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Dynamics of clinical and immunological parameters in the integrated management of endo-periodontal lesions, including laser therapy

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Abstract

Aim. To determine the dynamics of clinical changes and indicators of local immunity in integrating the diode laser into the treatment of the endo-periodontal lesion.

Methods. We performed a prospective study of 110 patients of both sexes aged 25–55 years with endo-periodontal lesions. The patients were randomized into two groups — the main group (n=54), whose received root canal treatment and periodontal pockets with a diode laser in addition to standard therapy, which included endodontic and periodontal treatment, and control group (n=56), whose patients received only standard treatment. The Green–Vermillion oral hygiene index and Russell's periodontal index, as well as the levels of immunoglobulin (Ig) A, tumor necrosis factor-alpha (TNF-alpha) and cytokine interleukin-10 (IL-10) in the mixed saliva of patients, were determined during the study. Quantitative data were described using median, lower and upper quartiles. These data were visualized using boxplots. The Mann–Whitney U test was used to compare differences between an independent set of quantitative data. Differences were considered significant at a confidence level of $p < 0.05$.

Results. The median oral hygiene index decreased from 2.9 to 1.0 ($p < 0.001$) in the main group and from 2.9 to 1.6 ($p < 0.001$) in the control group. The median Russell's periodontal index decreased from 3.38 to 1.3 ($p < 0.001$) in the main group and from 3.95 to 2.0 ($p < 0.001$) in the control group. The median immunoglobulin A content decreased from 5.25 to 3.13 mg/L ($p < 0.001$) in the main group and from 5.23 to 4.21 mg/L ($p < 0.001$) in the control group. The tumor necrosis factor-alpha level decreased from 16.65 pg/ml in the main group and 18.28 pg/ml in the control group to 3.96 and 8.44 pg/ml ($p < 0.001$), respectively. The median cytokine interleukin-10 levels increased from 0.83 to 2.94 pg/ml ($p < 0.001$) in the main group and from 1.29 to 2.13 pg/ml ($p < 0.001$) in the control group.

Conclusion. The use of a diode laser in the treatment of endo-periodontal lesions has a positive effect on the dynamics of clinical and immunological parameters, as evidenced by a statistically significant decrease in clinical indices, as well as the normalization of the immunoglobulin A and cytokine levels in mixed saliva.

Keywords: endodontic treatment, periodontitis, diode laser, local immunity, cytokines.

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Background. Inflammatory periodontal diseases are one of the most essential dental diseases. Despite advances in theoretical and practical dentistry, the incidence of inflammatory periodontal diseases is increasing, and the age threshold for the incidence of inflammatory processes in periodontal tissues tends to decrease. According to the World Health Organization, approximately 95% of adults and 80% of children have signs of periodontal disease. One of the urgent problems in contemporary dentistry is the study of combined lesions of the periodontium and endodontium [1–3].

Currently, concomitant endoperiodontal lesions (EPLs) represent the most complicated clinical cases with the poorest prognosis. Doctors, who most often faced with a similar problem, recommend removing the affected teeth, but with correct diagnostics and prescription of combination therapy, the prognosis can be significantly improved [3,4].

EPL is caused by progressive inflammation; therefore, the study of immunological parameters of the tissues surrounding the pathological focus is of great interest. Inflammatory processes in periapical tissues become a source of auto- and hetero-

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sensitization of the body, which reduces immune resistance. Currently, most researchers recognize an immune link in the pathogenesis of EPL [4–7]. According to the literature, indices of tissue immunity of the oral cavity in the presence of inflammatory periodontal and endodontal diseases are used to confirm the treatment efficiency and to determine the prognosis of reparative processes [8, 9].

The immune response to periodontal pathogens leads to the release of inflammatory mediators and cytokines, namely, low-molecular-weight glycoproteins acting in picomolar concentrations, regulating interactions, and activating immune response [7–10]. Cytokines are represented by molecules that have the ability to influence various components of the immune and inflammatory response [10, 11].

