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INFLUENCE OF DENTAL PROSTHESES MATERIALS ON THE CONDITION OF ORAL MUCOSA LOCAL HOMEOSTASIS

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ВЛИЯНИЕ МАТЕРИАЛОВ ОРТОПЕДИЧЕСКИХ КОНСТРУКЦИЙ НА СОСТОЯНИЕ ЛОКАЛЬНОГО ГОМЕОСТАЗА СЛИЗИСТОЙ РТА

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Objective. To study the influence of base materials used in the manufacture of removable dentures on the immune homeostasis of the oral mucosa, and, as a consequence, on the clinical condition of the oral mucosa and periodontium of supporting teeth. To create fundamental principles for the development of a pathogenetically substantiated choice of basic dental materials of various chemical natures for removable prosthetics based on the analysis of the parameters of immune homeostasis of the oral mucosa.
Materials and methods. 154 patients aged 40 to 85 using dentures based on acrylic, polyurethane plastics and thermoplastics for 6 months, participated in the study. Indicators of immune homeostasis and the identified clinical manifestations of the influence of the prosthesis material such as chronic periodontitis and gingivitis were compared using the statistical method of conjugate multifield tables.

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Results. The indicators CD4+/CD8+, CD11/CD303, CD68, CD204, CD163, Ki-67 phenotypic markers were determined in gingival biopsies of the prosthetic bed of patients using dentures based on acrylic, polyurethane and thermoplastic for 6 months. Analysis of the statistical significance of differences proved the influence of the prosthesis material on indicators of cellular immune homeostasis, with a shift of homeostasis towards the pro-inflammatory phenotype, and the suppression of the anti-inflammatory factor in circulating monocytes.
Conclusions. The study shows that, although each type of removable dentures has its own advantages and disadvantages, the response of the cellular immunity of the oral mucosa to polyurethane dentures is less than to acrylic and thermoplastic ones in relation to the control group. The use of polyurethane prostheses is reasonable as temporary ones during the healing stage of surgical interventions in the oral cavity, in particular tooth extraction and implantation. This type of prosthesis can be recommended as a permanent one for patients with a severe allergic reaction, especially to polymer compounds and dyes.
Keywords. Denture material, cellular immunity, immune homeostasis, oral mucosa, denture biopsies, phenotypic markers.

Цель. Изучить влияние различных материалов съемных протезов на состояние слизистой оболочки рта и пародонта зубов посредством исследования локального иммунного гомеостаза.
Материалы и методы. В исследовании приняли участие 154 пациента в возрасте от 40 до 85 лет, для лечения которых использовались протезы на основе акриловых, полиуретановых пластмасс и термопластов. В качестве материала исследования представлены данные иммуногистохимического анализа биоптатов десневого ложа 154 пациентов, пользовавшихся в течение 6 месяцев съемными протезами с базисами на основе акрилов, термопластов и полиуретана. С помощью статистического метода спряженных многопольных таблиц показатели локального иммунитета сопоставлены с обнаруженными клиническими проявлениями влияния материала протеза – хроническим пародонтитом и гингивитом.
Результаты. Определены показатели фенотипических маркеров CD4+/CD8+, CD11/CD303, CD68, CD204, CD163, Ki-67 в десневых биоптатах протезного ложа пациентов, использующих съемные протезы с базисами из акрила, полиуретана и термопласта через 6 месяцев с момента окончания протезирования. По результатам анализа статистической значимости различий доказано влияние материала базиса протеза на показатели клеточного локального иммунитета, которое соответствует сдвигу гомеостаза в сторону провоспалительного фенотипа, и подавление противовоспалительного фактора в циркулирующих моноцитах.
Выводы. В исследовании показано, что пользование съемными протезами ведет к изменению локального клеточного иммунитета слизистой рта: данные параметры при пользовании протезами на основе термопластов, акриловых и полиуретановых пластмасс имеют существенные различия. Изменения показателей локального гомеостаза слизистой рта напрямую коррелируют с клиническими проявлениями в области протезного ложа и тканей пародонта. Изменения морфологических и клинических параметров слизистой рта при пользовании протезами на основе полиуретана минимальны по отношению к параметрам контрольной группы.
Ключевые слова. Материал съемных протезов, клеточный иммунитет, иммунный гомеостаз, слизистая оболочка рта, биоптаты протезного ложа, фенотипические маркеры.

