▲ – statistical significance of differences with the group of animals with bacterial-immune periodontitis on the 30th day using acrylic bases (p<0.001).

Analyzing changes in the content of IL-6 in blood serum, it should be noted that its level also increased significantly in the experimental group on the 30th day of the development of inflammation in periodontal tissues – 1.33 folds (p<0.01) against the control (Table 1).

In the study of interleukin-6 after the use of an acrylic base in the condition of bacterial-immune periodontitis, an increase in its level was established in comparison with the control group and animals with an inflammatory process on the 30th day of the experiment: 1.92 folds (p<0.001) and 1.45 folds (p<0.001), respectively.

A similar tendency to increase the level of IL-6 was recorded in the blood serum of rats with nylon bases of removable prostheses and periodontitis. The concentration of this cytokine exceeded the control values 1.57 folds (p<0.001). Compared to data on the 30th day without prostheses, the level of interleukin-6 was 1.19 folds higher (p<0.01).

It should also be noted that the results of the study showed that the level of IL-6 in the experimental group with periodontitis and prosthetics with nylon bases was significantly lower 1.22 folds (p<0.001) compared to the group with inflammation and acrylic structures (Fig. 1).

As for changes in the level of the anti-inflammatory cytokine IL-10, its concentration in the blood serum of animals under the conditions of the simulated inflammatory process changed in the opposite direction. It should be noted that this indicator on the 30th day was reliably lower than the data of the intact group of rats 1.67 folds (p<0.001) (Table 1), which is evidence of the active development and course of the inflammatory process in the periodontal tissues during this period.

Analyzing the obtained indicators of anti-inflammatory interleukin, it is necessary to pay attention to its decrease under the condition of prosthetics with acrylic bases in periodontitis in the experiment. IL-10 content in blood serum was 3.14 folds lower than that of intact animals (p<0.001), and 1.88 folds (p<0.001) of the group with bacterial-immune periodontitis on the 30th day.

The anti-inflammatory interleukin-10 content also decreased in animals with used nylon bases of prostheses. The influence of this type of plastic on the course and development of inflammation in this model of the pathological process is confirmed by a decrease in the level of IL-10 in blood serum (2.17 folds; p<0.001), compared to the control group.

It should be noted that during the fixation of nylon prostheses, during the development of this inflammatory process, there was a 1.30-fold decrease in anti-inflammatory cytokine indicators (p<0.01), compared to such data of animals with bacterial-immune periodontitis on the 30th day of the experiment, with no prosthetics, which indicates an increase in the manifestations of the inflammatory process in the periodontal tissues. When comparing the indicators of anti-inflammatory interleukin against the background of prosthetics with different types of bases of removable structures, it should be noted that the level of interleukin-10 was significantly higher under the condition of using nylon plastic, namely 1.45 folds (p<0.01) compared to the data in rats with acrylic bases (Fig. 2).

A decrease in the level of anti-inflammatory cytokines and an increase in the level of pro-inflammatory cytokines in the blood serum of experimental animals led to an imbalance in their ratio (IL-1β / IL-10). Comparison of this ratio showed that it was 3.28 folds higher (p<0.001) in rats with simulated experimental bacterial-immune periodontitis on the 30th day, compared to the control group (Table 2).

As a result of changes in the number of pro- and anti-inflammatory interleukins in the blood serum of animals against the background of the use of acrylic bases in simulated inflammation in the periodontium, there was a significant shift in their ratio (IL-1β / IL-10). Statistical processing of the results showed that this ratio was significantly higher (10.63 folds; p<0.001) compared to control animals (Fig. 3). The experimental study also showed that when acrylic structures were fixed, the ratio of pro- and anti-inflammatory interleukins significantly increased, compared to the group of animals with periodontitis on the 30th day of the experiment (3.2 folds; p<0.001).

Enzyme immunoassays also revealed a significant difference between IL-1β / IL-10 ratios in animals with nylon prostheses compared to animals with acrylic prostheses. When using nylon plastic, this indicator was 1.91 folds lower (p<0.001).