The clinical efficacy of laser therapy in dentistry has been the subject of many studies in different countries. These studies have confirmed the biostimulating effect of laser therapy, such as on the inflammatory, immune, and proliferative processes occurring in periodontal tissues [12–19]. The literature analysis of this issue revealed that the diode laser has significant clinical prospects, and the study of the problem of its use in the complex treatment of EPL remains relevant [15–19].

This study aimed to determine clinical changes and indices of tissue immunity when using a diode laser in the treatment of EPL.

Materials and methods of research. A randomized controlled trial conducted in the Kazan State Medical University was approved by the local ethics committee of Kazan State Medical University (Protocol No. 6, dated 06/28/2016). A total of 110 patients (40 men and 70 women) with EPL (primary endodontic/secondary periodontal lesions according to the Simon–Glik classification, 1972) were enrolled in the study. Differences by gender in the compared groups were not significant ($p = 0.198$).

Patients with EPL were distributed into two groups by simple randomization. The inclusion criteria were age 25–55 years and absence of aggravated somatic pathology (such as infection caused by the human immunodeficiency virus, tuberculosis, recent heart attack and stroke, and cancer). In the main group, 54 patients received the root canal treatment with a diode laser and laser curettage of periodontal recesses in addition to the standard treatment of EPL, which included professional oral hygiene, endodontic treatment, and periodontal treatment. In the control group, 56 patients received only standard treatment (i.e., professional oral hygiene, endodontic treatment, and curettage).

Clinical and immunological studies were performed in all patients with EPL prior to treatment. Clinical results were analyzed after 10 days as well as after 1, 3, and 6 months of treatment, and immunological studies were performed after 3 and 6 months.

Treatment protocol. At the first visit, after obtaining informed consent, all patients were taught oral hygiene with a selection of personal hygiene products. Then, all patients received professional oral hygiene care. At the next visit, endodontic treatment was performed, including instrumentation of root canals with Reciproc, Mtwo (VDW) systems up to the apex size with minimum of 30–40 according to ISO[1], irrigation of root canals with 3% sodium hypochlorite solution, and 17% ethylenediaminotetraacetic acid solution with passive ultrasonication using the VDW ULTRA device (Germany).

The main group underwent decontamination with laser radiation using a high-intensity dental diode laser Dr. Smile (Italy) with a wavelength of 980 nm, average treatment power of 1.25 W, and a peak power of 2.5 W, in a pulsed mode. The canal was irradiated with a laser, not reaching the apex by 1 mm, at 5 s per canal for three times, and irrigated with sodium hypochlorite solution and ethylenediaminotetraacetic acid. This procedure was not performed to the control group. The final stage was root canal obturation with gutta-percha using a sealer based on epoxy resins.

At the next visit (after 3–7 days), the main group underwent laser curettage of periodontal pockets using a diode laser. The average power of the procedure was 0.75 W, and the peak power was 2.5 W, with the pulsed mode. The exposure was 30 s per pocket, performed three times, and washed with 3% hydrogen peroxide solution. No bandages were applied. In the control group, periodontal pocket curettage was performed using Gracey curettes with application of antiseptic dressings (2% chlorhexidine in combination with metronidazole).

In this study, we examined the efficiency of EPL treatment with the inclusion of diode laser treatment of root canals and periodontal pockets as a combination therapy. During clinical examination, the hygienic state of the oral cavity was determined using the Green–Vermillion hygiene index (Oral Hygiene Index-Simplified, OHI-S) and the Russell periodontal index (PI). The state of tissue immunity was determined by levels of immunoglobulin A (IgA) and cytokines, such as tumor necrosis factor α (TNFα) and interleukin-10 (IL-10) in the mixed saliva of the patients. In the experiment using enzyme-linked immunosorbent assay, a set of reagents from Vector-Best, Novosibirsk, was used.

[1] ISO, International Organization for Standardization.