INTRODUCTION

Partial absence of teeth (partial secondary adentia) is one of the most common diseases: according to the results of various studies, it affects from 44 to 100 % of the population of the Russian Federation over 40 years old, depending on age and region. The absence of teeth not only affects chewing and speech functions, but also causes changes in the facial skeleton and can lead to psychological changes, disruption of social adaptation, changes in nutrition, and even contribute to the development of various diseases due to changes in the composition of oral fluid.

A population survey revealed a high level of need for dental orthopedic care – 69.9 %; already at the age of 20–29 years this figure is 55.6 %, and at the age of 60–69 years – 86.1 %, at the age of 70 years and older – 72.8 % [1].

Based on the results of the analysis of changes in the practice of dental orthopedic treatment in the regions of Russia over a 10-year period, it was revealed that the proportion of patients with partial removable dentures increased, compared to 2008, from 60 % (with clasp dentures – 67 %) to 64 % (with clasp dentures – 74 %), while the proportion of complete removable dentures decreased over this period by 6 %. Currently, with the increase in the number of elderly people, there is also an increase in patients with partial teeth loss, which increases the need for treatment.

Removable dentures, in addition to their advantages, have a number of disadvantages. More than 24 % of users of partial removable dentures complain of unsatisfactory fixation, 18 % of face aesthetic problems, more than 18 % are forced to adapt to poor-quality dentures, and 8 % face fractures of supporting teeth[1].

The impact of prosthetic materials on the immune system induces protective immune responses against pathogens and in many cases contributes to the pathogenesis and progression of diseases of the oral mucosa (OM). The resulting disruption of the homeostasis of the OM tissues causes periodontitis, one of the most common inflammatory diseases.

A large number of studies have been devoted to the study of the mechanisms of disturbance of homeostasis of monocytes and macrophages as the main cellular components of immunity in gingivitis and periodontitis [2]. Insufficient information on the impact of various base materials with different chemical natures used in dental prostheses on the local immunity of the oral mucosa in different periods after prosthetics emphasizes the importance of studying this issue and the need to develop recommendations for prosthetics with removable dentures based on the data obtained [3].

The influence of various materials used for the manufacture of removable dentures (acrylates, polyurethanes, thermoplastics) on the condition of the oral mucosa and periodontal tissue, as well as on local immune homeostasis, was studied. *The aim of the study* was to create a basis for pathogenetically substantiated selection of basic dental materials of various chemical nature in removable dentures using analysis of local immune homeostasis indicators of the oral mucosa.

MATERIAL AND METHODS

The study involved 154 people. They were divided into three experimental groups depending on the prosthesis material: acrylic, polyurethane, thermoplastic. By age, the participants were divided into groups according to G. Craig's classification of periods: middle adulthood – 40–59 years, late adulthood – 60 years. A control group was also selected, where prosthetics with a removable prosthesis was not required.

An assessment of the required sample size to confirm the statistical significance of the intergroup difference in the results of the effect of the prosthesis material on homeostasis parameters at a significance level

of $\alpha = 0.05$ and power of 0.80 for four groups showed that at least 16 people are required per group (Statistica 10.0).

The characteristics of the morphological substrate that supports cellular immunity of the oral mucosa were investigated when interacting with various materials of partial dentures, such as acrylic, polyurethane resins and thermoplastics. These materials can contribute to the occurrence of common inflammatory diseases such as chronic gingivitis and periodontitis.

Immunohistochemical analysis on paraffin sections was performed using standard methods for determining the phenotype of immunocompetent cells. Antigens on the surface of lymphocytes were identified using monoclonal antibodies that had similar binding properties and were distributed in tissues according to a certain stage of development of the cell population – the so-called clusters of differentiation (CD). CD molecules are membrane phenotypic markers of the corresponding cells.

The major immune cell populations of the oral mucosa include antigen-presenting cells such as monocytes / macrophages, dendritic cells, and epidermal Langerhans cells, as well as neutrophils and granulocytes. The presence of B cells is minimal, and the proportion of γδT cells is small – 12 %. Widespread $CD4^+$ clusters of differentiation characterize activated T helper cells – inducers of the immune response. They regulate the strength of the immune response to a foreign substance and control the stability of the internal state of the body (immune homeostasis). An increase in the number of T-helper lymphocytes indicates hyperactivity of the immune system, while a decrease indicates immunological deficiency [4].

$CD8^+$ – cytotoxic T-lymphocytes – T-killers and T-suppressors, $CD8^+$ also defines dendritic cells – leukocytes specializing in the presentation of antigens to T-lymphocytes, necessary for the activation of the T-cell response [5].

