# Evaluation of the effectiveness of photodynamic disinfection on the cytokine profile of oral fluid in patients with chronic generalized periodontitis

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**Abstract**

INTRODUCTION. An emerging and promising direction in dentistry is the use of photodynamically activated disinfection as part of comprehensive therapeutic and preventive protocols. This method contributes to the improvement of clinical periodontal status, enhances immune function, and positively influences the outcomes of periodontal treatment. However, the pathogenetic mechanisms underlying the effectiveness of this therapy remain insufficiently understood and require further investigation.

AIM. To evaluate the effectiveness of laser-assisted photodynamic disinfection on the clinical condition of periodontal tissues and the cytokine profile of oral fluid in patients with moderate chronic generalized periodontitis.

MATERIALS AND METHODS. A total of 62 patients aged 35 to 45 years with moderate chronic generalized periodontitis were examined. They were randomly assigned to two groups: a control group (receiving standard periodontal treatment) and a main group (receiving photodynamically activated disinfection in combination with standard treatment). Clinical and radiographic examinations were performed, along with the measurement of cytokine levels in oral fluid (IL-1β, IL-4, IL-6, IL-8, IL-10, TNF-α, and IFN-γ) before treatment, and at 14 days, 3 months, and 6 months after treatment initiation.

RESULTS. Photodynamically activated disinfection led to a significant improvement in the clinical condition of periodontal tissues and normalization of periodontal and hygiene indices. In addition, patients in the main group demonstrated a restoration of cytokine balance in periodontal tissues, with a marked reduction in pro-inflammatory cytokines IL-1β, IL-6, IL-8, TNF-α ($p < 0.01$), and IFN-γ ($p < 0.001$), as well as an increase in anti-inflammatory cytokines IL-4 ($p < 0.05$) and IL-10 ($p < 0.05$), compared to baseline levels.

CONCLUSIONS. In patients with moderate chronic generalized periodontitis, therapeutic and preventive measures contribute to improved clinical periodontal conditions, as reflected in the periodontal and hygiene indices. However, patients in the main group receiving photodynamically activated disinfection exhibited significantly greater improvements in periodontal indices and normalization of the cytokine profile ($p < 0.001$).

**Keywords:** chronic generalized periodontitis, interleukins-1β, -4, -6, -8, -10, tumor necrosis factor-alpha, interferon-gamma, photodynamically activated disinfection

# Оценка эффективности влияния фотоактивируемой дезинфекции на состояние цитокинового профиля ротовой жидкости у пациентов с хроническим генерализованным пародонтитом

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**Резюме**

ВВЕДЕНИЕ. Перспективным направлением в стоматологии становится использование в комплексе лечебно-профилактических мероприятий фотоактивируемой дезинфекции, которая улучшает клиническое состояние тканей пародонта и иммунный статус, способствует улучшению результатов

пародонтологического лечения. Однако патогенетические механизмы эффективности данного метода терапии требуют продолжения исследований.

ЦЕЛЬ. Оценка эффективности лазерной фотоактивируемой дезинфекции на клиническое состояние тканей пародонта и цитокиновый профиль ротовой жидкости у пациентов с хроническим генерализованным пародонтитом.

МАТЕРИАЛЫ И МЕТОДЫ. Обследованы 62 пациента с хроническим генерализованным пародонтитом средней степени тяжести в возрасте 35-45 лет, разделенные случайным образом на две группы – сравнения (получали стандартное лечение) и основную (получали фотоактивируемую дезинфекцию на фоне стандартного лечения). Проведены клиническое и рентгенологическое обследования с определением в ротовой жидкости уровней IL-1β, IL-4, IL-6, IL-8, IL-10, TNF-α и IFN-γ до лечения, через 14 дней, 3 и 6 месяцев.

РЕЗУЛЬТАТЫ. Фотоактивируемая дезинфекция тканей пародонта у пациентов способствует значительному улучшению состояния тканей пародонта, нормализации пародонтальных и гигиенических индексов. Также у пациентов этой группы происходит восстановление цитокинового баланса тканей пародонта: наблюдается снижение уровня провоспалительных цитокинов IL-1β, IL-6, IL-8, TNF-α ($p < 0,01$), IFN-γ ($p < 0,001$) и повышение уровня противовоспалительных IL-4 ($p < 0,05$) и IL-10 ($p < 0,05$) по сравнению с данными до лечения.

