

EFFECTIVENESS OF LASER THERAPY IN COMPLEX TREATMENT OF HERPETIC STOMATITIS

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Yulia G. Kolenko, Tetiana O. Timokhina, Nina S. Khrol, Oksana V. Kononova, Olesya V. Lynovytska

BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE

ABSTRACT

The aim: The purpose of research is to improve the effectiveness of treatment by applying laser in complex treatment in patients with herpetic stomatitis.

Materials and methods: Were examined 47 people (22 men and 25 women) with acute herpetic stomatitis. The patients' age was from 20 to 72 years. All patients underwent immunological tests such as (T-lymphocytes (CD3 +), T-helpers (CD4 +), cytotoxic T-lymphocytes (CD8 +), the content of immunoglobulins IgM, IgG, IgA and sIgA in saliva to assess the immunological reactivity of the organism.

Results: Clinical observations have shown that when using laser therapy, the results of treatment were better than in the control group. Positive dynamics was observed as early as 1-2 days after the start of laser use and was more pronounced when used in the early stages of the disease. The use of the laser promoted a more rapid suspension of new lesions, a decrease in pain syndrome, and a more rapid regression of herpetic lesions. We have found significant improvements in the parameters of cellular and humoral immunity in patients of the main group.

Conclusions: Treatment of herpetic stomatitis is relevant and requires further improvement and the search for new methods. The use of a laser in the complex treatment of herpetic stomatitis has a positive effect on the course and immunological status of patients with herpetic stomatitis. The manifestations of the disease healed faster, and the pain syndrome was less severe. Duration between illness and treatment decreased on 19.7% and 26%. It is advisable to include the method of treatment using a laser in the complex therapy of herpetic stomatitis.

KEY WORDS: herpetic stomatitis, laser, cellular and humoral immunity

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INTRODUCTION

Herpetic lesions of the oral mucosa are among the most serious diseases. These lesions are found in different climate zones, while the frequency of occurrence varies widely depending on population groups with different living standards. All over the world, there is a tendency in the spread of the herpes simplex virus [1,2]. The increased incidence is related to the prevalence of asymptomatic and undiagnosed forms of the disease, but this is an objective process, unfortunately, is not accompanied by a radical change to this disease, both doctors and the people.[3]. Today, the problem of herpetic stomatitis is relevant for doctors of many specialties such as dentists, dermatologists, pediatricians, therapists and family doctors. According to modern estimates, the infection of the population with the herpes simplex virus is very high and even approaches 100% [3,4].

During herpes simplex virus latency, under certain conditions, causes an exacerbation of the disease, that manifested as herpetic stomatitis.

The precipitating factors in the development of herpetic stomatitis relate a change in the quantitative composition of the microflora of the oral cavity, chronic diseases of the upper respiratory tract, traumatic removal of the lower

third molars, neuropsychiatric stress and emotional stress, radiation therapy and tobacco smoking.

Thus, the activation of the chronic inflammatory process in herpetic stomatitis is the result of a synergistic interaction between the protective forces of macroorganism and virus; therefore, it will not be effective enough to take only various antiviral drugs by individuals with initially reduced functional activity of the immune system [5].

THE AIM

Objective of work is to improve the effectiveness of treatment by applying laser in complex treatment in patients with herpetic stomatitis.

MATERIALS AND METHODS

Were examined 47 people (22 men and 25 women) with acute herpetic stomatitis, who appealed to the dental medical center of the National Medical University, named after A.A. Bogomolets, at the Department of Therapeutic Dentistry. The etiology of lesions caused by the herpes simplex virus was determined on the basis presence a typical clinical symptoms of the disease and by performing a PCR test (polymerase chain reaction).



Fig. 1. Herpetic eruptions on the red border of the lower lip.



Fig. 2. Herpetic eruptions on the red border of the upper lip and around the nose.

The age of patients with herpetic stomatitis was from 20 to 72 years old. Set average age - 42.2 years old.