In this study, we classified different cell types, including T helper ($CD4^+$) and T suppressor ($CD8^+$) cells, which have a specific $CD4^+/CD8^+$ ratio. We also studied cell populations that express adhesion molecules such as integrins ($CD11^+/CD303^+$) on the surface of various cells including dendritic cells, monocytes, granulocytes, B and NK lymphocytes, the scavenger receptor $CD163^+$, and typed the scavenger receptor $CD204^+$, which is expressed on macrophages and some types of dendritic cells, as well as the Ki-67^+ protein in epithelial cells [6]. Comparison of three or more groups by a quantitative indicator whose distribution differed from normal was performed using the nonparametric Kruskal – Wallis test, multiple comparisons of two groups were performed using the Mann – Whitney U test with Bonferroni correction.

Statistical data processing was performed using Statistica 10.0, IBM SPSS Statistics 27.0 programs.

RESULTS AND DISCUSSION

Quantitative indices of macrophage CD markers were assessed for compliance with normal distribution using the Shapiro-Wilk test. It was shown that most of the data (about 70 %) had a non-normal

distribution, the probability of error was $p < 0.05$ (the achieved significance level was $p = 0.001$). Data with non-normal distribution are described using the median (*Me*) and the lower and upper quartiles (Q1–Q3); for normally distributed data, the mean value and 95 % confidence interval (CI) are indicated. The relationships between the prosthesis material and the patient's age group after 6 months of prostheses use are presented in Table 1.

The influence of the removable denture material factor on the absolute values of the phenotypic markers $CD68^+$, $CD4^+/CD8^+$, $CD11^+/CD303^+$, $CD204^+$, $CD163^+$, $Ki67^+$ (Kruskal – Wallis test, $p = 0.0001$) was proven; the data statistically significantly differ from the indicators of the control group (Mann – Whitney test, $p < 0.008$, Bonferroni correction) with the exception of the difference in the level of CD163, $CD11^+/303^+$, $Ki\text{-}67^+$ in the "60+" age group: *p polyurethane – control* = 0.169, which confirms an insignificant deviation from the norm when using polyurethane dentures.

Multiple pairwise comparisons in the age group 40–59 years confirm the statistical significance of differences in the levels of CD markers of immunocytes for different materials of removable dentures. In this case, in the group using orthopedic structures made of thermoplastic, the highest levels of all differentiation clusters $CD204^+$ are observed, lower in the groups with acrylic dentures and even lower in the group using polyurethane dentures (Mann – Whitney test, $p < 0.008$).

Table 1

Phenotypic markers indicators

Material	Age, years	Parameter		
		$CD68^+$	$CD4^+/CD8^+$	$CD11^+/CD303^+$
		Average (95 % CI)	*Me* ($Q_1 - Q_3$)	*Me* ($Q_1 - Q_3$)
Acryl	40–59	3.95 (3.77–4.13)	2.81 (2.60–3.04)	1.34 (1.20–1.41)
	60+	2.52 (2.41–2.63)	1.72 (1.43–1.92)	1.02 (0.98–1.18)
Thermoplast	40–59	6.52 (6.34–6.70)	3.21 (3.00–3.45)	1.62 (1.72–2.08)
	60+	3.46 (3.31–3.61)	2.10 (1.86–2.39)	1.17 (1.23–1.64)
Polyeurethane	40–59	3.19 (3.09–3.29)	2.26 (1.93–2.43)	1.25 (1.05–1.43)
	60+	1.69 (1.58–1.80)	1.63 (1.47–1.88)	0.99 (0.87–1.12)
Control	40–59	1.53 (1.35–1.71)	1.33 (1.17–1.89)	1.22 (1.01–1.41)
	60+	1.04 (0.88–1.20)	1.02 (0.81–1.14)	0.93 (0.79–1.05)
Material	Age, years	CD204+	CD163+	Ki67+
		Me ($Q_1 - Q_3$)	*Me* ($Q_1 - Q_3$)	*Me* ($Q_1 - Q_3$)
Acryl	40–59	3.04 (3.39–2.79)	2.95 (2.55–3.01)	8.67 (8.17–8.79)
	60+	2.23 (2.40–1.83)	2.23 (2.03–2.32)	7.24 (6.81–7.59)
Thermoplast	40–59	3.38 (3.57–3.15)	3.49 (3.26–3.76)	9.58 (9.36–9.93)
	60+	2.63 (2.44–2.89)	3.04 (2.86–3.67)	7.82 (7.45–8.13)
Polyeurethane	40–59	2.72 (2.58–2.98)	2.15 (1.93–2.60)	7.63 (7.44–7.74)
	60+	2.09 (1.88–2.44)	1.78 (1.53–2.43)	6.82 (6.49–7.12)
Control	40–59	1.69 (1.49–1.89)	1.86 (1.67–1.96)	6.75 (6.27–7.06)
	60+	1.40 (1.26–1.48)	1.64 (1.31–1.83)	6.37 (5.87–6.59)

