

Article

Clinical application of photobiomodulation therapy to reduce the severity of acute pain after septoplasty

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Abstract: The purpose of the study: to evaluate the effectiveness of photobiomodulation (PBM) in the early postoperative period after septoplasty. Materials and methods: 62 patients have undergone septoplasty under general anaesthesia. Among them, there were 40 men and 22 women from 18 to 44 years of age. After septoplasty, the nasal cavity was tamponaded with foam tampons in glove rubber. The patients were divided into two groups of 31 participants, with the equal number of men and women in each of them. Patients of group 2 underwent PBM in 3 hours, 6 hours and 24 hours after septoplasty. The emitter heads generated infrared pulsed laser radiation of 0.890 microns wavelength and the power of 10 W. The emitter heads were installed for 2 minutes in the projection of the lateral cartilage and large cartilage of the nasal wing on both sides. In 48 hours after the operation, nasal swabs were removed in patients of both groups. In group 2, intranasal PBM therapy with a nozzle was performed in the continuous, modulated mode of operation in the red optical range, with the wavelength of 0.63 microns and radiation power of 8 mV for 2 minutes. Ultra-low frequency (ULF), high frequency (HF), low frequency (LF), and total heart rate variability (HRV) power were evaluated, as well as the pain syndrome. Results. ULF was significantly lower in group 2 (8086±3003 msec²), compared to group 1 (18580±2067 msec²) (p<0.001). LF was significantly higher in group 1 (1871±405 msec²), compared to group 2 (1095±190 msec²) (p<0.005). In group 2, HF was lower – 1157±220 msec² versus 1630±263



msec² in group 1 ($p < 0.01$). In group 2, the total HRV power was also lower (13498 ± 3226 msec²) than in group 1 (26808 ± 2371 msec²) ($p < 0.001$). In the first three hours after the septoplasty, pain intensity did not differ between the groups. In group 2, pain decrease was observed after 6 hours, compared to the previous period ($p < 0.05$). The pain continued to decrease in both groups, and 48 hours after septoplasty, patients either did not feel pain, or it was minimal and did not cause obvious discomfort. At the same time, in the period from 6 to 24 hours after septoplasty, patients who did not undergo PBM experienced significantly higher pain syndrome than patients with PBM ($p < 0.001$). Conclusion. The use of PBM therapy with nasal tamponade after septoplasty helps to reduce pain severity as well as an inflammatory response to the surgical stress and, consequently, leads to less pronounced changes in the autonomic nervous system in response to the surgery.

Keywords: septoplasty, pain, photobiomodulation, heart rate variability.

1. Introduction

Surgical correction of the curved nasal septum (CNS), or septoplasty, is one of the most common rhinosurgical operations. Nosebleeds, nasal septum hematoma, acute rhinosinusitis and pain syndrome are considered the most frequent complications after septoplasty [1, 2]. Septoplasty consists of the muco-suprachondral and/or muco-periosteal leaves separation and curved areas of the cartilaginous and/or bony parts of the nasal septum removal. As a rule, smooth sections of the extracted cartilaginous part of the nasal septum are placed back between the two leaves of the epiglottis. At the same time, the nasal cavity is tamponed after surgery to avoid complications [3].

The issue of patients' rehabilitation after septoplasty remains of essential importance. This may include both the question of anaesthesia and analgesia therapy quality, and the choice of local medicines application. For example, it was previously demonstrated that septoplasty by itself [4], as well as low-quality anaesthesia, may provoke the development of distress syndrome, which is an imbalance of the autonomic nervous system, severe pain syndrome and failure of life quality in the early postoperative period, which is confirmed by both changes in the balance of the autonomic nervous system (ANS) and changes in heart rate variability (HRV) [5].

Nowadays to reduce the appearance of side effects after septoplasty, such as pain, tissue oedema, inflammation, ecchymosis, etc, photobiostimulation (PBM) has been increasingly used [6]. This technique is based on the accelerating tissue repair principle, and therefore, the surgical wound healing [7, 8]. PBM therapy is a form of low-intensity laser therapy. PBM uses non-ionizing light sources, such as lasers or light-emitting diodes with a wavelengths 600-1000 nm and power less than 500 MW [9], to induce a photochemical reaction that leads to increase ATP synthesis in mitochondria, signal transmission in biological membranes and cells, DNA synthesis, cell proliferation, differentiation, and modulation of pro- and anti-inflammatory mediators, and, as a consequence, a reduction in pain and inflammation [10-12]. PBM is widely used to treat various diseases and conditions, such as wounds, diabetic ulcers, pain, inflammation, blood diseases, musculoskeletal complications, coronary heart disease, tissue repair and regeneration [13-14].