Complaints and personal clinical history of each patient were carefully examined. Particular attention was paid to the nature of the disease; possible causes herpetic stomatitis and its exacerbations, prior therapy and its effectiveness, diet, work, the presence of somatic diseases and stress. Allergy status also was taken into account. More than half of the patients (57.4%) sought for medical care on 2-3rd day after the disease manifested itself. Most of the patients had concomitant diseases such as hypertension, coronary heart disease, diabetes mellitus, cholelithiasis, gastric ulcer and duodenal ulcer, chronic pancreatitis, chronic bronchitis, bronchial asthma, chronic adnexitis, etc. Herpes simplex virus were also detected in two patients with malignant tumors and in one patient infected with HIV.

The condition of the skin of the oral region, the red border of the lips, corners of the mouth and oral mucosa, palatine arches, tonsils, posterior pharyngeal wall and tongue were clinically assessed. Their color, moisture, consistency, and the presence of rashes were noted. Particular attention was paid to the rehabilitation of the oral cavity: the presence of decayed teeth, sharp edges of teeth, amalgam fillings; the presence of prostheses made of dissimilar metals, orthodontic appliances, the condition of periodontal tissues.

Herpetic eruptions prevailed in the area in the red border of the upper or lower lips in 23 (48.9%) cases (Fig. 1), in 11 (23.5%) cases in the area of the hard palate and gingival margin, in 3 x cases (6.4%) accounted for lesions of the soft palate, in seven (14.8%) - lesions in the area of the red border of the lips and nasal passages (Fig. 2), and in three cases (6.4%) - on the lateral surface of the tongue. The disease was mild to moderate, and therefore the patients were mostly on outpatient treatment.

All patients underwent immunological tests to assess the immunological reactivity of the organism. In order to study various factors of immunity was carried out sampling of peripheral blood from a vein in the patient in dynamics: before treatment and on the 5-7th day after treatment. T-lymphocytes (CD3 +), T-helpers (CD4 +), cytotoxic T-lymphocytes (CD8 +) were identified using TAs labeled with fluorescein-5 isothiocyanate (FITC).

The results were recorded on a FACSCalibur flow cytometer (Becton Dickinson) using the «Simulset» software in a specially designed panel. The content of immunoglobulins IgM, IgG, IgA and sIgA in saliva was determined using the classical method of radial immunodiffusion according to Mancini.

The patients were divided into 2 groups. All patients received general therapy according to the protocols of herpetic stomatitis treatment. Patience from main group,

Table I. Localization of herpetic stomatitis.

Research groups	Q-ty of patients	The number of patients with different localization				
		red border of the upper or lower lip	hard palate and gingival margin	soft palate	red border of lips and nasal passage	lateral border surface of the tongue
Main group (1 group)	29	15 (51,72%)	6 (20,69%)	2 (6,9%)	4 (13,79%)	2 (6,9%)
Control group (2 group)	18	7 (38,89%)	5 (27,78%)	1 (5,56%)	3 (16,67%)	1 (5,56%)

Table II. Results of clinical studies of herpetic stomatitis treatment in the observation groups.

Groups	Clinical characteristics		
	Epithelialization of erosion (days)	Reduction or complete disappearance of mouth pain and discomfort (days)	Normalization of the general condition of patients (days)
Main	5--7	1--2	2--3
Control	8--12	3--6	5--6

Table III. Indicators of the body's immunological reactivity by using various treatment methods of herpetic stomatitis.