In the age group "60+", the differences in the values of phenotypic markers for the materials "acrylic – polyurethane" are less pronounced, and the statistical significance of the differences was not confirmed: $CD11^+/CD303^+$ ($p_{acrylic - polyurethane} = 0.319$), which corresponds to the same level of reaction of dendritic cells, macrophages and Langerhans cells to these materials.

The distribution of $CD68^+$ in the groups 40–59 years and "60+" corresponds to the normal distribution (Shapiro-Wilk test, $p > 0.008$), the homogeneity of variances was confirmed (Levene's test, $p > 0.85$), the ANOVA analysis of variance showed the influence of the "prosthesis material" factor on the $CD68^+$ values, the Tukey post-hoc test proved the presence of statistically significant differences between all groups ($p < 0.0002$), with the exception of "acrylic – polyurethane" in both age groups (40–59: pacrylic – polyurethane = 0.219; "60+": pacrylic – polyurethane = 0.020).

The influence of the removable denture material on the level of phenotypic markers $CD68^+$, $CD4^+/CD8^+$, $CD11^+/CD303^+$, $CD204^+$, $CD163^+$, $Ki67^+$ was confirmed. The results are statistically significantly different from the control group data, with the exception of some markers in the 60+ age group. In particular, the levels of CD163, $CD11^+/CD303^+$ and $Ki\text{-}67^+$ when using polyurethane prostheses do not differ significantly from the norm. A high degree of imbalance and activation of the inflammatory immune response six months after implantation also leads to a significant increase in $CD4^+/CD8^+$: the ratio between helper and suppressor T-lymphocytes increased by 2.4 times for thermoplastics, 2 times for acrylic and 70 % for polyurethane. This indicates an imbalance between the mechanisms of inflammation and reparation, which corresponds to the transition to a chronic form of inflammation, the level of which is highest for thermoplastics, lower for acrylic and polyurethane.

The established statistically significant ratio of CD marker levels in biopsies of the mucous membrane of the prosthetic bed after 6 months of using prostheses made of different materials and the values of the control group are presented in Table 2.

Table 2

Ratio of CD marker levels to control levels

Material	Age, years	$CD4/CD8^+$	$CD163^+$	$CD68^+$	$CD11^+/303^+$	$CD204^+$	$Ki\text{-}67^+$
Acryl	40–59	2.11	1.40	2.58	1.10*	1.79	1.28
Thermoplast		2.41	1.92	4.34	1.32	2.00	1.42
Polyeurethane		1.69	1.15	2.08	1.02*	1.60	1.13
Acryl	60 and older	1.69	1.36	2.42	1.09	1.59	1.13
Thermoplast		2.06	1.85	3.32	1.25	1.87	1.23
Polyeurethane		1.53	1.09*	1.62	1.06*	1.49	1.08*

Note: * – differences with the data of the control group are not statistically significant.

Comparison of immune cell populations in the control group and patients using dentures based on different materials for 6 months shows a significant increase in inflammatory cells in biopsies, which corresponds to an active proinflammatory cellular response of gingival immunocytes to the effects of denture materials [7]. The prosthesis material has a significant effect on the level of $CD68^+$ protein, which is a marker for monocytes / macrophages. This protein is expressed on various cells, such as myeloid and dendritic cells, fibroblasts, neutrophils, osteoclasts and Langerhans cells. When using thermoplastics as a prosthesis material, the level of $CD68^+$ protein increases by 4.3 times, compared to other materials, such as acrylic and polyurethane. To determine the quantitative content of activated monocytes in biopsies of the prosthetic bed, the researchers use the scavenger receptor CD163. The expression level of this receptor also increases by more than 90 % when using thermoplastics, compared with the use of acrylic and polyurethane. The $CD163^+$ receptor triggers intracellular signals, including the secretion of interleukin-6 (IL-6), which acts as a proinflammatory cytokine during traumatic tissue injury and other damage leading to inflammation [8].

Analysis of absolute values and ratios of phenotypic markers shows that the number of proinflammatory macrophages, neutrophils, dendritic cells and Langerhans cells in biopsies of the prosthetic bed in patients using thermoplastics increases almost 6 times, compared with the data of the control group. In patients who use polyurethane and acrylic-based prostheses, this increase is 3–3.5 times.

