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The Impact of Low-Intensity Laser Therapy in Rhinosinusitis

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ABSTRACT

Rhinosinusitis (RS) is a frequent problem in modern otolaryngology. But all the available methods do not make it possible to completely cure this pathology. The answer to this question may be an alternative treatment that is carried out on animals in order to find new technologies to eliminate RS. Little is known about alternative treatment options for rhinosinusitis. We sought to evaluate the effectiveness of low-intensity laser therapy (LILT) for RS in experimentally induced models of RS in rabbits, since the tissue of the nasal sinuses is almost identical to human.

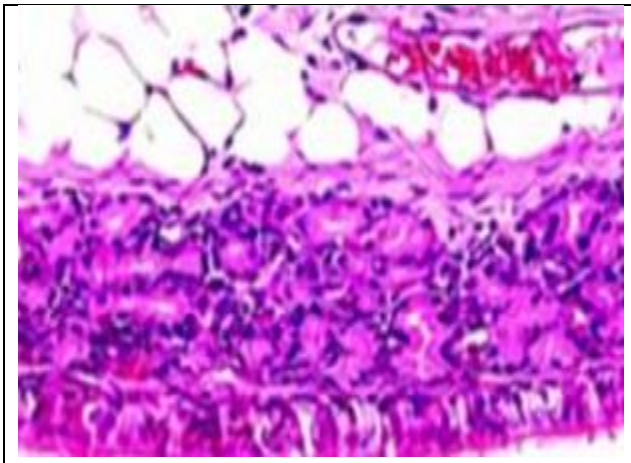
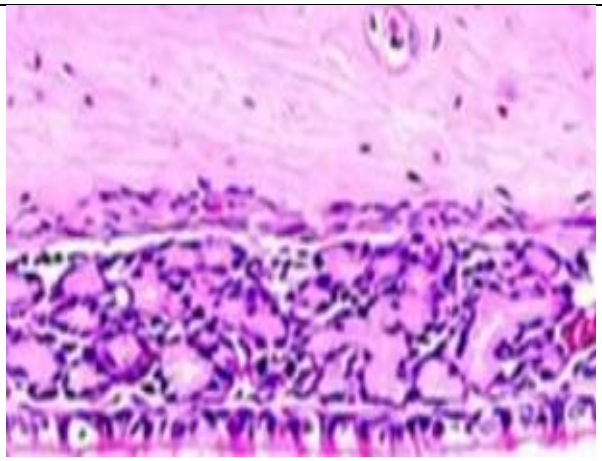
Relevance. Rhinosinusitis (RS) is one of the most common inflammatory diseases of the upper respiratory tract, characterized by nasal congestion, postnasal congestion, rhinorrhea and facial pain [1,2,3]. Standard treatment for RS includes appropriate drug therapy, such as saline lavage, antibiotics, and topical/systemic steroids. Endoscopic surgery of the paranasal sinuses was performed to treat cases of refractory or recurrent RS, despite appropriate drug therapy. However, there is not enough information about alternative treatment for RS. Some data have appeared on the effectiveness of low-level laser therapy (LILT), but since many studies were conducted on rats, the obvious advantages and disadvantages of this method were not evaluated. Low—level laser therapy (LILT) is a form of phototherapy that involves radiation using photon energy at low levels to change biological activity without thermal damage [4]. Compared to high-level lasers, LILT uses energy at low levels sufficient to stimulate tissue response, which leads to tissue regeneration [5]. Thus, LILT is considered non-toxic and non-allergenic and is widely used for medical purposes, such as tissue repair, anesthesia and treatment of diseases of the musculoskeletal system [6,7,8,9]. LILT is also applied to the upper and lower respiratory tract [10,11]. Due to its anti-inflammatory effect, it can be assumed that LILT may also be effective as an additional treatment for RS. We decided to use rabbits for this. Using rabbit models for RS has several advantages. Firstly, anatomically, rabbit RS is comparable to human RS due to the fact that they have a relatively large maxillary sinus. Secondly, histologically, it is easy to obtain sufficient inflamed mucous membrane of the nose and paranasal sinuses for microscopic analysis.

The purpose of the study. To evaluate the effectiveness of low-intensity laser therapy (LILT) in RS on experimentally induced models of MS in rabbits

Materials and methods of research. Eighteen female New Zealand white rabbits (8 weeks old,

3.1–3.5 kg) were used for the study. Before the start of RS, all rabbits were acclimatized in an animal room with sufficient food and water for 1 week. Rabbits were randomly divided into four groups (n=18 in total): the negative control group (n=3), the positive control group (n=5), the natural recovery group (n=5) and the laser control group, the treated group (n=5). Before the RS induction procedure, 15 rabbits (positive control, natural recovery groups and laser-treated) were anesthetized by intramuscular injection of 50 mg/kg ketamine hydrochloride and 5 mg/kg xylazine hydrochloride. Then, with the help of a surgical drill, a window was made into the maxillary bone about 3 cm in size . A piece of Merocel sponge measuring 3×5×25 mm (Medtronic-Xomed, USA) was inserted into one sinonasal cavity, and the other cavity was left untreated as a control side. Two weeks later, the Merocel sponge was removed, and the rabbits were killed. Meanwhile, in the natural recovery group, natural recovery was achieved within 1 week by reopening the sinus mouth after removal of the Merocel sponge. In the laser treatment group, laser irradiation was additionally performed for 1 week. None of the rabbits received any medications, such as antibiotics or steroids, before or during the procedure. In addition, rabbits in the group receiving laser treatment were subjected to LILT (multi-wave and multi-power (AlGaInP 670 nm at 3 MW, GaAs 830 nm at 20 MW), OptowellCo., Ltd., Jeonju, Republic of Korea for 1 week. Laser irradiation was applied to the nasal cavity of rabbits under anesthesia.