ВЫВОДЫ. У пациентов с хроническим генерализованным пародонтитом средней степени тяжести проводимые лечебно-профилактические мероприятия приводят к улучшению клинического состояния тканей пародонта с корреляцией пародонтологических и гигиенических индексов. Однако у пациентов основной группы, которым проводилась фотоактивируемая дезинфекция, наблюдается более значимое улучшение пародонтальных индексов, нормализация уровня цитокинового баланса ($p < 0,001$).

## INTRODUCTION

Inflammatory periodontal diseases rank 11th globally in prevalence according to the Global Burden of Disease Study [1]. The highest prevalence of chronic periodontitis is observed in the elderly (82%), followed by adults (73%) and adolescents (59%) [2; 3]. Globally, periodontal diseases are more frequently diagnosed in younger populations, with prevalence rates ranging from 4% to 76% in developed countries and from 50% to 90% in developing countries [4].

Inflammatory periodontal diseases represent a significant public health concern and are closely associated with various risk factors [5]. However, the local immune response plays a central role in the development of inflammation [6].

In active clinical stages of chronic generalized periodontitis, the pro-inflammatory cytokines IL-1β, IL-6, and TNF-α form a "classical" inflammatory triad. These cytokines initiate the expression of additional pro-inflammatory interleukins, their receptors, and other mediators of inflammation, while also signaling a reduction in IL-10 secretion [7–9]. During advanced inflammatory processes, there is an increase in phagocytic activity, antigenic proliferation of Th1, Th2, and Th17 cells, B-cell activation, and neutrophil release [7]. In this context, IL-6 exhibits strong pro-inflammatory properties, accelerating B-cell maturation, immunoglobulin secretion, and Th17 cell proliferation [10].

Th17 cells, in turn, produce a group of pro-inflammatory cytokines, including IL-17, IL-21, and IL-23. IL-17 promotes the expression of high levels of chemoattractants and increases the release of inflammatory mediators by macrophages and periodontal ligament cells, resulting in their elevated concentration within periodontal tissues [7]. Pro-inflammatory cytokines (IL-1β, IL-6, IL-17, TNF-α) contribute to the differentiation of monocytes into osteoclasts and accelerate bone resorption [7; 11–13].

The pathogenesis and chronicity of periodontal inflammation also involve cytokines such as IL-25, IL-31, IL-33, and the soluble CD40 ligand, which participate in the activation, differentiation, and regulation of interleukins, chemokines, and immune cell expression [10; 11]. Under physiological conditions, cytokines help maintain immune homeostasis within the periodontium, regulate neutrophil activity, and coordinate immune cell cooperation, thereby preserving epithelial barrier integrity [14].

The levels of pleiotropic cytokines in oral fluid and blood serum are positively correlated with clinical parameters of periodontitis. Thus, assessing cytokine profiles in whole saliva provides a convenient and effective tool for monitoring the severity of the inflammatory response [15].

Despite the extensive literature devoted to the immune-inflammatory aspects of chronic periodontitis, its underlying pathogenetic mechanisms remain insufficiently understood [11].

Currently, numerous comprehensive treatment strategies and modern pharmacological agents have been developed for the management of periodontitis.

However, despite significant advancements, existing methods have not achieved long-term clinical stability or sustained remission. According to the latest treatment guidelines published by the European Federation of Periodontology, a staged therapeutic approach is recommended [16].

A promising component of the comprehensive management of inflammatory periodontal diseases is photodynamically activated disinfection, which can improve key periodontal parameters such as clinical attachment loss or gain, bleeding on probing, and pocket depth. It also reduces inflammatory marker levels, thereby slowing disease progression and prolonging remission periods [17; 18].

Nonetheless, the pathogenetic mechanisms underlying the therapeutic efficacy of this method – particularly its influence on the cytokine profile of oral fluid – remain to be fully elucidated. This gap in knowledge defines the relevance and objective of our study.

## AIM

Evaluation of the Effectiveness of Laser Photodynamically Activated Disinfection on the Clinical Condition of Periodontal Tissues and the Cytokine Profile of Oral Fluid in Patients with Chronic Generalized Periodontitis.