Indicators	Main group		Control group	
	Before treatment	After treatment	Before treatment	After treatment
CD3 ⁺ , %	55,20 ± 1,42	62,0 ± 1,50	55,50 ± 2,10	56,80 ± 1,86
CD4 ⁺ , %	32,10 ± 1,80	36,60 ± 2,67	32,20 ± 1,86	31,70 ± 0,95
CD8 ⁺ , %	23,80 ± 1,30	27,0 ± 1,02	22,40 ± 1,23	23,10 ± 1,09
CD4 ⁺ /CD8 ⁺	1,34 ± 0,03	1,35 ± 0,04	1,43 ± 0,06	1,37 ± 0,12
NK-cells, %	11,10 ± 0,78	11,70 ± 1,79	12,0 ± 1,59	11,30 ± 1,03
CICs	0,102 ± 0,01	0,07 ± 0,005	0,132 ± 0,055	0,1 ± 0,005

Note: Reliability Indicator ($P < 0.001$).

Table IV. Indicators of the level of immunoglobulins in saliva in patients with CGS before and after treatment.

Indicators	Main group		Control group	
	Before treatment	After treatment	Before treatment	After treatment
IgM, m%	8,74 ± 0,7	3,45,0 ± 0,50	8,68 ± 0,10	6,23 ± 0,4
IgG, m%	13,52 ± 1,20	9,33 ± 0,67	13,48 ± 0,86	11,13 ± 0,5
IgA, m%	7,20 ± 0,50	15,74 ± 0,3	7,40 ± 0,4	7,8 ± 0,4
sIgA, m%	8,9 ± 0,2	21,94 ± 0,2	8,8 ± 0,6	11,49 ± 0,12

Note: Reliability Indicator ($P < 0.001$).

as a local treatment were used a diode laser to treat affected areas by continuous wave 0.400 mm / 980 nm for 60 seconds at 0.7 w. Patients from control group were used topical antiviral drugs locally.

Data were analyzed by using Statistical Package for Social Sciences software for Windows, version 18.0 (SPSS Inc., Chicago, USA). Descriptive statistical analysis was performed to tabulate our results. The reliability was assessed at the 5% significance level. Values were recorded and subjected to analysis of variance (ANOVA) and Tukey post-hoc test with $P < 0.001$ as statistically significant.

RESULTS

In terms of age, premorbid background and severity of the course, both groups of patients were similar. Localization of herpetic lesions were not significantly different (Table I).

The assessment of the therapeutic effectiveness of the use of laser therapy was carried out taking into account following clinical data: patient complaints, the rate of regression of herpetic elements, the duration of treatment and the results of immunological studies.

Clinical observations have shown that, the results of using laser treatment were better compared to the control group. Positive dynamics was observed on 1-2 day after starting use of the laser, and was more pronounced already on early stages of the disease. The use of the laser promoted a more rapid suspension of new lesions, decrease pain syndrome, a more rapid regression of herpetic lesions (Table II).

The use of laser therapy led to a reduction in the duration of bubbles and erosions from 5.9 ± 1.08 days in the control group to 2.58 ± 0.7 days in the main group. Were observe an intensity decrease of pain syndrome in the first 2-3 days after treatment in 38.9% of patients in the control group

and in 79.3% of patients in the main group, and after 4 days of treatment, the intensity of pain syndrome decreased in 100% of patients from main group and in 75.8 % of patients in the control group. The formation and falling off of crusts also occurred faster in the patients of the main group.

In the study of the immunological status, positive changes were also noted in all links of immunity (Table III).

The use of laser therapy in the main group of patients showed an increase in the content of CD3 + lymphocytes from 55.2 ± 1.42 to $62 \pm 1.5\%$ compared to $56.8 \pm 1.86\%$ in the control group; there was also an increase in the content of CD4 + lymphocytes from 32.1 ± 1.8 to $36.6 \pm 2.67\%$ compared to $31.7 \pm 0.95\%$ in the control group and CD8 + lymphocytes from 23.8 ± 1.3 to $27.0 \pm 1.02\%$ versus $23.1 \pm 1.09\%$ in the control group ($P < 0.001$). The number of NK cells did not change significantly. The indices of circulating immune complexes (CICs) significantly improved in the group where laser therapy was used (Table III).