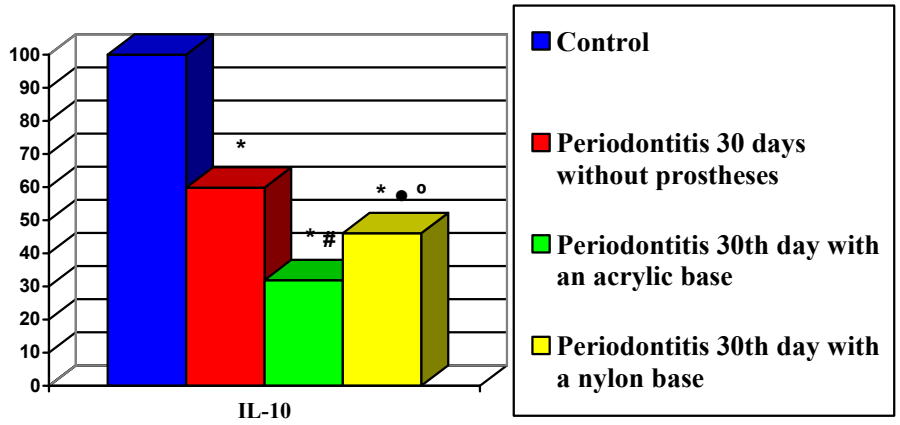

Fig. 2. Changes in the content of interleukin-10 in the blood of animals under the conditions of the development of bacterial-immune periodontitis and the use of prosthetic bases (in % of control)

Note. * – statistical significance of differences with the intact group of animals (p<0.001); # – statistical significance of differences with the group of animals with bacterial-immune periodontitis on the 30th day without using bases (p<0.001); ● – statistical significance of differences with the group of animals with bacterial-immune periodontitis on the 30th day without using bases (p<0.01); º – statistical significance of differences with the group of animals with bacterial-immune periodontitis on the 30th day using acrylic bases (p<0.01).

Table 2

Changes in the ratio of pro-inflammatory and anti-inflammatory cytokines in the blood of experimental animals with experimental bacterial-immune periodontitis and under the condition of fixation of prosthetic bases (M±m)

Research conditions and indicators		Study duration (days)	Number of rats	IL-1β / IL-10
Control (intact) group		–	10	0.32±0.02
Animals with experimental bacterial-immune periodontitis	No prosthetics	30	8	1.05±0.06 p_1<0.001
	Acrylic base	30	8	3.40±0.16 p_1<0.001; p_2<0.001
	Nylon base	30	8	1.78±0.06 p_1<0.001; p_2<0.001; p_3<0.001

Note. p_1 – statistical significance of differences with an intact group of animals; p_2 – statistical significance of differences with the group of animals with bacterial-immune periodontitis on the 30th day without prosthetics; p_3 – statistical significance of differences with a group of animals with bacterial-immune periodontitis on the 30th day with acrylic bases.

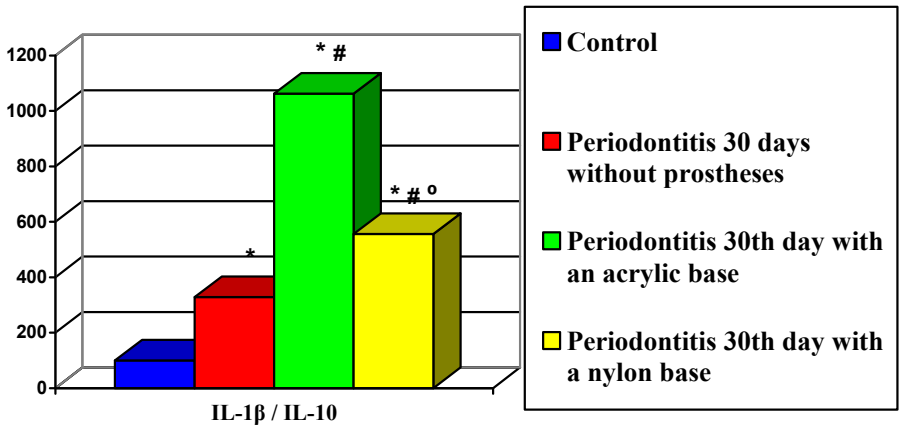

Fig. 3. Changes in the ratio of pro-inflammatory and anti-inflammatory interleukins in the blood of animals under the conditions of the development of bacterial-immune periodontitis and the use of prosthetic bases (in % of control)