## MATERIALS AND METHODS

Clinical studies were conducted at the Department of Therapeutic Dentistry of Bashkir State Medical University (BSMU), Ministry of Health of the Russian Federation, and at the dental clinic Ibradent LLC. A total of 62 patients aged 35 to 45 years with moderate chronic generalized periodontitis (ICD-10: K05.3) and 21 individuals with intact periodontium (control group) were examined. The mean age of the participants was $41.98 \pm 4.30$ years; 24 (38.71%) were male and 38 (61.29%) were female.

The comprehensive dental examination included assessment of complaints and medical history, clinical evaluation of periodontal and dental tissues, and measurement of periodontal indices:
– CPI (P.A. Leus, 1988);
– PMA (C. Parma, 1960);
– SBI (H.P. Muhlemann, S. Son, 1971);
– OHI-S (J.K. Green, J.K. Vermillion, 1964), which assesses the amount of dental plaque in the gingival sulcus.

To confirm the diagnosis and assess the condition of the alveolar bone, cone-beam computed tomography (CBCT) was used.

Patients with periodontitis were randomly divided into two equal clinical groups: a comparison group and a main group. The main group received standard treatment according to clinical guidelines, supplemented with photodynamically activated disinfection using toluidine blue as a photosensitizer and the Soga PDT-I device with a wavelength of 570–690 nm and energy density of 75 mW/cm$^2$. Examinations were performed at baseline, after 10–14 days, and at 3 and 6 months. Patients in the comparison group received standard treatment only, according to clinical guidelines.

Laboratory testing of oral fluid samples included determination of the concentrations of interleukins IL-1β, IL-4, IL-6, IL-8, IL-10, tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ) using enzyme-linked immunosorbent assay (ELISA) with reagent kits from Vector-Best JSC (Russia) on the Personal Lab analyzer (Italy). Sample collection, storage, and preparation for analysis were performed according to the manufacturer's recommendations [19].

Oral fluid was collected in the morning, fasting and prior to tooth brushing, by expectoration into a sterile centrifuge tube with a tightly sealed cap. Salivation was physiologically stimulated through active tongue and cheek muscle movements. Samples were stored at −18°C to −20°C for no longer than 5 days prior to analysis. Before testing, samples were thawed slowly at room temperature and centrifuged at 2800 rpm for 15 minutes. The supernatant was used for analysis.

Statistical analysis was performed using R 4.3 statistical software. Data distribution was presented as median and interquartile range: Me [Q1–Q3]. The Mann–Whitney U test was used for between-group comparisons and comparisons with reference values. The Wilcoxon signed-rank test was used for comparisons of pre- and post-treatment values (paired data). Differences were considered statistically significant at $p \leqslant 0.05$.

## RESULTS

A comprehensive dental examination was conducted on 62 patients with moderate chronic generalized periodontitis (ICD-10: K05.3).

Before the initiation of therapeutic and preventive measures, patients most commonly reported the following complaints:
– pain in the gingival area (93%);
– soreness and gingival bleeding during eating and tooth brushing (95%);
– halitosis (89%);
– tooth mobility (31%);
– development of traumatic occlusion (58%).

Clinical examination of the periodontal tissues revealed:
– congestive venous hyperemia in 91% of patients;
– the presence of supra- and subgingival calculus in 100%;
– blunting of interdental papillae and gingival edema in 90%, and Grade II tooth mobility.

The depth of periodontal pockets ranged between 4.6 and 5 mm.

Orthopantomographic analysis showed:
– bone resorption of the interradicular septa in all patients, ranging from one-third to one-half of the root length, focal osteoporosis, and the formation of vertical bone defects in localized areas.

The median values of periodontal indices at baseline were as follows:
– CPI – 2.79 [2.57–3.12];
– SBI – 2.61 [2.43–2.69];
– PMA – 46.6 [42.5–49.0];
– the simplified oral hygiene index (OHI-S) – 2.47 [2.19–2.70].

The dynamics of hygiene and periodontal indices in patients with moderate chronic generalized periodontitis undergoing either photodynamically activated disinfection or standard treatment are presented in Table 1.