The prosthesis material has a significant impact on the level of $CD68^+$ protein, which is a marker for monocytes / macrophages. This protein is expressed on various cells, such as myeloid and dendritic cells, fibroblasts, neutrophils, osteoclasts and Langerhans cells.

The high level of homeostasis disturbance and activation of the proinflammatory immune response 6 months after prosthetics also determines a significant increase in the $CD4^+/CD8^+$ level, corresponding to the ratio of T-lymphocytes helpers and suppressors, which increased by 2.4 times for thermoplastics, 2 times for acrylics and by 70 % for polyurethane. This indicates an imbalance between the mechanisms of inflammation and reparation and corresponds to the transition to a chronic form of inflammation, the level of which is maximum for thermoplastics, weaker for acrylic and polyurethane.

Changes in the heterogeneous population of $CD11^+/CD303^+$ markers are an indicator of the reaction of the cellular immunity of the oral mucosa to various prosthesis materials. Myeloid dendritic cells expressing the CD11c receptor specialize in the presentation of antigens to T lymphocytes. These cells demonstrate an increased ability to engulf necrotic cells, recognize viral antigens, and cross-present antigen with $CD8^+$ T cells. These cells exhibit an enhanced capacity to engulf necrotic cells, recognize viral antigens, and cross-present antigen with $CD8^+$ T cells. After cleavage from the membrane, the free (soluble) form can play

an anti-inflammatory role and serve as a diagnostic parameter for macrophage activation in inflammatory diseases. Plasmacytoid dendritic cells express exclusively the surface marker $CD303^+$ [9]. Analysis of the data in Table 2 shows an increase in the $CD11^+/CD303^+$ population by more than 30 % for thermoplastics, while for materials such as acrylic and polyurethane, the parameters do not differ significantly from the control group level.

Changes in the parameters of cellular immunity were accompanied by an increase in the Ki-67 protein of the epithelial cells of the gingival mucosa by 42 % for the group where the dentures were made of thermoplastics, 28 and 13 % for the group using acrylic and polyurethane dentures. Thus, polyurethane dentures are characterized by a long-term inflammatory process, manifested by a high level of proliferative activity of cells in the biopsy samples of the gingival bed. For patients aged 60 years and older, after 6 months, inflammation is active under the polyurethane prosthesis, the deviation of the cell proliferation level from the norm is 23 %.

In the group of patients aged 60 years and older, an increase in all parameters of cellular immunity was also noted: the highest for the thermoplastic group, average for acrylics and lower for polyurethanes. The data are also an indicator of the activation of the immune system, given that with increasing age, deviations from the norm decrease and this is associated with a decrease in the body's reactivity.

A significant difference in the obtained indicators of phenotypic markers from the norm is a sign of activation of the T-system of the oral mucosa immunity; the objective of the study is to compare the changes identified in the oral mucosa immune system with the clinical manifestations of the influence of the material – chronic periodontitis, gingivitis.

These indicators of cellular immunity correlate with clinical manifestations in the oral cavity, in particular such as hyperemia, swelling and exacerbation of inflammatory phenomena. All patients underwent the Schiller-Pisarev test to determine the fact of the inflammatory process.

Six months after prosthetics, a high level of imbalance in the body and activation of the immune system, which promotes inflammation, was recorded. The $CD4^+/CD8^+$ level (the ratio of T-lymphocytes helpers and suppressors) increased significantly for all three types of prosthesis materials, but the greatest increase was in thermoplastic prostheses (2.4 times), then in acrylic (2 times) and by 70 % in polyurethane. This indicates an imbalance between the mechanisms of inflammation and reparation, which can lead to a chronic form of inflammation. The level of inflammation was highest for thermoplastic prostheses, less pronounced for materials such as acrylic and polyurethane.

Multifield contingency tables (IBM SPSS Statistics 27.0) were used to assess the strength of the relationship between nominal variables. The material of the removable denture in the table is considered as a risk factor for the development of prosthetic complications in the form of chronic gingivitis, mild, moderate and severe periodontitis. Data on the diagnosis of oral mucosal tissue diseases were analyzed in the SPSS

Statistics system in order to identify a statistical relationship between the material of the removable denture and the severity, prevalence in the group, and stage of the disease. Table 3 presents data on the total number of patients (n = 154), in groups and by severity of the recorded disease (mild periodontitis, moderate periodontitis, severe periodontitis).

