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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

CLINICAL AND IMMUNOLOGICAL FEATURES OF THE COURSE OF INFLAMMATORY PERIODONTAL DISEASES IN ALLERGIC PATHOLOGY AND THE RATIONALE FOR PATHOGENETIC THERAPY

Specialty: 3226.01 – Dentistry

Field of science: Medical sciences

Applicant: **Saida Rahib Abdullayeva**

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The work was performed at the Department of Therapeutic Dentistry of the Azerbaijan Medical University.

Scientific supervisor: Doctor of Medical Sciences, Professor
Rizvan Movsum Mammadov

Scientific consultant: Doctor of Medical Sciences, Professor
Jabrail Teymur Mammadov

Official opponents: Doctor of Medical Sciences, Associate Professor
Ramida Vagif Shadlinskaya

Doctor of Medical Sciences, Associate Professor
Ziba Vagif Gasimova

Doctor of Philosophy in Medical Sciences
Togrul Gulhuseyn Abdullayev

Dissertation Council FD 2.53 of the Supreme Attestation Commission under the President of the Republic of Azerbaijan operating at the A. Aliyev Azerbaijan State Advanced Training Institute for Doctors

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GENERAL CHARACTERISTICS OF THE WORK

Relevance of the study Chronic generalized periodontitis (CGP) occupies a leading position in the structure of inflammatory diseases of the oral cavity and represents one of the key problems in modern dentistry due to its high prevalence, progressive course, and significant risk of tooth loss[1,2,3].

According to the World Health Organization, oral diseases affect more than 3.5 billion people, with severe forms of periodontitis diagnosed in approximately 19% of the adult population, underscoring the scale and medico-social significance of this pathology.

At the present stage, CGP is regarded not as an isolated local infectious-inflammatory process, but as a multifactorial immunoinflammatory disease resulting from complex interactions between microbial biofilm and the immune mechanisms of the macroorganism. Its pathogenesis involves disturbances in innate and adaptive immunity, cytokine dysregulation, genetically determined features of the inflammatory response, and systemic immunoinflammatory changes that determine the severity, clinical course, and progression of the disease[4,5,6].

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[1] Nazir M.A., Al-Ansari A., Al-Khalifa K.S., et al. Global prevalence of periodontal disease // Scientific World Journal. 2020. Article 2146160.

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[5] Neurath M.F., Finotto S. Cytokines in gingivitis and periodontitis: current roles in pathogenesis and therapy // *Frontiers in Immunology*. — 2024. — Vol. 15. — Article 1435054. DOI: 10.3389/fimmu.2024.1435054

[6] Neurath M.F., Finotto S. Cytokines in gingivitis and periodontitis // *Frontiers in Immunology*. — 2024. — Vol. 15. — Article 1348779. DOI: 10.3389/fimmu.2024.1348779.

In recent years, particular importance has been attached to studying the relationship between chronic generalized periodontitis and systemic diseases, given its ability to reflect and modify the overall immunoinflammatory status of the body. CGP has been shown to be associated with various somatic pathologies, including cardiovascular diseases, diabetes mellitus, and metabolic disorders, confirming its systemic nature[7,8].

At the same time, the interaction between CGP and allergic pathology has been much less studied. Despite some research on bronchial asthma, allergic rhinitis, and atopic dermatitis, the relationship between chronic generalized periodontitis and food allergy remains virtually unexplored[9,10].

The insufficient study of the immunopathogenetic mechanisms of the combined course of chronic generalized periodontitis and food allergy, along with the limited number of comprehensive clinical-immunological studies, underscores the need for in-depth analysis of local and systemic components of the immune response in this patient category.

Of particular relevance is the study of oral fluid as a non-invasive biological substrate that reflects the state of local immune homeostasis in the oral cavity and is directly related to the condition of periodontal tissues. Analysis of cytokine levels and secretory immunoglobulin A allows assessment of the characteristics of mucosal immunity in chronic inflammation.

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[7] Martinez-Garcia M., Hernandez-Lemus E. The molecular comorbidity network of periodontal disease // International Journal of Molecular Sciences. 2024. Vol. 25, No 18. Article 10161.

[8] Simpson T.C., Weldon J.C., Worthington H.V., et al. Treatment of periodontal disease for glycemic control in diabetes mellitus // Cochrane Database of Systematic Reviews. 2015. Issue 11. CD004714.

[9] Sakonidou E., Manousakis E., Paliatsos A., et al. Evaluation of salivary cytokines (IL-4, IL-6, IL-10, TNF-α) in children with food allergy and atopic conditions // *Allergy and Asthma Proceedings*. — 2023. — Vol. 44, No. 2. — P. 127–134. DOI: 10.2500/aap.2023.44.220052.

[10] Nagler C.R., Rachid R., Smith T.J., et al. Immune regulation and disruption in food allergy: tolerance mechanisms and pro-inflammatory pathways // *Immunological Reviews*. — 2024. — Vol. 309, No. 1. — P. 87–102. DOI: 10.1111/imr.13397.