In nasal surgery, the problem of the postoperative quality of life of patients occupies a special place [15]. In addition to pain, nasal cavity tamponade presents significant inconveniences for patients. At the same time, there is an opinion that after septoplasty, instead of tamponade, splines should be used [15]. However, both tamponade and splints have their own advantages and disadvantages [5]. It seems interesting to search for non-invasive methods of rehabilitation of patients after septoplasty with nasal cavity tamponade. Resolving this issue will likely shorten the period of nasal cavity tamponade after septoplasty and improve the quality of life of patients.

The literature review shows that after septoplasty, PBM is applied intranasally after the removal of tampons, or immediately in the case of splints [15]. At the same time, there are practically no data on the evaluation of PBM effectiveness, when exposed during tamponade in the first two days after septoplasty.

Considering all of the above, this study was conducted to evaluate the effectiveness of PBM therapy in the early postoperative period in patients after septoplasty.

2. Patients and Methods

2.1. Rhinosurgery.

The study was approved by the Ethics Committees of the RUDN University Medical Institute. 62 patients have undergone septoplasty under general anesthesia. 40 men and 22 women from 18 to 44 years of age were included in the study. The participants were randomly assigned to two



groups of 31 patients each, with the equal number of men and women in both groups. The women underwent septoplasty during the periovulatory period. This phase of the ovarian-menstrual cycle is known to have a lower risk of nosebleeds after rhinosurgery [16]. Immediately after the operation, all the patients received anterior nasal tamponade with gauze swabs in glove rubber for 2 days. All the patients underwent septoplasty using local infiltration anesthesia with 1% procaine solution (250 mg) along with 0.1% epinephrine solution (10 mg) and general anesthesia using fentanyl (30 mcg/ml), propofol (150 mg), cisatracurium bezilate (nimbex) (6 mg), tranexamic acid (tranexam) (1000 mg), atropine (0.5 mg) and metoclopramide (cerucal) (10 mg). To avoid the development of acute bacterial inflammation of the paranasal sinuses, oral antibacterial therapy of azithromycin 500 mg once in the morning for three days with the first dose in the morning on the day of surgery was prescribed.

Exclusion criteria from the study were age less than 18 years, cardiovascular diseases, diabetes, endocrinological diseases, kidney diseases, oncological diseases, mental disorders, menstrual disorders and gynecological diseases, bronchial asthma, chronic hepatitis, chronic diseases of the gastrointestinal tract.

2.2. PBM therapy.

3 hours, 6 hours, and 24 hours after the septoplasty, group 2 patients received PBM therapy. The emitter heads generated infrared pulsed laser radiation with a wavelength of 0.890 microns and a power of 10 W. The emitter heads were placed in the projection of the lateral cartilage and the prominent cartilage of the nasal wing on both sides for 2 minutes.

48 hours after the operation, nasal swabs were removed in patients of both groups, and in group 2, intranasal PBM therapy with a nozzle was performed in the continuous, modulated mode of operation in the red optical range, with the wavelength of 0.63 microns and radiation power of 8 mV. The emitter heads were placed in both halves of the nose for 2 minutes.

2.3. HRV and pain syndrome analysis.

To assess the HRV, daily Holter electrocardiogram (ECG) was recorded using MT-200 devices (Schiller, Swiss). The ECG recording system was installed in patients 30 minutes before the septoplasty and removed 24 hours after it. The HRV parameters were studied in the frequency range: low frequencies (LF) in msec^2 , ultra-low frequencies (ULF) in msec^2 , high frequencies (HF) in msec^2 and total power (Total power) in msec^2 .

Pain syndrome was assessed using a visual-analogue scale (Fig. 1) at 1, 3, 6, 12, 24 and 48 hours after septoplasty and in group 2 immediately after PBM therapy sessions. The patients were asked to place a vertical line or dot at a point on the scale that they thought corresponded to the pain they were experiencing. The scale length was 100 mm. The pain intensity was measured in mm.