Table 1. Changes in the level of tumor necrosis factor α in the saliva of patients with endoperiodontal lesions, depending on the treatment method (pkg/ml)

Follow-up stage	Treatment method				p
	Standard treatment + diode laser		Standard treatment		
	Me	Q_1–Q_3	Me	Q_1–Q_3	
1. Before treatment	16.65	11.96–24.54	18.28	11.33–25.26	0.56
2. After 3 months	12.59	9.84–18.64	15.05	10.02–20.11	0.27
3. After 6 months	3.96	2.41–5.21	8.44	5.16–10.49	0.0005*
$p_{1–2–3}$	0.0006*	0.0007*			
$p_{1–2}$	0.012*	0.003*			
$p_{2–3}$	0.0004*	0.0005*			

Note: *differences between indicators were significant ($p < 0.05$).

Table 2. Changes in the interleukin-10 level with time in the saliva of patients with endoperiodontal lesions, depending on the treatment method (pkg/ml)

Follow-up stage	Treatment method				p
	Standard treatment + diode laser		Standard treatment		
	Me	Q_1–Q_3	Me	Q_1–Q_3	
1. Before treatment	0.83	0.63–1.28	1.29	0.74–1.41	0.012*
2. After 3 months	1.36	0.95–2.06	1.79	1.16–2.04	0.111
3. After 6 months	2.94	2.14–4.15	2.13	1.89–2.51	0.0006*
$p_{1–2–3}$	0.0004*	0.0004*			
$p_{1–2}$	0.0004*	0.0005*			
$p_{2–3}$	0.0002*	0.0003*			

Note: *differences between indicators were significant ($p < 0.05$).

Statistical processing of data was performed using parametric and nonparametric methods in accordance with the results of testing the populations compared for normality of distribution. Quantitative data are indicated as median with lower and upper quartiles. Such variables were represented graphically by means of box diagrams. The Mann–Whitney *U*-test was used to compare independent populations of quantitative data.

Results and discussion. In this study, we compared indicators of the immunological status of the oral cavity of patients with EPL depending on the chosen treatment method, namely, use of a diode laser (main group) or a standard method (control group). Table 1 shows the data when assessing changes in the level of TNFα in the saliva.

In the comparison of results, a significant negative trend of the TNFα level was found in the saliva of both groups ($p < 0.001$). However, with the use of both diode laser and standard treatment, the decrease was significant both after 3 months ($p = 0.012$ and $p = 0.003$, respectively) and after 6 months from the start of follow-up ($p < 0.001$ in both cases).

However, the decrease in the TNFα level in the saliva of the main group was more pronounced than that in the control group, as the median values decreased from 16.65 to 3.96 pkg/ml and from 18.28 to 8.44 pkg/ml, respectively ($p = 0.0003$). As a result, the TNFα levels achieved after 6 months in the main group were significantly lower ($p = 0.0008$) than in the control group.

Furthermore, we compared changes in the IL-10 level with time in the saliva of patients with EPL, depending on the treatment method (Table 2).

In both groups, the level of IL-10 in the saliva increased significantly ($p < 0.001$). For 6 months, an increase in the level of IL-10 was noted in all patients. Moreover, the increase in the level of IL-10 in the main group, despite the initially lower level ($p = 0.012$), was more pronounced, so the median level of IL-10 increased from 0.83 to 2.94 pkg/ml. With standard treatment, the level of IL-10 increased by less than two times, from 1.29 to 2.13 pkg/ml. As a result of such changes with time, after 6 months of follow-up, the level of IL-10 of the main group was significantly higher than that of the control group ($p < 0.001$).