As shown, pairwise intergroup comparison of periodontal and hygiene indices revealed no statistically significant differences between the main group and the comparison group before treatment ($p > 0.2$). After treatment, significant improvements were observed in CPI, SBI, PMA, and OHI-S indices at 14 days, 3 months, and 6 months compared to baseline in both groups ($p < 0.05$). Additionally, statistically significant intergroup differences were noted in the dynamics of these indices over time –at 14 days, 3 months, and 6 months – except for OHI-S, which showed no significant differences at 3 and 6 months ($p > 0.1$).

At 14 days after treatment, a notable downward trend in the periodontal and hygiene indices was observed in the main group:
- CPI decreased by 1.53-fold to 1.82 [1.46–2.27];
- SBI by 1.44-fold to 1.83 [1.67–1.91];
- PMA by 1.9-fold to 30.0 [25.5–32.0];
- OHI-S by 1.82-fold to 1.36 [1.17–1.47].

In the comparison group, receiving standard care per clinical guidelines, the reductions were more modest:
- CPI by 1.33-fold to 2.09 [1.79–2.44];
- SBI by 1.21-fold to 2.13 [1.89–2.41];
- PMA by 1.55-fold to 30.0 [25.5–32.0];
- OHI-S by 1.52-fold to 1.62 [1.24–2.04].

At 3 months post-treatment, patients in the main group demonstrated clinical stabilization of periodontal tissues, with further reductions compared to baseline:
- CPI decreased by 1.91-fold to 1.46 [1.11–1.65];
- SBI by 1.91-fold to 1.38 [1.06–1.72];
- PMA by 2.06-fold to 22.6 [18.5–27.3];
- OHI-S by 1.93-fold to 1.28 [1.07–1.34].

In the comparison group, the respective reductions were:
- CPI by 1.65-fold to 1.69 [1.25–1.83];
- SBI by 1.32-fold to 1.94 [1.71–2.22];
- PMA by 1.91-fold to 24.4 [21.3–27.0];
- OHI-S by 1.69-fold to 1.46 [1.14–1.75].

At the 6-month follow-up, patients in the main group showed sustained clinical improvement due to photodynamically activated disinfection.

**Table 1.** Dynamics of Periodontal and Hygiene Indices in Patients with Moderate Chronic Generalized Periodontitis Undergoing Standard Treatment and Treatment with Photodynamically Activated Disinfection, Me [$Q_1$–$Q_3$]

**Таблица 1.** Динамика пародонтологических и гигиенических индексов у пациентов с хроническим генерализованным пародонтитом средней степени тяжести при стандартном лечении и лечении с применением фотоактивируемой дезинфекции, Me [$Q_1$–$Q_3$]

| Study period | Patient group | n | Indices, scores, % | | | |
|---|---|---|---|---|---|---|
| | | | KPI, scores | SBI, % | PMA, % | OHI-S, scores |
| Before treatment | O | 31 | 2.79 [2.68–3.12] $p = 0.926$ | 2.64 [2.43–2.75] $p = 0.874$ | 46.6 [42.5–49.5] $p = 0.926$ | 2.47 [2.11–2.70] $p = 0.814$ |
| | C | 31 | 2.79 [2.46–3.12] | 2.57 [2.38–2.69] | 46.4 [42.5–49.0] | 2.47 [2.19–2.75] |
| After 14 days | O | 31 | 1.82 [1.46–2.27] $p = 0.016$ $p_1 < 0.001$ | 1.83 [1.67–1.91] $p = 0.001$ $p_1 < 0.001$ | 24.5 [19.6–28.7] $p = 0.018$ $p_1 < 0.001$ | 1.36 [1.17–1.47] $p = 0.175$ $p_1 < 0.001$ |
| | C | 31 | 2.09 [1.79–2.44] $p_1 < 0.001$ | 2.13 [1.89–2.41] $p_1 = 0.002$ | 30.0 [25.5–32.0] $p_1 < 0.001$ | 1.62 [1.24–2.04] $p_1 < 0.001$ |
| After 3 months | O | 31 | 1.46 [1.11–1.65] $p = 0.272$ $p_1 < 0.001$ | 1.38 [1.06–1.72] $p = 0.008$ $p_1 < 0.001$ | 22.6 [18.5–27.3] $p = 0.042$ $p_1 < 0.001$ | 1.28 [1.07–1.34] $p = 0.178$ $p_1 < 0.001$ |
| | C | 31 | 1.69 [1.25–1.83] $p_1 < 0.001$ | 1.94 [1.71–2.22] $p_1 < 0.001$ | 24.4 [21.3–27.0] $p_1 < 0.001$ | 1.46 [1.14–1.75] $p_1 < 0.001$ |
| After 6 months | O | 31 | 1.22 [0.96–1.43] $p = 0.042$ $p_1 < 0.001$ | 1.06 [0.77–1.23] $p = 0.025$ $p_1 < 0.001$ | 20.4 [16.7–22.6] $p = 0.036$ $p_1 < 0.001$ | 1.16 [0.91–1.33] $p = 0.643$ $p_1 < 0.001$ |
| | C | 31 | 1.52 [0.97–1.64] $p_1 < 0.001$ | 1.43 [1.23–1.73] $p_1 < 0.001$ | 24.0 [19.1–27.4] $p_1 < 0.001$ | 1.16 [0.97–1.63] $p_1 < 0.001$ |