Thus, a comprehensive study of the relationship between immunological parameters and clinical manifestations of chronic generalized periodontitis in patients with food allergy constitutes a relevant scientific task and provides the foundation for developing pathogenetically substantiated approaches to diagnosis and treatment.

The aim of the study: To evaluate the associations between cytokine levels in oral fluid and blood serum (IL-1β, IL-2, IL-4, IL-6) and clinical indicators of chronic generalized periodontitis in patients with food allergy.

The study objectives:

1. To determine the levels of cytokines IL-1β, IL-2, IL-4, and IL-6 in the blood serum of patients with chronic generalized periodontitis and concomitant food allergy.
2. To determine the levels of cytokines IL-1β, IL-2, IL-4, and IL-6 in the oral fluid of patients with chronic generalized periodontitis and concomitant food allergy.
3. To determine the levels of total IgE in blood serum and sIgA in oral fluid, and to evaluate their influence on the immune response in patients with chronic generalized periodontitis of varying severity and concomitant food allergy.
4. To analyze the cytokine profile in different biological fluids (oral fluid and blood serum) in patients with chronic generalized periodontitis and food allergy in order to identify pathogenetically significant immunological changes.
5. To substantiate a pathogenetically oriented approach to the diagnosis and treatment of patients with chronic generalized periodontitis and concomitant food allergy.

Research methods:

- clinical and periodontal examination
- immunological investigations
- allergological investigations
- statistical processing of the obtained data

Main provisions submitted for defense

- In patients with chronic generalized periodontitis accompanied by food allergy, the inflammatory process is characterized by higher clinical activity, manifested by increased periodontal pocket depth,

intensified gingival bleeding, and progression of destructive processes, largely than in patients without an allergic background.

- The presence of food allergy in patients with chronic generalized periodontitis is accompanied by changes in the immune system, characterized by elevated total IgE in blood serum, a shift in the cytokine balance toward a Th2-dominant profile, and increased concentrations of IL-4 and IL-6.

- In patients with chronic generalized periodontitis accompanied by food allergy, pronounced changes in the cytokine profile are observed in oral fluid, characterized by elevated levels of pro-inflammatory cytokines IL-1β, IL-6, and disruption of regulatory immune response mechanisms, reflecting the activity of the local inflammatory process in periodontal tissues.

- Decreased concentration of secretory immunoglobulin A in oral fluid in patients with chronic periodontitis accompanied by food allergy indicates impairment of local mucosal immunity, weakening of the barrier function of the oral mucosa, and creation of conditions for persistence of the inflammatory process.

- Comprehensive assessment of clinical periodontal indicators and immunological markers (IL-1β, IL-2, IL-4, IL-6, IgE, sIgA) demonstrates that they are pathogenetically significant markers of activity and progression of chronic generalized periodontitis modified by an allergic background.

- A pathogenetically substantiated algorithm for laboratory examination of patients with chronic generalized periodontitis accompanied by food allergy has been developed; it expands diagnostic capabilities and promotes the implementation of a personalized approach to treatment in this patient category.

Scientific novelty of the research

- A comprehensive clinical and immunological study was conducted in patients with mild and moderate chronic generalized periodontitis combined with food allergy, including assessment of dental status, total immunoglobulin E levels, and the profile of pro- and anti-inflammatory cytokines.

- A comparative analysis of the levels of pro- and anti-inflammatory cytokines in peripheral blood and oral fluid was

performed in patients with chronic generalized periodontitis with and without food allergy.

- It was established that the combination of chronic generalized periodontitis with food allergy is associated with more pronounced alterations in the cytokine profile, characterized by increased levels of pro-inflammatory mediators and imbalance between pro- and anti-inflammatory cytokines.

- The diagnostic significance of changes in cytokine levels in peripheral blood and oral fluid was demonstrated; these indicators may be considered informative immunological markers of the severity of the inflammatory process in periodontal tissues.

- Correlations were identified between total IgE levels, indicators of allergic sensitization, and clinical indices of periodontal tissue inflammation, confirming the role of the allergic component in the pathogenesis of chronic periodontitis.

- The effectiveness of including the antihistamine drug cetirizine in the комплексive therapy of patients with chronic generalized periodontitis and food allergy was scientifically substantiated, which was accompanied by improvement of clinical periodontal parameters and normalization of immunological indicators.

- The obtained results expand current concepts regarding the pathogenesis of chronic generalized periodontitis as a systemic immunoinflammatory disease, the course of which is significantly modified by the presence of allergic pathology.

- It was proven that food allergy acts not merely as an incidental concomitant condition, but as a significant pathogenetic factor influencing the direction of the immune response, the severity of inflammatory and destructive changes in periodontal tissues, and the resistance of the disease to standard therapeutic interventions.

- The role of cytokines IL-1β, IL-2, IL-4, IL-6, total IgE, and secretory immunoglobulin A in the development and maintenance of chronic periodontal inflammation under conditions of allergic sensitization was theoretically substantiated.