Figure 1. Visual-analogue scale for assessing the intensity of acute pain syndrome.

2.4. Statistical analysis.

All statistical data processing was performed using the JASP software package, version 0.14.0 (the University of Amsterdam, Netherlands) for Windows[®]. Continuous variables (pain value, LF, ULF, HF, Total power) were presented as mean±error of mean and analyzed using the t-test of independent samples after checking normality using the Shapiro-Wilk test. Normally distributed data were evaluated using the Student's t-test of independent samples, and abnormally distributed data were assessed using the Mann-Whitney's U-test. The values of $p < 0.05$ were considered statistically significant.

3. Results

3.1. Heart rate variability.

Student's t-test showed that after the sessions of PBM therapy, the ultra-low-frequency component of HRV spectral analysis was significantly lower in group 2 ($8086 \pm 3003 \text{ msec}^2$), compared to group 1 ($18580 \pm 2067 \text{ msec}^2$) ($p < 0.001$) (Fig. 2a). The low-frequency component of HRV was significantly higher in group 1 ($1871 \pm 405 \text{ msec}^2$), compared to group 2 ($1095 \pm 190 \text{ msec}^2$) ($p < 0.005$), which indicates an increase in the sympathetic tension of the ANS in the group without



FBMT (Student's t-test) (Fig. 2b). According to the Mann-Whitney U-test based on the high-frequency component of HRV analysis, a decrease in the activity of the parasympathetic nervous system during the perioperative day was also recorded in group 2 as a whole – $1157 \pm 220 \text{ msec}^2$ versus $1630 \pm 263 \text{ msec}^2$ in the first group ($p < 0.01$) (Fig. 2c). In group 2, the total HRV power was significantly lower ($13498 \pm 3226 \text{ msec}^2$) than in group 1 ($26808 \pm 2371 \text{ msec}^2$) ($p < 0.001$) (Student's t-test) (Figure 2d).

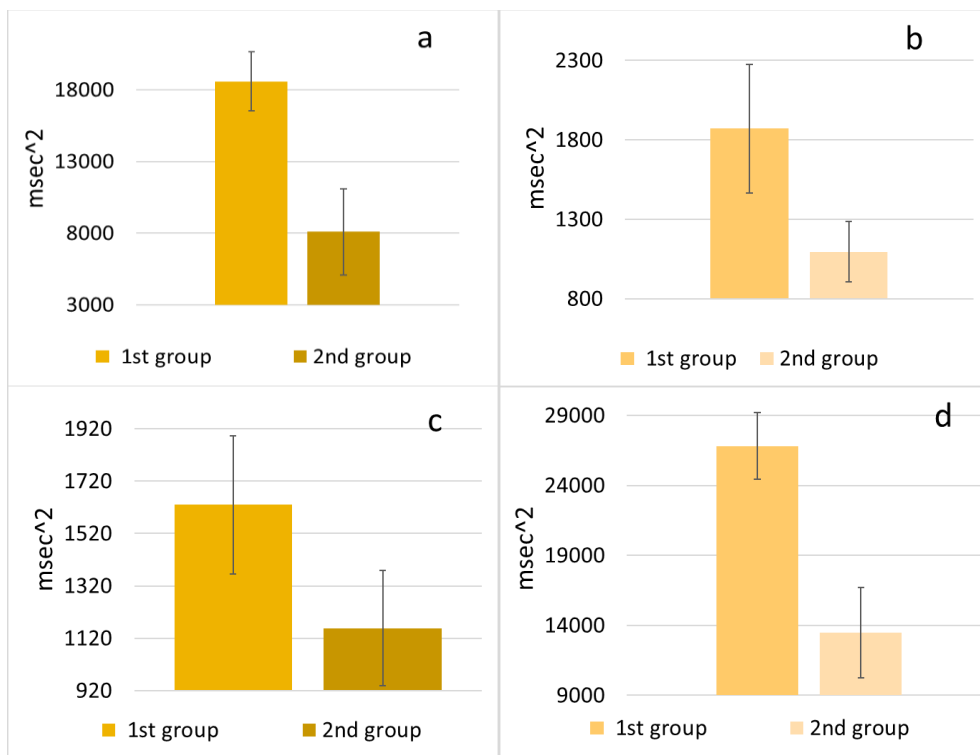


Figure 2. Changes in the frequency of heart rate variability with the use of PBMT after septoplasty and without it: a-ULF, b-LF, c-HF, d-Total power. The error bars indicate standard error.