*Note:* C – comparison clinical group; M – main clinical group; $p$ – difference compared to the comparison group (Mann–Whitney U test); $p_1$ – difference before and after treatment within the same group (Wilcoxon signed-rank test).

*Примечания*: С – клиническая группа сравнения, О – основная клиническая группа; $p$ – различие с группой сравнения (критерий Манна-Уитни), $p_1$ – до и после проведения лечебно-профилактических мероприятий (критерий Вилкоксона).

Reductions compared to baseline were as follows:
– CPI by 2.29-fold to 1.22 [0.96–1.43];
– SBI by 2.49-fold to 1.06 [0.77–1.23];
– PMA by 2.28-fold to 20.4 [16.7–22.6];
– OHI-S by 2.13-fold to 1.16 [0.91–1.33].

In the comparison group, the CPI and SBI decreased respectively by:
– 1.84-fold to 1.52 [0.97–1.64];
– 1.80-fold to 1.43 [1.23–1.73];
– PMA by 1.93-fold to 24.0 [19.1–27.4].

The dynamics of the OHI-S index did not significantly differ between groups, with similar reductions of 2.13-fold observed in both groups:
– main group: 1.16 [0.91–1.33];

– comparison group: 1.16 [0.97–1.63].

Clinical manifestations of chronic generalized periodontitis were accompanied by significant changes in cytokine concentrations in oral fluid samples (Table 2).

ELISA data showed that, before treatment, patients in the main group had elevated levels of pro-inflammatory cytokines:
– IL-1β by 271.9%;
– IL-6 by 231.0%;
– IL-8 by 319.2%;
– TNF-α by 529.4%;
– IFN-γ by 418.9%, compared to conditional normal values.

**Table 2.** Cytokine Concentrations (pg/mL) in Oral Fluid of Patients with Chronic Generalized Periodontitis Undergoing Comprehensive Treatment Including Photodynamically Activated Disinfection, Me [$Q_1$–$Q_3$], $n = 31$

**Таблица 2.** Содержание цитокинов (в – пг/мл) в ротовой жидкости у пациентов с хроническим генерализованным пародонтитом при включении в комплексное лечение фотоактивируемую дезинфекцию, Me [$Q_1$–$Q_3$], $n=31$