The analysis of contingency tables showed a high degree of relationship between the factor of influence of the material and the signs of chronic gingivitis, periodontitis of mild, moderate and severe severity: Pearson criterion – 56.7 ($p < 0.01$), Cramer's V criterion for multi-field tables – 0.458, contingency coefficient – 0.622 ($p < 0.001$) – corresponds to a strong relationship (Figure).

Table 3

Contingency table "Prosthesis material – diagnosis"

Material		No	Gingivitis	Mild periodontitis	Moderate periodontitis	Severe periodontitis	Total
Control	Quantity	31	5	0	0	0	36
	% in orthopedic structure	86.1	13.9	0.0	0.0	0.0	100
Polyeurethane	Quantity	6	21	9	2	0	38
	% in orthopedic structure	15.8	55.3	23.7	5.3	0.0	100
Acryl	Quantity	4	21	13	3	0	41
	% in orthopedic structure	9.8	51.2	31.7	7.3	0.0	100
Thermoplast	Quantity	2	12	15	9	1	39
	% in orthopedic structure	5.1	30.8	38.5	23.1	2.6	100
Total	Quantity	43	59	37	14	1	154
	% in orthopedic structure	27.9	38.3	24.0	9.1	0.6	100

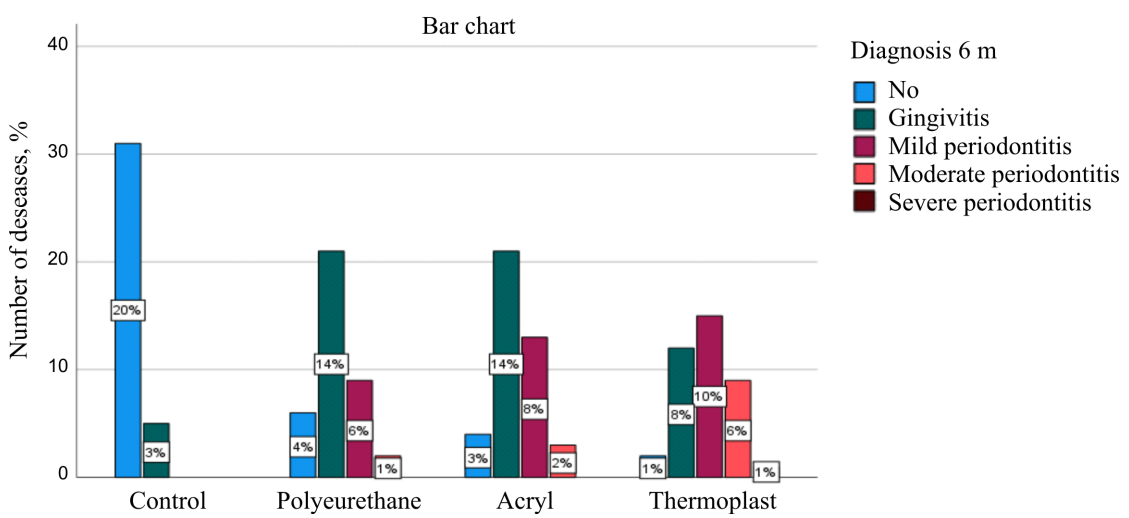

Fig. Distribution of patients with recorded diagnoses after 6 months in groups using different removable denture materials

The distribution of the severity of complications among patients using removable dentures depends significantly on the material of the orthopedic structure: in the control group, after 6 months, the occurrence of gingivitis is recorded in 13.9 %, in the group using polyurethane plastics – 84.2 %, of which 23.7 % were mild periodontitis and 5.3 % were moderate periodontitis, in the group using acrylic plastics – 90.2 %, of which 31.7 % were mild periodontitis and 7.3 % were moderate periodontitis, the largest number of patients with a diagnosis of periodontitis – 64.2 %, of which 23.1 % were moderate periodontitis and 2.6 % were severe periodontitis in the group using thermoplastic dentures. Data on the prevalence of complications in the form of gingivitis and periodontitis in groups with different materials for the bases of removable dentures correlate well with the results of the Schiller – Pisarev test, Spearman correlation coefficient $\rho = 0.84$.

Let us determine the quantitative values of phenotypic CD markers corresponding to clinical manifestations in the form of gingivitis and periodontitis. Patients in each age group were divided into three groups: without complications, complications in the form of gingivitis. Patients with complications of prosthetics in the form of periodontitis of mild, moderate and severe severity were combined into the third group to determine the average parameters of local cellular immunity.