- It was shown that a comprehensive analysis of immunological indicators in oral fluid combined with serum data provides an integrated understanding of the nature of the immune response and the

direction of the inflammatory process, which is of considerable importance for understanding the mechanisms underlying the comorbid course of chronic generalized periodontitis and food allergy.

Practical significance

1. The expediency of a comprehensive assessment of the immunological status of patients with chronic generalized periodontitis was demonstrated, including determination of the levels of cytokines IL-1β, IL-2, IL-4, IL-6, total IgE in blood serum, and sIgA in oral fluid.

2. A pathogenetically substantiated algorithm for laboratory examination was developed, enabling the identification of immune and allergic factors modifying the course of chronic generalized periodontitis and allowing the obtained data to be used for the individualization of therapeutic strategies.

3. The necessity of taking allergological status into account when selecting therapeutic approaches was substantiated, which contributes to increased treatment effectiveness and reduction in the frequency of recurrences of the inflammatory process.

4. The obtained results may be used in the development of personalized diagnostic and treatment algorithms aimed at optimizing the management of patients with chronic generalized periodontitis combined with food allergy.

Aprobation of the study results

The main provisions and results of the dissertation were presented and discussed at national and international scientific and practical conferences devoted to current issues in dentistry, allergology, immunology, and interdisciplinary aspects of medicine, including the Ə. Əliyev Scientific and Practical Conference (Baku, 2022); the International Scientific and Practical Conference “Science of the 21st Century: Challenges, Formation, Development” (Petrozavodsk, 2023); the A. Aliyev Scientific and Practical Conference (Baku, 2024); and the International Scientific and Practical Conference “Modern Medicine: New Approaches and Current Research” (Moscow, 2025).

The dissertation materials were discussed at the extended meeting of the Department of Therapeutic Dentistry (07.07.2025,

Protocol No. 9), at the scientific seminar operating under Dissertation Council ED 2.50 of Azerbaijan Medical University (31.10.2025, Protocol No. 15), and at the scientific seminar operating under Dissertation Council FD 2.53 of the A. Aliyev Azerbaijan State Advanced Training Institute for Doctors (12.05.2026, Protocol No. 1).

Application of the research results to practice

The results of the dissertation have been implemented into the clinical practice of the Department of Therapeutic Dentistry of Azerbaijan Medical University and the World Med Dental Clinic.

The obtained data are used in the diagnosis, assessment of severity, and comprehensive examination of patients with inflammatory periodontal diseases, including chronic generalized periodontitis associated with food allergy.

The developed clinical and immunological approaches are applied in patient assessment using cytokine profile parameters and total IgE indicators, contributing to improved diagnostic efficacy and the individualization of therapeutic strategies.

Practical recommendations developed on the basis of the study results have been introduced into the treatment process and are used in selecting комплекс therapy for patients with chronic generalized periodontitis associated with allergic pathology, including the use of Cetirizine as part of pathogenetically substantiated treatment.

The study materials are also used in the educational process at the Department of Therapeutic Dentistry of Azerbaijan Medical University in the training of students, interns, and clinical residents.

Study Setting. The research work was carried out at the Dental Clinic of the Azerbaijan Medical University, as well as at the World Med Dental Clinic.

Place of the study. The research work was carried out at the Dental Clinic of the Azerbaijan Medical University, as well as at the "World Med" Dental Clinic in Baku.

Publications. A total of 13 scientific papers on the topic of the dissertation were published in journals and proceedings recommended by the Higher Attestation Commission under the President of the Republic of Azerbaijan, including 9 articles and 4 abstracts. Among

them, 1 article was published in a journal indexed in the international Scopus database, 2 articles were published in foreign peer-reviewed scientific journals, and 2 abstracts were published abroad.

Volume and structure of the dissertation. The dissertation is presented on 178 pages of typewritten text (196303 characters) and consists of an introduction (14701 characters), a literature review (31613 characters), materials and methods of the study (26631 characters), three chapters of original research results and their discussion (99653 characters), conclusions, findings, and practical recommendations (23705 characters), a list of references, and appendices.

The work is illustrated with 22 figures and contains 21 tables. The list of references includes 170 sources, among them 134 publications by foreign authors reflecting the current state of research on the studied problem.

MATERIALS AND METHODS OF THE STUDY

The present study was carried out in 2019–2022 and had a comprehensive clinical and immunological design. The study included examination of patients with mild and moderate chronic generalized periodontitis (CGP), occurring both as an isolated condition and in combination with IgE-mediated food allergy.