3.2. Pain syndrome.

In the first three hours after the surgical intervention, the intensity of pain severity did not differ between the groups. The Mann-Whitney U-test showed that in group 1, the intensity of pain increased after 6 hours, compared to 3 hours after surgery, but there was no significant difference recorded. In group 2, the intensity of pain syndrome began to decrease after 6 hours, compared to the previous period ($p < 0.05$) (Mann-Whitney U-test) (Fig. 3). Further, the pain syndrome continued to decline in both groups, and 48 hours after the septoplasty, the patients either did not feel pain, or it was minimal and did not cause pronounced discomfort. At the same time, in the period from 6 to 24 hours after surgery, the patients who did not undergo PBMT experienced significantly higher pain syndrome than the patients with PBMT ($p < 0.001$) (Mann-Whitney U-test) (Fig. 3, Table 1).

Table 1. Intensity of acute pain syndrome after septoplasty.

Time after surgery	1 hour, mm	3 hours, mm	6 hours, mm	12 hours, mm	1st days, mm	2nd days, mm
Group 1	17.15±2.46	21.82±2.83	25±2.02	21.64±2.36	16.68±1.01	3.68±1.01
Group 2	14.16±2.31	18.88±2.45	16.43±2.08	12.83±2.38	10.84±1.15	3.84±1.15



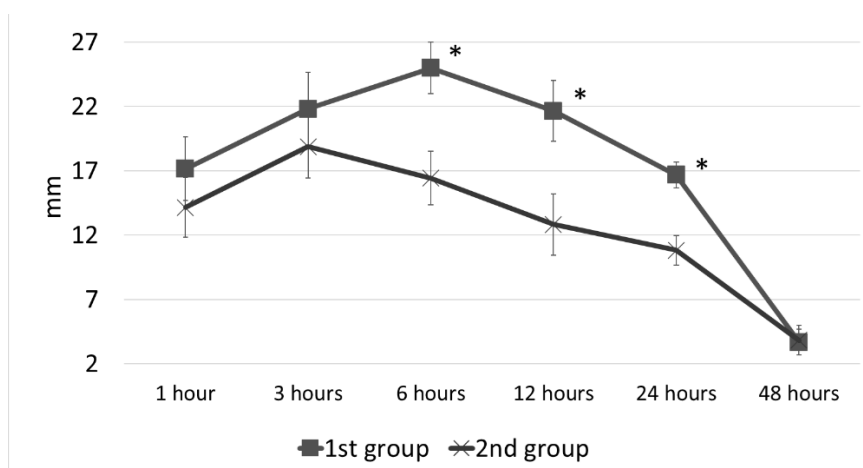


Figure 3. The intensity of pain syndrome after septoplasty. * - significant differences between the groups at $p < 0.001$. The error bars indicates standard error.

4. Discussion

The presented study is one of the few that shows the effectiveness of the use of PBMT in patients with nasal cavity tamponade in the first two days after septoplasty.

It is known that the removal of tampons is advisable 2 days after surgery, when there is a decrease in inflammatory processes with simultaneous restoration of the mucous membrane, normalization of blood supply to cartilaginous and bone tissues [1, 2], so it becomes relevant to use PBM therapy during the first two days after surgery. To date, it has not been found in the literature that PBM therapy is carried out with intranasal swabs with a high frequency of therapy sessions on the first day after rhinosurgical interventions in patients after septoplasty.

It is generally assumed that the PBM biological effect mechanism implies the absorption of light by chromophores [17, 18]. PBM therapy results in the following effects: reduction of oedema and inflammation, reduction of pain, collagen synthesis, increased elasticity, increased tissue perfusion and increased tissue vascularization, increased cell proliferation, especially fibroblasts, which generally leads to the restoration of damaged tissues [6]. Recent studies have shown the effectiveness of PBM therapy in a variety of conditions, from diabetic foot to androgenetic alopecia and post-chemotherapy mucositis, as well as wound healing and inflammation reduction [7, 8, 17 - 19]. PBM therapy may play a role in reducing the number of new postoperative haemorrhages in the maxillofacial region. At the same time, PBMT is positioned as a unique alternative to other interventions since it is an easy-to-use and minimally invasive method [6].