The results of the study. The thickness of the epithelium was significantly hypertrophied in the MS-induced groups (positive control groups and natural recovery groups), while the thickness of the epithelium decreased almost to the control thickness with the help of LILT (laser-treated group) ($p<0.001$, negative control compared with positive control), groups; ($p<0.001$, negative control against natural recovery groups). Total infiltration of inflammatory cells was noticeably observed in the positive control and natural recovery groups compared to the negative control group ($p=0.09$, the negative and positive control group; $p<0.001$, the negative and natural recovery groups). Interestingly, the infiltration was significantly restored with the help of LILT (laser-treated group) compared to that in the natural recovery group ($p=0.002$). Similarly, the infiltration of goblet cells, eosinophils and mast cells was significantly observed in the positive control and natural recovery groups compared to the negative control group ($p<0.001$, negative control compared to positive control groups; $p<0.001$, negative control compared to positive control groups, natural recovery groups, while cellular infiltration decreased markedly in the laser-treated group compared to that in the natural recovery group ($p<0.001$).

	
after surgery without the use of medication	**after using LILT**

Thus, histopathological analysis showed that RS can be treated more effectively with the help of LILT. In Figure 1 comparative morphological pictures are given after the operation performed without the use of drugs and with the use of LILT.

In Figure 1 we can see the accumulation of neutrophils in the area of tissue on which no drugs were used, whereas on the second one their number is significantly less. This shows a decrease in the inflammatory process after the use of LILT compared to placebo. In addition, the effectiveness of LILT against experimentally induced RS was confirmed by the levels of mRNA and protein. mRNA levels of typical cytokines Th1 and Th17, IFN-γ and IL-17, in the mucous membrane of the paranasal sinuses increased after induction of MS (positive control group) compared with negative control. Slightly reduced mRNA expression was observed in the natural recovery group compared to the positive control group. Interestingly, the relative expression of mRNA, as a rule, was restored in the group receiving laser treatment, although without statistical significance. Similarly, the Th2 cytokine IL-5 showed similar trends to those for IFN-γ and IL-17.

IFN-γ protein levels measured by Western blotting were markedly increased in the positive control group compared to those in the negative control group. IFN-γ protein levels in the laser-treated group showed a marked decrease compared to the natural recovery group, but without statistical significance ($p=0.243$). The level of IL-5 protein showed a similar result according to Western blotting. On the other hand, the expression of the IL-17 protein did not undergo significant changes in all groups.

Discussion. The present study has shown that NLT significantly improves experimentally induced RS. Radiologically experimentally induced RS was confirmed using a piece of surgical sponge. Histopathologically, the infiltration of inflammatory cells was significantly observed in experimentally induced RS rabbits compared to the negative control group. Immunologically, the expression of inflammatory cytokines was increased in the experimentally induced RS groups compared to the negative control group. These parameters were restored after surgical removal of the sponge. In addition, LILT led to accelerated improvement compared to natural recovery. Summing up all these results, it can be assumed that LILT has a therapeutic effect on RS, from a histological point of view, it has been shown that LILT increases the deposition of collagen fibers, promotes fibroblast proliferation and enhances microcirculation in local tissues, which leads to beneficial physiological cycles. Our histopathological results based on the thickness of the epithelium have shown that LILT can significantly reduce tissue fibrosis depending on the thickness of the epithelium. Moreover, we have demonstrated that LILT significantly reduces the deposition of goblet cells, eosinophils and mast cells in the nasal sinus mucosa. Based on these histological data, it can be considered that LILT is suitable for the nasal mucosa and paranasal sinuses. In our study, the representative expression of cytokines Th1 (IFN-γ) and Th17 (IL-17) was increased in experimentally induced MS rabbits compared to the negative control group. It is noteworthy that the expression of these cytokines was improved in rabbits treated with LILT, compared with rabbits recovering naturally.

Although our rhinogenic model induced mainly bacteriological and neutrophilic inflammation, allergic markers such as IL-5 expression showed similar results for the expression of cytokines Th1 and Th17. In addition, elevated serum levels of total IgE in experimentally induced RS rabbits were restored in laser-treated rabbits. Thus, allergy and RS affect each other in the mucous membrane of the respiratory tract. In addition, according to clinical studies, year-round allergy plays a significant role in chronic and recurrent acute RS [52].

Conclusions. The use of LILT in combination with standard treatment leads to rapid healing, compared to standard treatment only.This model of rabbits with RS allows us to fully assess the changes occurring in the sinus tissues that are similar to human ones.

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