Patient selection and clinical dental examination were conducted at the clinical base of the Department of Therapeutic Dentistry of the Azerbaijan Medical University, as well as at the “World Med” Dental Clinic.Immunological investigations were performed at the Department of Immunology of the Azerbaijan Medical University during 2019–2021. Identification of patients with food allergy, allergological examination, and diagnosis were carried out at the Department of Allergology and Immunology of the Azerbaijan Medical University. Depending on the presence of concomitant allergic pathology, the patients were divided into three groups: the main group — 56 patients with CGP combined with food allergy (mean age 29.3 ± 1.25 years); the comparison group — 66 patients with CGP without allergic pathology (33.1 ± 3.5 years); and the control group — 30 practically healthy individuals (25.8 ± 1.7 years).

The distribution of the examined patients by sex and age is presented in Table 1.

Table 1

Characteristics of the examined patients by sex and age

Indicator	Main group (CGP + FA), n = 56	Comparison group (CGP), n = 66	Control group, n = 30	p
Age, years (M ± m)	29.3 ± 1.25	33.1 ± 3.5	25.8 ± 1.7	p > 0.05
Men, n (%)	24 (42.9%)	30 (45.5%)	14 (46.7%)	p > 0.05
Women, n (%)	32 (57.1%)	36 (54.5%)	16 (53.3%)	p > 0.05

Note: No statistically significant differences in age or sex were identified between the examined groups (p > 0.05).

The obtained data indicate the comparability of the examined groups in terms of age and sex. No statistically significant differences between the groups were identified with regard to age composition or sex distribution (p > 0.05), which allows the formed samples to be considered homogeneous and makes it possible to correctly interpret the subsequently identified clinical and immunological differences as being обусловлены the characteristics of the disease course and the presence of concomitant food allergy.

The groups were formed according to inclusion and exclusion criteria. The study included patients aged 18 to 55 years with mild and moderate chronic generalized periodontitis in the presence or absence of food allergy. Patients with severe forms of CGP, systemic autoimmune diseases, diabetes mellitus, as well as pregnant and lactating women were excluded from the study.

Additionally, individuals who had received immunomodulatory, glucocorticosteroid, or antihistamine therapy less than 4 weeks before the beginning of the study were excluded.

Clinical periodontal examination was carried out according to a unified protocol using the PMA and PBI indices, periodontal pocket depth (PPD), clinical attachment loss (CAL), as well as the DMFT and OHI-S indices. Allergological examination included medical history

assessment, clinical evaluation, and laboratory confirmation of IgE-mediated sensitization.

The immunological study was performed using blood serum and oral fluid samples. The levels of cytokines IL-1β, IL-2, IL-4, and IL-6, total IgE in blood serum, as well as secretory immunoglobulin A (sIgA) in oral fluid were determined. Blood samples were collected on an empty stomach, while oral fluid samples were collected in the morning before food intake and oral hygiene procedures. The parameters were determined using the enzyme-linked immunosorbent assay (ELISA) method with certified test kits.

The study was conducted in accordance with the international ethical standards set forth in the Declaration of Helsinki of the World Medical Association. The study protocol was approved by the local ethics committee. All patients were informed about the aims and methods of the study and signed written informed consent forms.

Statistical analysis of the results was performed using IBM SPSS Statistics software (Version 25.0, IBM, USA). At the first stage, descriptive statistics were carried out. The normality of quantitative data distribution was assessed using the Shapiro–Wilk test.

With normal distribution, the results were presented as mean values and standard error of the mean ($M \pm m$). Parametric methods were used for intergroup comparisons, including Student's t-test for independent samples and one-way analysis of variance (ANOVA) when comparing more than two groups.

When the distribution deviated from normality, the data were presented as median and interquartile range (Me [Q1–Q3]). Nonparametric methods, including the Mann–Whitney U test, were used for analysis. Qualitative variables were analyzed using Pearson's χ^2 test or Fisher's exact test. Correlation analysis was performed using Spearman's rank correlation coefficient. Differences were considered statistically significant at $p < 0.05$.

RESULTS OF THE STUDY AND THEIR DISCUSSION

This section presents the results of the clinical and dental examination of patients with mild and moderate chronic generalized

periodontitis. The patients were divided into groups depending on the presence or absence of concomitant allergic pathology.

Clinical examination of patients with chronic generalized periodontitis revealed gingival bleeding, edema and hyperemia of the marginal gingiva, the presence of supra- and subgingival dental deposits, and deepening of periodontal pockets. In patients of the main group, these manifestations were more pronounced and widespread.

Comparative analysis of the clinical course of chronic generalized periodontitis demonstrated that the presence of concomitant food allergy aggravates the severity of the inflammatory process in periodontal tissues. Patients of the main group showed higher values of clinical periodontal indices reflecting the intensity of inflammation and the degree of destructive changes. More pronounced gingival bleeding, increased periodontal pocket depth, and more frequent episodes of disease exacerbation were observed. The chronic inflammatory process in patients with food allergy was characterized by diffuse periodontal tissue involvement and less pronounced clinical remission, indicating the influence of systemic immunoinflammatory mechanisms on the local course of the disease.