| Study period | Class group | IL-1β | IL-4 | IL-6 | IL-8 | IL-10 | TNF-α | IFN-γ |
|---|---|---|---|---|---|---|---|---|
| Before treatment | O | 58.2 [50.2–67.2] $p < 0.001$ $p_1 = 0.894$ | 17.3 [15.2–19.8] $p = 0.022$ $p_1 = 0.797$ | 12.66 [11.5–15.7] $p < 0.001$ $p_1 = 1.0$ | 46.6 [39.7–48.9] $p < 0.001$ $p_1 = 0.833$ | 148.4 [127.4–154.2] $p < 0.001$ $p_1 = 0.437$ | 32.4 [24.9–38.4] $p < 0.001$ $p_1 = 0.366$ | 161,5 [135,5–173,8] $p < 0,001$ $p_1 = 0,078$ |
| | C | 61.6 [49.2–69.8] $p < 0.001$ | 16.2 [12.8–18.9] $p < 0.001$ | 12.96 [10.59–15.79] $p < 0.001$ | 57.2 [44.6–55.6] $p < 0.001$ | 137.5 [115.5–147.6] $p < 0.001$ | 30.4 [20.5–35.9] $p < 0.001$ | 134,0 [107,1–154,2] $p < 0,001$ |
| After 14 days | O | 55.2 [48.8–63.2] $p < 0.001$ $p_1 = 0.124$ $p_2 = 0.095$ | 17.3 [15.6–21.4] $p = 0.036$ $p_1 = 1.0$ $p_2 = 1.0$ | 10.56 [9.72–12.1] $p < 0.001$ $p_1 = 0.072$ $p_2 = 0.031$ | 41.4 [36.4–45.5] $p < 0.001$ $p_1 = 0.054$ $p_2 = 0.133$ | 120.5 [112.7–155.5] $p = 0.002$ $p_1 = 0.078$ $p_2 = 0.008$ | 27.2 [21.1–32.4] $p = 0.001$ $p_1 = 0.081$ $p_2 = 0.056$ | 118,1 [94,4–132,2] $p < 0,001$ $p_1 = 1,0$ $p_2 = 0,037$ |
| | C | 60.8 [48.2–68.9] $p < 0.001$ $p_2 = 1.0$ | 17.2 [14.9–19.4] $p = 0.006$ $p_2 = 0.672$ | 11.88 [10.2–13.24] $p < 0.001$ $p_2 = 1.0$ | 49.6 [41.5–83.2] $p < 0.001$ $p_2 = 1.0$ | 122.5 [113.4–134.0] $p < 0.001$ $p_2 = 0.417$ | 31.3 [27.4–34.4] $p < 0.001$ $p_2 = 0.533$ | 119,3 [87,7–132,4] $p < 0,001$ $p_2 = 0,213$ |
| After 3 months | O | 36.4 [28.4–43.6] $p = 0.041$ $p_1 = 0.037$ $p_2 = 0.024$ | 23.3 [19.4–24.8] $p = 1.0$ $p_1 = 0.004$ $p_2 = 0.002$ | 8.85 [8.05–9.66] $p < 0.001$ $p_1 = 0.032$ $p_2 = 0.027$ | 26.4 [21.4–31.5] $p = 0.025$ $p_1 = 0.046$ $p_2 = 0.002$ | 229.5 [202.5–287.5] $p = 0.773$ $p_1 = 0.001$ $p_2 < 0.001$ | 10.7 [5.8–15.5] $p = 0.263$ $p_1 = 0.029$ $p_2 < 0.001$ | 60,3 [52,7–72,6] $p = 0,042$ $p_1 = 1,0$ $p_2 < ,001$ |
| | C | 52.8 [45.4–61.8] $p = 0.002$ $p_2 = 0.018$ | 19.8 [18.3–21.7] $p = 0.364$ $p_2 = 0.005$ | 10.2 [9.03–11.52] $p = 0.001$ $p_2 = 0.003$ | 32.4 [24.3–38.4] $p = 0.004$ $p_2 = 0.005$ | 174.1 [144.1–182.6] $p = 0.701$ $p_2 = 0.001$ | 16.4 [10.2–20.4] $p = 0.004$ $p_2 = 0.005$ | 59,6 [46,3–65,7] $p = 0,039$ $p_2 < 0,001$ |
| After 6 months | O | 25.4 [17.8–28.4] $p = 0.912$ $p_1 = 0.034$ $p_2 < 0.001$ | 22.6 [19.5–25.1] $p = 1.0$ $p_1 = 0.031$ $p_2 = 0.002$ | 6.24 [4.85–7.68] $p = 0.075$ $p_1 = 0.038$ $p_2 < 0.001$ | 15.6 [14.3–19.8] $p = 0.958$ $p_1 = 0.041$ $p_2 < 0.001$ | 245.6 [99.1–272.4] $p = 0.081$ $p_1 = 0.039$ $p_2 < 0.001$ | 8.21 [6.16–8.33] $p = 0.934$ $p_1 = 0.036$ $p_2 < 0.001$ | 47,7 [38,6–51,1] $p = 0,281$ $p_1 = 0,219$ $p_2 < 0,001$ |
| | C | 36.8 [30.2–43.4] $p = 0.182$ $p_2 < 0.001$ | 23.4 [19.3–26.7] $p = 1.0$ $p_2 = 0.003$ | 7.97 [6.99–8.64] $p = 0.034$ $p_2 < 0.001$ | 20.2 [14.3–26.2] $p = 0.783$ $p_2 < 0.001$ | 205.5 [200.5–246.3] $p = 0.232$ $p_2 < 0.001$ | 9.5 [6.2–15.3] $p = 0.248$ $p_2 = 0.001$ | 56,8 [45,2–59,2] $p = 0,388$ $p_2 < 0,001$ |
| Control | | 21,4 [16,2–26,8] | 22.4 [19.4–28.6] | 5.48 [1.79–6.23] | 14.6 [12.1–16.3] | 195.5 [166–336] | 6.12 [5.22–7.14] | 38.5 [26.6–44.2] |