Hersant et al. evaluated the effect of low-intensity laser on flap survival results in facial plastic surgery. The authors showed that PBM therapy increases flap survival as well as wound healing. However, some possible effects of skin ageing were reported [20]. Enwemeka et al. found highly efficient tissues restoration promoted by PBMT during all three phases and pain reduction [21].

The effects of PBM therapy described above, significantly damaged tissues restoration and neovascularization, provide edema and inflammatory reaction reactions, a reduction in haemorrhage likelihood [6] and, consequently, pain in the tissue after septoplasty. With the intranasal use of PBM therapy, systemic effects are also achieved through blood cells and components [22], which probably can contribute to a positive neurotherapeutic impact [23]. The tissues adjust to the nasal cavity have an abundant blood supply with relatively slow blood flow. PBMT has shown to improve blood rheology [24], reduce blood viscosity [25], and enhance blood clotting status [26, 27] in various pathological conditions. In group 2, significantly lower intensity of pain syndrome, a decrease in its power compared to patients of group 1, indicates relatively low inflammatory reactions of the blood system in the damaged area after PBMT [28].

In patients with PBM therapy, HRV indicators had significantly lower total power than those without PBM therapy, for example, an ULF component often associated with circadian rhythms [29]. An increase in ULF power indicates a failure of circulatory rhythms due to surgical traumatization against the background of inflammatory phenomena in the group without PBM therapy. The high-frequency component of HRV shows the parasympathetic nervous system tonus, while LF, according to a number of authors, can reflect both sympathetic (mainly) and parasympathetic one [30]. The decrease in LF and HF after septoplasty with the use of PBM therapy demonstrates the reduction in sympathetic and parasympathetic tonus after the correction of CNS. The shift in the balance of the ANS towards its sympathetic component is physiologically justified and corresponds to the severity of the stress factors impact. However, an increase in the tonus of the parasympathetic nervous system under stress may indicate an inadequate response of the body and



correspond to distress syndrome [31], which may reflect the degree of surgical damage in the maxillofacial region [32]. Thus, it was shown that after septoplasty, LF of HRV could sharply decrease [30]. In our study, a group of patients with the classic variant of postoperative rehabilitation had increased activity of both the sympathetic and parasympathetic parts of the ANS. Studies have shown a relationship between blood rheology, cognitive function [28], and mood improvement [27]. It has been suggested that the systemic effects of PBM therapy after blood irradiation may also ultimately have a neuroprotective effect [23, 33, 34]. Intranasal blood irradiation is also known to have the same neurological consequences as intravenous or intravascular PBM therapy [35]. Those findings may also provide insight into lower pain syndrome, lower changes in the ANS balance in response to surgical damage after septoplasty in patients with photobiomodulation in the early postoperative period.

5. Conclusions

To sum up, in our study, the group of patients with PBM therapy showed better results regarding pain syndrome decrease and HRV compared to the classical patients' rehabilitation after septoplasty. In our opinion, it is necessary to further develop protocols for the patients' rehabilitation after septoplasty with various types of nasal tamponade.