The data presented in Table 4 show that in periodontitis, the median values of differentiation clusters are significantly higher: thus, the values for the $CD68^+$ marker in periodontitis are 2 times higher than in gingivitis, and exceed the norm by almost 4.3 times.

The severity and prevalence of gingivitis and periodontitis in abutment teeth due to the influence of the prosthesis material depend on the interaction between the microbial triggers and the host immune system, a process in which monocytes and macrophages play an important role. Macrophages can be phenotypically classified into the M1 phenotype, which promotes the proinflammatory phase of the immune response, while M2 macrophages promote the healing and resolution phase [10].

Analysis of the $CD4^+/CD8^+$ ratio, which characterizes the ratio of T-helpers and T-suppressors, on average for the age group of 40–59 years, revealed that the state of the immune system for the norm is normoergic, for the diagnosis of gingivitis – 2.6 on the

Table 4

Quantitative values of CD markers of immunocytes in gingiva of prosthetic bed of patients with clinical manifestations

Parameter	Age, years	$CD163^+$	$CD204^+$	$CD4^+/CD8^+$	$CD11^+/CD303^+$	$CD68^+$	Ki67
Norm	40–59	1.82	1.70	1.36	1.38	1.52	6.45
	60+	1.60	1.52	1.10	1.27	1.03	6.14
Gingivitis	40–59	2.19	2.67	1.78	2.29	3.22	7.53
	60+	1.78	2.27	1.59	1.90	1.71	6.98
Periodontitis	40–59	3.10	3.56	2.36	3.32	6.54	9.62
	60+	2.97	2.92	1.83	3.20	3.57	7.87

border of normoergic and hyperactive, which corresponds to an adequate reaction of the oral mucosa, while for the diagnosis of periodontitis with complications – 3.5, which corresponds to a hyperactive reaction.

The dependence of CD marker levels (in patients diagnosed with moderate and severe periodontitis) on the material of the removable denture was studied. The data of median values of the indices of differentiation clusters of immunocytes of the gingival prosthetic bed of patients for both age groups with a diagnosis of chronic periodontitis, using removable dentures made of different materials for 6 months, are presented in Table 5, the statistical significance of the differences was tested by a nonparametric median test ($p < 0.05$).

Table 5 shows the change in immune cell populations in groups of patients using removable dentures based on different materials and diagnosed with chronic periodontitis after 6 months.

In periodontitis, $CD11^+$ receptors and dendritic cells are of great importance [11]. In Table 5, the $CD11^+$ values for acrylic coincide with the control ones, for polyurethane they are slightly lower than the control values, for thermoplastics they are 29 % higher in the 40–59-year old group, and 33 % higher in the 60 year and older group, which explains the largest number of patients diagnosed with periodontitis in these groups.

The $CD4^+/CD8^+$ ratio analysis in the 40–59 age group allows us to assess the state of the immune system. Normally, this ratio is normoergic. For the diagnosis of gingivitis, the value is 2.6, which is on the border between the normoergic and hyperactive state and indicates an adequate response of the body's system to inflammation. However, for the diagnosis of periodontitis with complications, the value is 3.5, which corresponds to a hyperactive response of the immune system.

The data in Table 5 show that the $CD4^+/CD8^+$ ratio is 16 % higher when using thermoplastics as the base material compared to when using acrylates, suggesting that this is due to a reduction in the number of $CD8^+$ T cells. This corresponds to an increase in the content of M1 macrophages and a decrease in the content of M2 macrophages in the gingival tissues affected by periodontitis and may reflect a change in cellular immunity towards a pro-inflammatory phenotype – an increase in the level of pro-inflammatory factors and

Table 5

CD marker values in patients diagnosed with periodontitis

Parameter	Age, years	$CD163^+$	$CD204^+$	$CD4^+/CD8^+$	$CD11^+/CD303^+$	$CD68^+$	Ki67
Acryl	40–59	2.98	2.87	2.88	1.38	4.06	8.75
	60+	2.27	2.43	1.84	1.06	2.55	7.35
Thermoplast	40–59	3.51	3.47	3.34	1.78	6.65	9.64
	60+	3.21	2.79	2.25	1.41	3.56	7.92
Polyeurethane	40–59	2.59	2.78	2.38	1.27	3.24	7.68
	60+	2.02	2.17	1.70	1.02	1.79	7.03
Control	40–59	1.62	1.70	1.36	1.38	1.24	6.80
	60+	1.30	1.42	1.10	1.07	2.91	6.44

suppression of the anti-inflammatory factor in circulating monocytes. The obtained data are consistent with the results of a study indicating that the M1/M2 macrophage ratio is significantly higher in affected periodontium, indicating an imbalance between inflammation and reparation mechanisms [12].