When comparing the IgA level in the saliva of patients with EPL in the dynamics of treatment, depending on the method used, a negative

trend of the IgA level was noted during the treatment ($p < 0.001$); the IgA level decreased significantly throughout the follow-up period. At the start of the follow-up, the IgA levels in the saliva from both groups were comparable, namely, 5.25 g/L in the main group and 5.23 g/L in the control group ($p = 0.995$). Moreover, no significant differences were found in the IgA level 3 months after the start of treatment ($p = 0.283$). After 6 months, the median IgA level in the main group decreased to 3.13 g/L, while the level was significantly higher in the control group, amounting to 4.21 g/L, and the differences were significant ($p < 0.001$).

Thus, the use of a diode laser as part of the treatment protocol of patients with EPL lead to significantly more pronounced changes with time in the level of the studied cytokines in the saliva; thus, the levels of TNFα and IgA at the end of treatment were significantly lower and the level of IL-10 was higher than that with standard treatment.

We also compared the indicators of the dental status in the dynamics of EPL correction, depending on the treatment method applied. When comparing changes in OHI-S, depending on the treatment, a significant decrease in the OHI-S index was recorded in both groups ($p < 0.001$). With diode laser treatment, the median OHI-S index decreased from 2.9 to 1.0, but with standard treatment, the change was less pronounced and a decrease from 2.9 to 1.6 was noted. In the main group, as the decrease was significant both during the first 3 months and from month 3 to month 6 of follow-up ($p < 0.001$ and $p = 0.022$, respectively); in the control group, the changes were significant only in the first half of the follow-up period ($p < 0.001$), and from month 3 to month 6, the OHI-S index remained at the same level without noticeable changes over time ($p = 0.358$).

Significant differences were found in OHI-S index values compared depending on the treatment performed at the initial stage, as well as after 10 days and 1 month from the start of treatment ($p > 0.05$). After 3 months, the OHI-S index in the main group was significantly lower than that in the control group ($p = 0.001$), and after the follow-up period, due to a further decrease in the OHI-S index, the differences became even more pronounced, so the median was 1.0 in the main group and 1.6 in the control group ($p < 0.001$).

Further, PI changes in the compared groups were analyzed. We found significant PI changes both with the use of a diode laser and with standard treatment of patients with EPL ($p < 0.001$). In the main group, the decrease in PI was significant throughout the follow-up period, namely, both after 3 months and after 6 months ($p < 0.001$ in both cases). In the control group, PI decreased significantly after 3 months ($p < 0.001$), but after 6 months, compared with the previous stage, the level of significance of changes was close to critical one ($p = 0.051$).

As regards the difference in PI depending on the treatment used at different stages of follow-up, with an initially comparable level of PI ($p = 0.259$), at 10 days after the start of treatment, the PI in the main group was significantly lower than that in the control group ($p < 0.001$). At this stage, the median PI was 2.1 with diode laser treatment and 3.1 with standard treatment, that is, 1.5 times higher. The median PI between the diode laser treatment and standard treatment groups was 1.5 and 2.1 after 1 month ($p < 0.001$), 1.4 and 2.0 after 3 months ($p < 0.001$), and 1.3 and 2.0, respectively, by the end of the follow-up period ($p < 0.001$).

Despite the significant favorable tendencies of dental indices in both groups, changes in indicators in the latter half of the follow-up period with standard treatment were not significant. This explains the achievement of significantly lower indices and less severe pathological process with diode laser treatment compared with standard treatment at month 6.

CONCLUSIONS

1. The use of a diode laser in the combination treatment of EPLs improves both clinical parameters and the state of tissue immunity in patients with this pathology, normalizing the level of cytokines in the saliva.

2. We recommend the clinical application of diode lasers as an additional tool in the treatment of EPLs owing to their ability to reduce the intensity of inflammation and improve the tissue immunity of the oral cavity.

Author contributions. S.L.B. created the concept and design of the study and wrote the text; E.V.K. analyzed the data obtained, performed dental treatment and diagnostic studies, and wrote the text; I.G.M. created the study concept, analyzed the data, and wrote the text; I.Kh.V. performed laboratory diagnostics and the data analysis; Yu.V.B. collected and processed the materials and performed the literature review.

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