*Note:* C – comparison clinical group; M – main clinical group; $p$ – difference from the control group (patients with intact periodontium) according to the Mann–Whitney U test; $p_1$ – difference from the comparison group (Mann–Whitney U test); $p_2$ – difference before and after treatment within the same group (Wilcoxon signed-rank test).

*Примечания:* С – клиническая группа сравнения, О – основная клиническая группа, $p$ – различия с контролем – группой пациентов с интактным пародонтом (критерий Манна-Уитни), $p_1$ – с группой сравнения (критерий Манна-Уитни), $p_2$ – до и после лечебно-профилактических мероприятий (критерий Вилкоксона).

In the comparison group, cytokine levels increased by:
– IL-1β by 227.9%;
– IL-6 by 236.5%;
– IL-8 by 350.7%;
– TNF-α by 513.1%;
– IFN-γ by 348.1%.

Both groups also showed decreased levels of anti-inflammatory cytokines before treatment:
– IL-4 by 77.23% and 75.9%;
– IL-10 by 72.32% and 70.3%, respectively, compared to normal reference values.

Before the initiation of therapeutic and preventive interventions, patients in the main group with chronic generalized periodontitis exhibited a decrease in the levels of anti-inflammatory cytokines IL-4 and IL-10 in oral fluid samples by an average of 1.29-fold and 1.32-fold, respectively, compared to reference values. At the same time, the median concentrations of pro-inflammatory cytokines IL-1β, IL-6, IL-8, TNF-α, and IFN-γ were elevated by 2.72, 2.31, 3.19, 5.29, and 4.19 times, respectively, relative to conditional norms.

In the comparison group, a reduction in anti-inflammatory cytokines IL-4 and IL-10 was observed by 1.38-fold and 1.42-fold, respectively. Pro-inflammatory cytokines IL-1β, IL-6, IL-8, TNF-α, and IFN-γ were elevated by 2.88, 2.36, 3.90, 4.97, and 2.87 times, respectively, compared to the reference values.

All cytokine values in both groups significantly differed from the reference norm ($p < 0.001$) according to the Mann–Whitney U test.

## DISCUSSION

According to the obtained data, therapeutic and preventive interventions contributed to the improvement of the clinical condition of periodontal tissues in patients with chronic generalized periodontitis in both the main and comparison groups, as evidenced by the reduction in CPI, SBI, and PMA indices.

In the main group, however, the use of photodynamically activated disinfection of the periodontal complex proved to be a significant factor in further improving index values compared to the comparison group (treated according to standard clinical guidelines). These findings are consistent with those reported by Amoian B. et al. [20].

Overall, cytokines at the site of inflammation exhibit diverse and often opposing actions, frequently demonstrating synergistic, mutually activating, or antagonistic effects. This underscores the need to investigate the systemic interactions within the cytokine network in pathological conditions, rather than focusing solely on individual cytokines.

In patients with chronic generalized periodontitis, our study revealed an increase in the levels of pro-inflammatory cytokines–IL-1β, IL-6, IL-8, TNF-α, and IFN-γ–in oral fluid samples, accompanied by a decrease in anti-inflammatory cytokines–IL-4 and IL-10. This cytokine imbalance likely contributes to the progression and aggravation of the clinical periodontal condition.

Our findings are consistent with those reported by Medara N. et al. [11], Pan W. et al. [12], and Ramadan D.E. et al. [14].