Analysis of immunological parameters revealed significant differences between the examined groups of patients. In patients with chronic generalized periodontitis combined with food allergy, an increased level of total IgE in blood serum was detected, reflecting systemic allergic sensitization and a Th2-mediated immune response.

At the same time, patients of the main group demonstrated a decrease in the concentration of secretory immunoglobulin A (sIgA) in oral fluid to 112.5 ± 8.7 mg/L compared with the comparison group (156.3 ± 10.2 mg/L) and the control group (198.4 ± 12.1 mg/L), indicating impairment of local mucosal immunity.

In patients of the comparison group, changes in IgE levels were less pronounced, while sIgA values remained relatively stable (156.3 ± 10.2 mg/L), indicating less severe immune disturbances in the absence of an allergic background. The results of the study of cytokines and local immunity parameters in the examined groups are presented in Table 2.

Table 2

Immunological parameters in blood serum and oral fluid (M ± m)

Parameter	Biological medium	Main group (CGP + FA)	Comparison group (CGP)	Control group	p
IL-4, pg/mL	Blood serum	8.4 ± 0.6	4.2 ± 0.4	2.1 ± 0.3	p<0.05
IL-6, pg/mL	Blood serum	12.7 ± 0.9	7.3 ± 0.6	3.5 ± 0.4	p<0.05
sIgA, mg/L	Oral fluid	112.5 ± 8.7	156.3 ± 10.2	198.4 ± 12.1	p<0.05

Note: The differences between the main group, the comparison group, and the control group were statistically significant ($p < 0.05$).

Analysis of immunological parameters revealed statistically significant differences between the examined groups. Patients with chronic generalized periodontitis combined with food allergy demonstrated increased levels of IL-4 and IL-6 in blood serum compared with the comparison and control groups.

The concentration of IL-4 in patients of the main group was 8.4 ± 0.6 pg/mL, whereas in the comparison group this parameter was 4.2 ± 0.4 pg/mL and in the control group 2.1 ± 0.3 pg/mL ($p < 0.05$). The increased level of IL-4 indicates a shift of the immune response toward a Th2-dominant profile and activation of allergy-mediated inflammatory mechanisms.

The level of IL-6 in blood serum in patients of the main group reached 12.7 ± 0.9 pg/mL, which significantly exceeded the values of the comparison group (7.3 ± 0.6 pg/mL) and the control group (3.5 ± 0.4 pg/mL) ($p < 0.05$). Elevated IL-6 concentration reflects high inflammatory activity in periodontal tissues.

Simultaneously, patients of the main group demonstrated a decrease in the concentration of secretory immunoglobulin A in oral fluid to 112.5 ± 8.7 mg/L compared with the comparison group (156.3 ± 10.2 mg/L) and the control group (198.4 ± 12.1 mg/L) ($p < 0.05$). Reduced sIgA levels indicate impairment of local mucosal immunity and weakening of the barrier function of the oral mucosa.

In the comparison group, changes in immunological parameters were less pronounced, whereas the values of the control group

corresponded to physiological norms. The obtained data confirm the presence of more pronounced immunoinflammatory disturbances in patients with chronic generalized periodontitis in the presence of concomitant food allergy.

The performed correlation analysis revealed statistically significant relationships between immunological and clinical dental parameters. Direct correlations were established between total IgE levels and the PMA and PBI indices ($r = 0.46$ and $r = 0.42$, respectively; $p < 0.05$), indicating an association between allergic sensitization and the severity of inflammatory changes in periodontal tissues.

Positive correlations were also identified between total specific IgE and the PMA and PBI indices ($r = 0.51$, $p < 0.01$ and $r = 0.48$, $p < 0.05$, respectively). These findings indicate intensification of the inflammatory process in periodontal tissues with increasing severity of allergic sensitization.

Thus, IL-4, IL-6, total IgE, and sIgA levels reflect the activity of the inflammatory process, the degree of allergic sensitization, and the state of local immunity in patients with chronic generalized periodontitis and may be considered additional immunological markers of disease severity.

In order to determine the relationship between immunological disturbances and the severity of inflammatory changes in periodontal tissues, a correlation analysis between immunological and clinical dental parameters was performed. The results of the analysis are presented in Table 3.

Table 3

Correlation between immunological and clinical dental parameters

Parameter	Clinical dental index	Correlation coefficient (r)	p
Total IgE, IU/mL	PMA, %	0.46	$p < 0.05$
Total IgE, IU/mL	PBI	0.42	$p < 0.05$
Specific IgE (total)	PMA, %	0.51	$p < 0.01$
Specific IgE (total)	PBI	0.48	$p < 0.05$

Note: Statistically significant positive correlations were identified between immunological parameters and clinical dental indices ($p < 0.05$–0.01).

Based on the obtained clinical, immunological, and correlation data, a generalized pathogenetic model of chronic generalized periodontitis associated with food allergy was developed. The proposed model reflects the characteristics of immunoinflammatory disturbances arising in the combined course of periodontitis and allergic pathology and provides a more comprehensive understanding of the mechanisms underlying disease progression.