Note. * – statistical significance of differences with the intact group of animals ($p<0.001$); # – statistical significance of differences with the group of animals with bacterial-immune periodontitis on the 30th day without using bases ($p<0.001$); ° – statistical significance of differences with the group of animals with bacterial-immune periodontitis on the 30th day using acrylic bases ($p<0.001$).

Our research showed that in white rats with experimental bacterial-immune periodontitis, the content of pro-inflammatory cytokines of the first line, such as IL-1β and IL-6, in the blood serum increased significantly compared to intact animals. Interleukin-1β is a proinflammatory cytokine that activates T cells, NK cells, and NKT cells, and stimulates cytokine production by T cells [16]. IL-6 is a pro-inflammatory cytokine that plays an important role in regulating the immune response and inflammatory responses. An increase in their concentration indicates an active reaction of the body to inflammation, which is a consequence of acute and chronic inflammatory processes, in turn; an increase in the level of IL-6 in blood serum also indicates an increased activity of nonspecific defense mechanisms of the body and indicates an activation of the inflammatory process [17].

In the pathogenesis of periodontitis and bone resorption, a significant role is played by the increased secretion of anti-inflammatory IL-10, which prevents the formation of an effective inflammatory reaction, which is a necessary condition for the elimination of pathogens [18]. This can lead to clinical manifestations of periodontitis with mild symptoms, although at the same time serious destructive processes in the periodontal complex are observed [19]. IL-10, being an anti-inflammatory cytokine, plays a key role as an endogenous regulator of immune and inflammatory responses. It has the reverse ability to suppress the activation and functions of T-cells, NK-cells, macrophages, as well as to reduce the production of pro-inflammatory cytokines by these cells [20].

The analysis of the obtained data also indicates that the gradual increase in the IL-1β / IL-10 ratio, which is characteristic of the increase of the inflammatory reaction in periodontal tissues and the activation of the inflammatory reaction in the body of experimental animals against the background of the use of different types of base plastics and an imbalance in the cytokinegenesis system.

An increase in the content of pro-inflammatory cytokines (IL-1β and IL-6) and a decrease in the content of anti-inflammatory IL-10 in blood serum when using acrylic bases of removable orthopedic structures, in comparison with nylon prostheses, indicates a smaller negative impact of nylon plastic on the development and course of inflammatory processes in periodontal tissues.

Conclusions

1. On the 30th day of the study, simulated bacterial-immune inflammation in the periodontal complex was characterized by the most pronounced clinical manifestations of periodontitis; there was a reactive increase in the level of pro-inflammatory cytokines (IL-1β, IL-6) in the blood serum and a decrease in the level of the anti-inflammatory cytokine – IL-10.

2. Fixation of prosthetic bases made of different types of plastics under conditions of experimental bacterial-immune periodontitis contributed to an increase in the inflammatory process in the periodontal tissues. This was manifested by an increase in the level of pro-inflammatory cytokines, as well as a decrease in the concentration of anti-inflammatory interleukin-10 in blood serum.

3. In experimental animals with experimental inflammation in periodontitis and prosthetic acrylic bases of removable structures, a significant growth in the production of pro-inflammatory cytokines (IL-1β, IL-6) against the background of a decrease in the formation of anti-inflammatory IL-10 was found, compared to the indicators obtained in the group of animals with inflammation and nylon prostheses, which is characteristic of the more unfavorable effect of acrylic plastics on the key mechanisms of the development of the inflammatory process in the periodontium.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical statement

All authors declare that ethical approval is not required for this review study.

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