According to recent international studies, the progression of inflammation in periodontal tissues is associated with a significant elevation of IFN-γ and induced production of IL-1β and TNF-α in oral fluid samples [7; 11]. Moreover, IL-4 has been shown to suppress the production of IL-1β, TNF-α, IL-6, and IL-8 [7], while IL-10 levels decrease in oral fluid under inflammatory conditions [10], all of which corroborate our current findings.

The implementation of high-quality therapeutic and preventive measures contributes to the reduction of inflammatory activity in periodontal tissues, as evidenced by decreased levels of pro-inflammatory cytokines and increased levels of anti-inflammatory cytokines in oral fluid samples. These cytokine changes were more pronounced in the main group receiving photodynamically activated disinfection.

At 14 days following treatment, no significant changes in cytokine levels were observed in the comparison group (treated according to clinical guidelines). In contrast, the main group showed statistically significant reductions in the levels of IL-6 and IFN-γ, as well as an increase in the anti-inflammatory cytokine IL-10, indicating the therapeutic benefit of photodynamic disinfection.

IL-1β is a key pro-inflammatory mediator associated with periodontal disease. Previous studies comparing healthy individuals and patients with chronic periodontitis have demonstrated lower IL-1β levels in periodontally healthy subjects and a decrease in IL-1β following periodontal treatment in affected patients [10], which is consistent with our findings.

Follow-up at 3 and 6 months revealed sustained improvements in cytokine profiles in both the main and comparison groups, with statistically significant differences compared to baseline levels ($p < 0.05$).

The IL-10/IL-1β ratio, used as an indicator of cytokine balance, was significantly altered before treatment in both groups compared to reference values:
– main group: 2.54 [1.73–3.46];
– comparison group: 2.23 [1.08–2.96], ($p < 0.001$, Mann–Whitney U test).

After 6 months, this ratio increased significantly:
– in the main group, it rose to 9.67 [7.44–10.8];
– in the comparison group, to 5.58 [4.36–6.58], with both changes being statistically significant ($p < 0.001$, Wilcoxon signed-rank test) compared to pre-treatment values.

The IL-10/TNF-α ratio prior to therapeutic and preventive interventions was significantly reduced ($p < 0.001$) compared to the reference range, reaching:
– 3.84 [2.66–4.97] in the main group;
– 3.53 [2.72–4.48] in the comparison group.
At 6 months, this ratio increased markedly to:
– 29.9 [25.8–31.6] in the main group;
– 21.8 [18.8–24.2] in the comparison group.
These changes were statistically significant compared to baseline values ($p < 0.001$, Wilcoxon signed-rank test).

Thus, the comprehensive assessment of the cytokine network demonstrated more pronounced differences in the effectiveness of therapeutic approaches between the clinical groups. From this perspective, the balance between pro-inflammatory and anti-inflammatory cytokines emerges as a key factor in the chronicity of periodontal inflammation, aligning with the findings reported in previous studies [6; 12].

The ratio of IL-10, as one of the most important anti-inflammatory cytokines, to pro-inflammatory markers such as IL-1β and TNF-α in oral fluid revealed significant differences in treatment outcomes between the group managed according to standard clinical recommendations (comparison group) and the group treated with adjunctive photodynamically activated disinfection (main group).

While the clinical progression of moderate chronic generalized periodontitis is naturally influenced by the combined effect and variability of internal and external risk factors, the inclusion of laser photodynamic disinfection in the treatment protocol was shown to accelerate the restoration of cytokine balance in periodontal tissues.

## CONCLUSION

1. In patients with moderate chronic generalized periodontitis, therapeutic and preventive interventions lead to an improvement in the clinical condition of periodontal tissues, reflected in the correction of periodontal and hygiene indices. Moreover, patients receiving photodynamically activated disinfection demonstrate statistically significantly lower periodontal index values ($p < 0.05$).

2. The course of moderate chronic generalized periodontitis is characterized by a shift in the cytokine profile of oral fluid, with a significant increase in IL-1β, IL-6, IL-8, TNF-α ($p < 0.01$), and IFN-γ ($p < 0.001$), along with a decrease in IL-4 ($p < 0.05$) and IL-10 ($p < 0.05$).

3. The inclusion of laser photodynamically activated disinfection in the comprehensive treatment protocol for moderate chronic generalized periodontitis contributes to the stabilization of the cytokine balance in oral fluid samples, which serves as an important marker of periodontal tissue condition during the remission stage.

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