There was also an increase in the level of sIgA and a decrease in the level of secretory Ig G and IgM in saliva, which suggests that the inflammatory process subsided as a result of the antioxidant and anti-inflammatory activity of laser therapy (Table IV).

Using laser therapy in the main group of patients revealed increase content of secretory IgA from 8.9 ± 0.2 to 21.94 ± 0.2 mg% compared to 11.49 ± 0.12 mg% in the control group; there was also an increase in the IgA content from 7.20 ± 0.50 to 15.74 ± 0.3 mg% compared to 7.8 ± 0.4 mg% in the control group and a decrease in the IgG content from 13.52 ± 1.20 to 9.33 ± 0.67 mg% versus 11.13 ± 0.5 mg% in the control group ($P < 0.001$).

Thus, the use of a laser in the treatment of patients with herpetic stomatitis had a positive effect on the indicators of the body's immunological reactivity, and the conventional symptomatic therapy did not provide significant changes in any of the studied indicators of immunological reactivity - the violation of immune homeostasis remained uncompensated.

DISCUSSION

One of the most effective modern methods of treating diseases of periodontal tissues and oral mucosa is a diode laser. Scientific research has demonstrated that diode laser is capable to dissecting, coagulating and ablating biological tissue, and the whole process occurs quickly and silently [6,7,8,9]. The mechanism of high-energy laser with high continuous power based on the influence of the high-temperature factor, which is limited by a strictly local nature. Under the condition of a certain duration of temperature exposure, the tissue substrate "burns out" with the formation of a defect from the adjacent coagulation necrosis zone [10, 11, 12].

Thus, it was found that in patients with various pathologies of the soft tissues of the oral cavity using a diode laser with a wavelength of 970 nm, twice reduced the terms wound epithelialization (7.0 ± 0.5 days) [13].

In our study, it was found that the average duration of the disease and treatment in the control group was 12.4 ± 3.0 and 10.4 ± 2.7 , and in the main group - 9.0 ± 4.1 and 7.4 ± 2.3 days.

The laser also has an anti-inflammatory and repair-stimulating effect. Studies carried out in recent years have revealed the antibacterial potential of laser therapy [14,15,16]. The results of the study by M. Giannelli et al. (2012) demonstrated the bacteriostatic and bactericidal properties of a diode laser [17].

E.R. Kusek et al. (2012) published a study showing that a diode laser stimulates the immune defense system, reduces the pathogenicity of microflora, increases its sensitivity to antibiotics, and positively regulates the functions of a cement plaque in vitro [18]. M. Pourhajibagher et al. (2017) note that a 940 nm diode laser with a radial firing tip showed a satisfactory bactericidal effect without any thermal side effect on tissue [19].

As it is known, during inflammation, laser radiation causes general and local effects. The general effect is expressed in an increase in the content of nonspecific humoral defense factors (such as complement, interferon, and lysozyme), general leukocyte reaction, and increase in the phagocytic activity of micro- and macrophage systems. There is a desensitizing effect, activation of the immunocompetent system, cellular and humoral specific immunological protection, and increase in the general protective and adaptive reactions of the body [20,21,22].

We have found significant improvements in the parameters of cellular and humoral immunity in patients of the main group, which indicates that use of a laser helps to stop the inflammatory process.

Local laser radiation exposure is considered according to the main elements of the inflammatory response: exudation, alteration, proliferation [23, 24]. So, when studying the effect of laser radiation on the state of local immunity in the oral cavity in patients with purulent-inflammatory diseases of the maxillofacial region, it was found that the use of a laser normalizes secretory, humoral and cellular factors of local protection, promotes an increase in the phagocytic function of neutrophils and completely restores the relationship between cellular and humoral links of immunity.

CONCLUSIONS

1. Treatment of herpetic stomatitis is relevant and requires further improvement and the search for new methods.
2. The use of a laser in the complex treatment of herpetic stomatitis has a positive effect on the course and immunological status of patients with herpetic stomatitis. The manifestations of the disease healed faster, and pain syndrome manifested itself less. Duration between illness and treatment decreased on 19.7% and 26%.
3. It is advisable to include the method of laser treatment in complex therapy of herpetic stomatitis.