It was established that patients with food allergy demonstrate a shift of the immune response toward a Th2-dominant profile accompanied by increased levels of IL-4 and total IgE, activation of allergic inflammation, and impairment of local immune defense mechanisms. At the same time, a decrease in the protective potential of the oral mucosa was identified, manifested by alterations in secretory immunoglobulin A levels and contributing to weakening of the barrier function of periodontal tissues.

The development of immune imbalance creates conditions for persistence of the chronic inflammatory process, maintenance of cytokine activation, and progression of destructive changes in periodontal tissues. Elevated IL-6 levels contribute to enhancement of vascular and tissue reactions, impairment of microcirculation, and activation of resorptive processes in periodontal structures.

The developed pathogenetic model emphasizes the close relationship between local and systemic immune mechanisms and serves as a theoretical basis for the necessity of a comprehensive pathogenetically oriented approach to the diagnosis, prevention, and treatment of chronic generalized periodontitis in the presence of food allergy. The obtained results substantiated the need to expand the standard periodontal treatment regimen through inclusion of agents aimed at correction of the allergic component of inflammation and normalization of the immune response.

Taking into account the identified immunological disturbances, antihistamine therapy was included in the comprehensive treatment of patients with chronic generalized periodontitis associated with food allergy.

Cetirizine, a second-generation antihistamine characterized by high selectivity for peripheral H1 receptors and a favorable tolerability profile, was used in the study as a systemic corrective agent.

The use of cetirizine was considered a pathogenetically substantiated addition to the comprehensive therapy of patients with chronic generalized periodontitis and concomitant food allergy.

Taking into account the identified disturbances of local and systemic immune responses, as well as the need for a comprehensive effect on the main pathogenetic mechanisms of the disease, patient treatment was carried out in several stages. The initial stage of treatment included basic therapeutic and preventive measures aimed at eliminating local inflammatory factors and reducing microbial load.

The basic stage of therapy was performed in all patients regardless of the presence of concomitant allergic pathology and included a complex of standard therapeutic and preventive measures aimed at eliminating local inflammatory factors and normalizing the condition of periodontal tissues. Treatment began with professional oral hygiene procedures, including removal of supra- and subgingival dental deposits, thorough debridement and polishing of root surfaces, as well as elimination of local retention factors contributing to plaque accumulation and maintenance of the chronic inflammatory process.

Special attention was paid to correction of individual oral hygiene practices. All patients received instruction on proper tooth brushing techniques, selection of oral hygiene products, and adherence to oral care recommendations. Patients were informed about the role of microbial biofilm in the development of inflammatory periodontal diseases and the importance of regular control of oral hygiene status.

The implementation of basic therapeutic measures was aimed at reducing microbial load, decreasing the severity of the local inflammatory process, and improving the functional condition of periodontal tissues. Elimination of local inflammatory factors created optimal conditions for subsequent evaluation of the effectiveness of systemic therapy and for a more objective analysis of the influence of immunological and allergic mechanisms on the course of chronic generalized periodontitis.

In addition, the initial stage of treatment contributed to reduction of edema and gingival bleeding, improvement of microcirculation, and decreased activity of inflammatory reactions.

This provided more favorable conditions for the implementation of pathogenetically oriented comprehensive therapy in patients with chronic generalized periodontitis associated with food allergy.

In addition to standard periodontal treatment, patients of the main group received systemic antihistamine therapy with cetirizine according to the developed treatment regimen, which included administration of the drug at a dose of 10 mg once daily orally for 14 days, followed by maintenance therapy at a dose of 5 mg once daily for the subsequent 2 months.

This therapeutic regimen was aimed not only at relieving acute manifestations of allergic inflammation, but also at maintaining stable correction of immunoinflammatory disturbances identified in patients with chronic generalized periodontitis associated with food allergy. Continuation of antihistamine therapy in a maintenance regimen made it possible to reduce the severity of allergic sensitization, stabilize vascular permeability, and decrease the activity of the chronic inflammatory process in periodontal tissues.

Systemic antihistamine therapy was used as part of the comprehensive treatment of patients with chronic generalized periodontitis and concomitant food allergy throughout all stages of observation.

After comprehensive therapy, patients of the main group demonstrated significant positive dynamics in the clinical condition of periodontal tissues. Against the background of the performed treatment, a reduction in subjective complaints was observed, including decreased discomfort, itching sensation, and gingival bleeding during toothbrushing and food intake. Objective dental examination revealed a reduction in the severity of inflammatory changes in periodontal tissues.

Patients of the main group demonstrated reduced gingival bleeding, decreased edema and hyperemia of the marginal gingiva, improvement in periodontal tissue consistency, and reduction of signs of congestive inflammatory phenomena. Simultaneously, a reduction in periodontal pocket depth, decreased inflammatory exudation, and stabilization of tooth mobility were observed. Improvement in clinical condition was accompanied by positive dynamics of the main periodontal indices, including PMA, PBI, and oral hygiene indicators.