For patients using thermoplastic-based prostheses, elevated levels of the $CD4^+/CD8^+$ glycoprotein ratio, which are localized on the surface of T-lymphocytes, are observed. The ratio between T-helpers and T-suppressors is more than 3, which exceeds the hyperactivity threshold – 2.4 times, compared with the normal (control) value; when using acrylate materials as the base material, this excess is 2.2 times, and for polyurethane – 1.9 times. The level of $CD4^+$ T cells, which react to pathogens and trigger an immune response, is higher than the control sample; $CD8^+$ T cells react and neutralize the infection; T suppressor cells "switch off" CD4 activity when the immune response is sufficient. An increase in the Ki67 antigen level indicates activation of proliferation processes and promotes cell regeneration and the formation of connective tissue in the inflammation site [13].

Moreover, the change in the population of the main immune cells in patients with moderate and severe periodontitis using acrylic dentures, compared to the norm, is more than 10, which indicates the activation of immunocytes associated with the base material of the removable denture.

The $CD68^+$ antigen is active on various cells, such as blood monocytes, tissue macrophages, lymphocytes, fibroblasts and endothelial cells. When using thermoplastics, its level increases by 68 % compared to acrylics and exceeds the norm by more than 5 times, and when using polyurethane, its level exceeds the norm by 2.5 times.

The most significant deviation of the parameters of local immune homeostasis of the oral mucosa from the parameters of the control group was observed when using thermoplastic materials, while less significant changes in the parameters of local cellular immunity of the oral mucosa were noted when using acrylic base materials.

The control group included patients without periodontal tissue pathologies; in the experimental groups, the condition of the soft tissues in the area of the prosthetic bed and contact with the teeth was assessed before and after prosthetics after 6 months. Based on statistical analysis of the obtained data, a strong relationship was found between the material of the removable denture and changes in the parameters of cellular immunity, signs and severity of inflammation. In particular, when examining patients, the majority of them had hyperemic and edematous mucous membranes of the lips and cheeks after prosthetics. In the group where thermoplastic prosthetics were performed, a positive Schiller-Pisarev test was detected in 90.43 % of cases in the 40–59-year-old group and in 98.57 % in the 60-year-old and older group, and correlated with the proliferative activity index values. The lowest number of patients with a positive test was detected in the group where polyurethane-based prostheses were used, which correlates with the lowest proliferation index values in the experimental groups.

The severity of periodontal diseases also correlated with the increase in the indices of

local cellular immunity of the oral mucosa. It can be noted that in percentage terms within the studied groups, the highest prevalence of gingivitis and periodontitis was also in the groups where prosthetics were performed with thermoplastic prostheses, and the lowest – in the groups where polyurethane base materials were used. These data correlate with the increase in local cellular immunity indices, which were also maximum in the group with thermoplastics and minimum in the group with polyurethane prostheses. Thus, it can be concluded that changes in the parameters of local cellular immunity directly affect the condition of the mucous membrane of the prosthetic bed, as well as the clinical manifestations of inflammation and the degree of damage to periodontal tissues, causing the presence of inflammatory symptoms and signs detected by the main and additional examination methods.

Conclusions

1. Immune homeostasis was studied in patients with partial and complete secondary adentia before the start of prosthetics. The data obtained from the study indicate that significant changes in the parameters of the immune balance of the oral mucosa occur at the age of patients from 40 to 59 years due to increased activity of the body.

2. The use of removable dentures leads to a change in the local homeostasis of the oral mucosa. Changes in the parameters of local immune homeostasis of the oral mucosa when using dentures based on thermoplastics, acrylic and polyurethane plastics have significant differences.

3. Changes in the indicators of local homeostasis of the oral mucosa directly correlate with clinical manifestations in the area of the prosthetic bed and periodontal tissues, which is characterized by the appearance of inflammatory changes in the mucous membrane, such as hyperemia and edema, a positive Schiller-Pisarev test, as well as the severity of the disease of the periodontal tissues.

4. Changes in the morphological and clinical parameters of the oral mucosa when using polyurethane-based prostheses are minimal in relation to the parameters of the control group, which allows us to recommend the use of polyurethane prostheses as immediate prostheses at the healing stage during surgical interventions in the oral cavity, in particular tooth extraction and implantation, as well as permanent ones – for patients with allergic intolerance to dental materials, especially with allergic reactions to polymer compounds and dyes.

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