REFERENCES

1. Van Oeffelen L., Biekram M., Poeran J. et al. Update on Neonatal Herpes Simplex Epidemiology in the Netherlands: A Health Problem of Increasing Concern? *Pediatr Infect Dis J.* 2018;37(8):806-813.
2. Chaabane S., Harfouche M., Chemaitelly H. et al. Herpes simplex virus type 1 epidemiology in the Middle East and North Africa: systematic review, meta-analyses, and meta-regressions. *Sci Rep.* 2019;9(1):1136.

3. Rechenchoski D.Z., Faccin-Galhardi L.C., Linhares R.E.C., Nozawa C. Herpesvirus: an underestimated virus. *Folia Microbiol (Praha)*. 2017;62(2):151-156.
4. Pfaff F., Groth M., Sauerbrei A., Zell R. Genotyping of herpes simplex virus type 1 by whole-genome sequencing. *J Gen Virol*. 2016;97(10):2732-2741.
5. Zhang J., Liu H., Wei B. Immune response of T cells during herpes simplex virus type 1 (HSV-1) infection. *J Zhejiang Univ Sci B*. 2017;18(4):277-288.
6. Cobb C.M. Commentary: Is there clinical benefit from using a diode or Nd:YAG laser in the treatment of periodontitis? *J. Periodontol*. 2016; 87 (10): 1117–1131. DOI: 10.1902/jop.2016.160134.
7. Roncati M., Gariffo A. Systematic review of the adjunctive use of diode and Nd:YAG lasers for nonsurgical periodontal instrumentation. *Photomed. Laser. Surg.* 2014; 32 (4): 186–197. DOI: 10.1089/pho.2013.3695.
8. Kurtzman G.M., Hughes M.K. Evolution of Comprehensive Care, Part 3. Periodontal Treatment Continues to Evolve. *Dent. Today*. 2015; 34 (5): 90, 92, 94–97.
9. Cobb C.M., Blue M.S., Beaini N.E. et al. Diode laser offers minimal benefit for periodontal therapy. *Compend. Contin. Educ. Dent*. 2012; 33 (4): e67–e73.
10. Low S.B., Mott A. Laser technology to manage periodontal disease: a valid concept? *J. Evid. Based. Dent. Pract.* 2014; 14: 154–159. DOI: 10.1016/j.jebdp.2014.03.010.
11. Falkenstein F., Gutknecht N., Franzen R. Analysis of laser transmission and thermal effects on the inner root surface during periodontal treatment with a 940-nm diode laser in an in vitro pocket model. *J. Biomed. Opt.* 2014; 19 (12): 128–202. DOI: 10.1117/1.JBO.19.12.128002.
12. Ozgursoy O.B., Garvey C. Cost-effective and safe dental protection for trans oral laser microsurgery. *J. Otolaryngol. Head Neck Surg.* 2010; 39 (3): E16–E17.
13. Sgolastra F., Severino M., Gatto R., Monaco A. Effectiveness of diode laser as adjunctive therapy to scaling root planning in the treatment of chronic periodontitis: a meta-analysis. *Lasers. Med. Sci.* 2013; 28 (5): 1393–1402. DOI: 10.1007/s10103-012-1181-5.
14. Fekrazad R., Nokhbatolfighahaei H., Khoei F., Kalhori K.A. Pyogenic granuloma: surgical treatment with Er:YAG laser. *J. Lasers Med. Sci.* 2014; 5 (4): 199–205.
15. Chang P.C., Chien L.Y., Ye Y., Kao M.J. Irradiation by light-emitting diode light as an adjunct to facilitate healing of experimental periodontitis in vivo. *J. Periodontal. Res.* 2013; 48 (2): 135–143. DOI: 10.1111/j.1600-0765.2012.01511.x.
16. He W.L., Yu F.Y., Li C.J. et al. A systematic review and meta-analysis on the efficacy of low-level laser therapy in the management of complication after mandibular third molar surgery. *Lasers. Med. Sci.* 2014; 30 (6): 1779–1788. DOI: 10.1007/s10103-014-1634-0.