The most pronounced positive changes were observed in patients receiving comprehensive therapy including cetirizine. In this group, inflammatory signs decreased more rapidly, the intensity of vascular reactions diminished, and a more pronounced restoration of the functional condition of periodontal tissues was observed. This may be associated with reduction of the allergic component of inflammation and decreased severity of immunoinflammatory reactions.

The obtained results indicate a decrease in the activity of the chronic inflammatory process and slowing of the progression of destructive changes in periodontal tissues during comprehensive treatment including antihistamine therapy. Positive clinical dynamics confirm the expediency of a pathogenetically oriented approach to the treatment of patients with chronic generalized periodontitis associated with food allergy.

In addition, during the observation period, patients of the main group demonstrated more stable remission of the inflammatory process and improvement in oral hygiene indicators, suggesting a favorable effect of comprehensive therapy on the course of the disease and the condition of periodontal tissues as a whole.

Immunological evaluation of the effectiveness of the performed therapy demonstrated significant changes in local and systemic immune response parameters in patients of the main group. After completion of comprehensive treatment, pronounced positive dynamics of immunological indicators were observed, indicating decreased activity of inflammatory and allergic reactions.

Patients of the main group demonstrated decreased concentrations of IL-4 and IL-6 in both oral fluid and blood serum. Reduction of IL-4 levels reflected decreased activity of the Th2-mediated immune response and attenuation of the allergic component of the inflammatory process, whereas decreased IL-6 concentration indicated reduction in systemic and local proinflammatory activity. At the same time, a decrease in total and specific IgE levels was observed, indicating reduced allergic sensitization and decreased intensity of IgE-mediated immune reactions.

During therapy, an increase in the concentration of secretory immunoglobulin A in oral fluid was also observed, indicating

restoration of local mucosal immunity mechanisms and improvement of the barrier function of the oral mucosa. Normalization of sIgA parameters indicated enhancement of the protective potential of oral fluid and improvement of local immunological resistance of periodontal tissues to microbial and inflammatory factors.

The identified immunological changes were accompanied by positive clinical dynamics and correlated with decreased activity of the inflammatory process in periodontal tissues. The obtained results confirm the favorable effect of comprehensive therapy including cetirizine on the course of chronic generalized periodontitis in patients with concomitant food allergy.

Clinical observations demonstrated that cetirizine administration was accompanied by more pronounced and stable clinical improvement compared with the results of standard therapy. Patients of the main group showed a reduction in subjective complaints, including gingival bleeding, discomfort, and signs of inflammation of the oral mucosa. In addition, a decrease in the frequency of exacerbations of the inflammatory process and increased stability of the achieved clinical results during follow-up observation were observed.

It should be noted that the positive dynamics of immunological parameters persisted even after completion of the main treatment course, which may indicate a prolonged immunomodulatory effect of comprehensive therapy including the antihistamine component. Maintenance use of cetirizine contributed to stabilization of immunoinflammatory reactions and preservation of the achieved therapeutic effect.

Thus, the conducted study confirmed the significant role of immunoinflammatory and allergic mechanisms in the pathogenesis of chronic generalized periodontitis in patients with concomitant food allergy. It was established that the combined course of these pathologies is accompanied by more pronounced clinical manifestations of the inflammatory process, alterations in the cytokine profile, and disturbances of local mucosal immunity.

The obtained results indicate a close relationship between local and systemic immune reactions involved in maintaining chronic

inflammation and progression of destructive changes in periodontal tissues. The identified alterations in IL-1β, IL-4, IL-6, total IgE, and sIgA levels confirm the diagnostic and pathogenetic significance of immunological markers in this combined pathology.

The study results substantiate the necessity of a comprehensive approach to the diagnosis and treatment of patients with chronic generalized periodontitis taking into account allergological status and immunological parameters. Inclusion of antihistamine therapy in the comprehensive treatment regimen contributes to increased treatment effectiveness and stabilization of clinical outcomes.

Summarizing the results of the conducted study, it should be emphasized that chronic generalized periodontitis in patients with IgE-mediated food allergy represents not merely a combination of two nosological entities, but a complex immunopathological model based on systemic dysregulation of the cytokine network. In this case, local inflammation in periodontal tissues reflects deeper disturbances of immune homeostasis caused by prolonged antigenic stimulation and sensitization of the organism. This concept makes it possible to reinterpret the clinical course of the disease and explain its resistance to standard therapeutic approaches.

A fundamentally important conclusion of the study is that correction of the immune component of inflammation contributes to a more favorable clinical outcome. The inclusion of antihistamine therapy in the comprehensive treatment regimen resulted in a more pronounced reduction in inflammatory activity and stabilization of clinical parameters. This confirms the necessity of a pathogenetically oriented approach that takes into account the individual characteristics of the patient’s immune status. Thus, the therapeutic strategy should be aimed not only at elimination of the microbial factor, but also at modulation of the immune response.