17. Giannelli M., Formigli L., Lorenzini L., Bani D. Combined photoablative and photodynamic diode laser therapy as an adjunct to non-surgical periodontal treatment: a randomized split-mouth clinical trial. *J. Clin. Periodontol.* 2012; 39 (10): 962–970. DOI: 10.1111/j.1600-051X.2012.01925.x.
18. Kusek E.R., Kusek A.J., Kusek E.A. Five-year retrospective study of laser-assisted periodontal therapy. *Gen. Dent.* 2012; 60 (5): e291–e294.
19. Bozkurt S.B., Hakki E.E., Kayis S.A. et al. Biostimulation with diode laser positively regulates cementoblast functions, in vitro. *Lasers. Med. Sci.* 2017; 32 (4): 911–919. DOI: 10.1007/s10103-017-2192-z.
20. Pourhajibagher M., Chiniforush N., Ghorbanzadeh R., Bahador A. Photo-activated disinfection based on indocyanine green against cell viability and biofilm formation of *Porphyromonas gingivalis*. *Photo Diagnosis Photo In Ther.* 2017; 17 (3): 61–64. DOI: 10.1016/j.pdpdt.2016.10.003.
21. Cappuyns I., Cionca N., Wick P. et al. Treatment of residual pockets with photodynamic therapy, diode laser, or deep scaling. A randomized, split-mouth controlled clinical trial. *Lasers. Med. Sci.* 2012; 27 (5): 979–986. DOI: 10.1007/s10103-011-1027-6.
22. Dominguez A., Gómez C., García-Kass A.I., García-Núñez J.A. IL-1beta, TNF-alpha, total antioxidative status and microbiological findings in chronic periodontitis treated with fluorescence-controlled Er:YAG laser radiation. *Lasers. Surg. Med.* 2010; 42 (1): 24–31. DOI: 10.1002/lsm.20873.
23. Giannelli M., Bani D., Viti C. et al. Comparative evaluation of the effects of different photoablative laser irradiation protocols on the gingiva of periodontopathic patients. *Photomed. Laser. Surg.* 2012; 30 (4): 222–230. DOI: 10.1089/pho.2011.3172.
24. Decker E.M., Bartha V., von Ohle C. Improvement of antibacterial efficacy through synergistic effect in photodynamic therapy based on thiazinium chromophores against planktonic and biofilm-associated periodonto pathogens. *Photomed. Laser. Surg.* 2017; 35 (4): 195–205. DOI: 10.1089/pho.2016.4152.
25. Saglam M., Kantarci A., Dundar N., Hakki S.S. Clinical and biochemical effects of diode laser as an adjunct to nonsurgical treatment of chronic periodontitis: a randomized, controlled clinical trial. *Lasers. Med. Sci.* 2014; 29 (1): 37–46. DOI: 10.1007/s10103-012-1230-0.

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ORCID and contributionship:

Yulia G. Kolenko: 0000-0003-1659-3333 ^{A, B, D, E, F}

Tetiana O. Timokhina: 0000-0002-0220-0220 ^{B, C, D, F}

Nina S. Khrol: 0000-0001-7317-6590 ^{A, B}

Oksana V. Kononova: 0000-0002-7099-5168 ^{B, C}

Olesya V. Lynovytska: 0000-0001-6723-6921 ^C

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Tetiana O. Timokhina

Bogomolets National Medical University

1 Zoologichna st., 03057 Kyiv, Ukraine

tel: +380961111122

e-mail: tanyatimokhina@gmail.com

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