The obtained data allow chronic generalized periodontitis under conditions of allergic comorbidity to be regarded as an interdisciplinary problem requiring integration of knowledge from dentistry, allergology, and clinical immunology. Implementation of the developed recommendations into clinical practice contributes to increased treatment effectiveness, reduction in recurrence frequency,

and achievement of more stable remission. This has important social significance in the context of the growing prevalence of both inflammatory periodontal diseases and allergic pathology.

CONCLUSIONS

1. Patients with chronic generalized periodontitis combined with food allergy demonstrated more pronounced immunoinflammatory disturbances characterized by increased serum levels of IL-4 up to 8.4 ± 0.6 pg/mL and IL-6 up to 12.7 ± 0.9 pg/mL compared with the group of patients without allergic pathology (4.2 ± 0.4 pg/mL and 7.3 ± 0.6 pg/mL, respectively; $p < 0.05$). The identified changes indicate a shift of the immune response toward a Th2-dominant profile and high inflammatory activity [1,3,8,11].
2. It was established that the combined course of chronic generalized periodontitis and food allergy is associated with pronounced immunological changes accompanied by increased levels of IL-4 and IL-6, as well as a decrease in the concentration of secretory immunoglobulin A in oral fluid to 112.5 ± 8.7 mg/L compared with the group of patients without allergic pathology (156.3 ± 10.2 mg/L; $p < 0.05$). The identified changes indicate high activity of the local inflammatory process and impairment of local immune defense mechanisms [2,5,6].
3. It was proven that in patients with chronic generalized periodontitis and food allergy, elevated total IgE levels reflect the severity of systemic allergic sensitization and the involvement of the allergic component in maintaining the chronic inflammatory process in periodontal tissues. Statistically significant positive correlations were identified between total IgE levels and the clinical dental indices PMA and PBI ($r = 0.46$ and $r = 0.42$, respectively; $p < 0.05$) [7,8].
4. The identified changes in immunological parameters, including increased levels of IL-4, IL-6, and total IgE, as well as decreased sIgA concentration ($p < 0.05$), reflect the severity of immunoinflammatory disturbances in patients with chronic generalized

periodontitis and food allergy. The established immunological changes are accompanied by activation of allergy-mediated inflammatory mechanisms, impairment of local mucosal immunity, and contribute to the progression of inflammatory and destructive changes in periodontal tissues [9, 12, 13].

5. Comprehensive assessment of IL-4, IL-6, total IgE, and sIgA levels improves the diagnostic informativeness of chronic generalized periodontitis associated with food allergy. The established statistically significant correlations between total IgE levels and the clinical dental indices PMA and PBI ($r = 0.46$ and $r = 0.42$, respectively; $p < 0.05$) confirm the diagnostic significance of immunological parameters and contribute to the individualization of therapeutic strategies [5,6,7].

PRACTICAL RECOMMENDATIONS

1. During the examination of patients with chronic generalized periodontitis, it is recommended to take the presence of food allergy into account and to assess the levels of IL-4, IL-6, total IgE, and sIgA in order to identify concomitant immunoinflammatory disturbances.
2. Determination of IL-4, IL-6, total IgE, and sIgA levels is recommended for monitoring the activity of the inflammatory process, evaluating the effectiveness of therapy, and dynamic follow-up of patients with chronic generalized periodontitis and food allergy.
3. When selecting therapeutic strategies for patients with the combined course of chronic generalized periodontitis and food allergy, the characteristics of immune status and the possibility of using agents aimed at correcting the identified immunoinflammatory disturbances should be taken into consideration.
4. The results of the study may be used in the development of personalized diagnostic and therapeutic algorithms in dental practice taking into account the patient's allergological history.

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LIST OF ABBREVIATIONS

IgE – immunoglobulin E
sIgA – secretory immunoglobulin A
IgA – immunoglobulin A
IgG – immunoglobulin G
IL-1β – interleukin-1β
IL-2 – interleukin-2
IL-4 – interleukin-4
IL-6 – interleukin-6
TNF-α – tumor necrosis factor-α
CGP – chronic generalized periodontitis
FA – food allergy
DMFT – decayed, missing, and filled teeth index
OHI-S – Simplified Oral Hygiene Index (Green–Vermillion)
PMA – Papillary-Marginal-Alveolar Index
PBI – Papillary Bleeding Index
SBI – Sulcus Bleeding Index
PPD – periodontal pocket depth
CAL – clinical attachment loss
ELISA – enzyme-linked immunosorbent assay
ECLIA – electrochemiluminescence immunoassay
SPSS – Statistical Package for the Social Sciences
TLR – Toll-like receptors
NF-κB – nuclear factor κB
RANK – receptor activator of nuclear factor κB
RANKL – receptor activator of nuclear factor κB ligand
OPG – osteoprotegerin
Th1 – type 1 T-helper cells
Th2 – type 2 T-helper cells
Th17 – type 17 T-helper cells

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