It is likely that the use of PBMT in the future can serve as one of the ways to reduce the duration of nasal tamponade after septoplasty as a result of accelerating the reparative processes of the nasal septum mucosa. Thus, we will be able to approach solving the problem of the quality of life of patients in the early postoperative period after nasal septum surgery with the nasal tamponade use.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of Medical Institute of RUDN University (protocol N26, 18 feb 2021).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Pustovit O.M., Nasedkin A.N., Egorov V.I., Isaev, V.M., Isaev, E.V., Morozov, I.I. Using ultrasonic cavitation and photochromotherapy to increase nasal mucosa repair process after septoplasty and submucous vasotomy of the inferior nasal turbinates. *Golova I Sheya Head and neck Russian Journal*. 2018; 6(2): 20–26 (in Russian).
2. Sommer F., Hoffmann T.K. Septoplasty—a surgical or political challenge? *The Lancet*. 2019; 394: 276–277.
3. Kastyro I.V., Torshin V.I., Drozdova G.A., Popadyuk V.I. Acute pain intensity in men and women after septoplasty. *Russian Open Medical Journal*. 2017; 6 (3): 1–6.
4. Kastyro I.V., Inozemtsev A.N., Shmaevsky P.E., Khamidullin G.V., Torshin V.I., Kovalenko A.N., Pryanikov P.D., Guseinov I.I. The impact of trauma of the mucous membrane of the nasal septum in rats on behavioral responses and changes in the balance of the autonomic nervous system (pilot study). *J. Phys.: Conf. Ser.* 2020; 1611.
5. Popadyuk V.I., Kastyro I.V., Ermakova N.V., Torshin V.I. Septoplasty and tonsillectomy: acute stress response as a measure of effectiveness of local anesthetics. *Vestn Otorinolaringol.* 2016; 81 (3): 7–11.
6. Karimi S., Sadeghi M., Amali A., Saedi B. Effect of Photobiomodulation on Ecchymosis after Rhinoplasty: A Randomized Single-Blind Controlled Trial. *Aesthetic Plast Surg.* 2020; 44 (5): 1685–1691.
7. Suchonwanit P., Chalermroj N., Khunkhet S. Low-level laser therapy for the treatment of androgenetic alopecia in Thai men and women: a 24-week, randomized, double-blind, sham device-controlled trial. *Lasers Med Sci.* 2018; 1–8.
8. Alegre-Sánchez A., Saceda-Corralo D., Segurado-Miravalles G., de Perosanz-Lobo D., Fonda-Pascual, P., Moreno-Arrones O.M., Buendía-Castaño D., Perez-García B., Boixeda P. Pulsed dye laser on ecchymoses: clinical and histological assessment. *Lasers Med Sci.* 2018; 33 (3): 683–688.
9. Zein R., Selting W., Hamblin M.R. Review of light parameters and photobiomodulation efficacy: dive into complexity. *J. Biomed Opt.* 2018; 23.
10. Costa M.S., Pinfildi C.E., Gomes H.C., Liebano R.E., Arias V.E., Santos Silveira T., Ferreira L.M. Effect of low-level laser therapy with output power of 30 mW and 60 mW in the viability of a random skin flap. *Photomed Laser Surg.* 2010; 28 (1): 57–61.
11. Santos F.T., Santos R.S., Weckwerth V., Dela Coleta Pizzol K.E., Pereira Queiroz T. Is low-level laser therapy effective on sensorineural recovery after bilateral sagittal split osteotomy? Randomized trial. *J Oral Maxillofac Surg.* 2019; 77(1): 164–173.
12. Musstaf R.A., Jenkins D.F., Jha A.N. Assessing the impact of low-level laser therapy (LLLT) on biological systems: a review. *Int J Radiat Biol* 2019; 95(2): 120–143.
13. Chung H., Dai T., Sharma S.K., Huang, Y.Y., Carroll J.D., Hamblin M.R. The nuts and bolts of low-level laser (light) therapy. *Ann Biomed Eng.* 2012; 40: 516–533.



14. Arany P.R., Cho A., Hunt T.D., Sidhu G., Shin K., Hahm E., Huang G.X., Weaver J., Chen A.C.H., Padwa, B.L., Hamblin M.R., Barcellos-Hoff M.H., Kulkarni A.B., Mooney D.J. Photoactivation of endogenous latent transforming growth factor- β 1 directs dental stem cell differentiation for regeneration. *Sci Transl Med.* 2014; 6: 238-269.
15. Naik K. A Novel Way of Trans-Septal Splint Suturing Without Nasal Packing for Septoplasty. *Indian J Otolaryngol Head Neck Surg.* 2015; 67 (1): 48-50.
16. Findikcioglu K., Findikcioglu F., Demirtas Y., Yavuzer R., Ayhan S., Atabay K. Effect of the menstrual cycle on intraoperative bleeding in rhinoplasty patients. *Eur J Plast Surg.* 2009; 32: 77-81.
17. Kazemikhoo N., Vaghardoost R., Dahmardehei M., Mokmeli S., Momeni M., Nilforoushadeh M.A., Ansari F., Razagi M.R., Razagi Z., Amirkhani M.A., Masjedi M.R. Evaluation of the effects of low level laser therapy on the healing process after skin graft surgery in burned patients (a randomized clinical trial). *J Lasers Medi Sci.* 2018; 9 (2): 139.
18. Tchanque-Fossuo C.N., Ho D., Dahle S.E., Koo E., Li C.S., Jagdeo R.R.I. A systematic review of lowlevel light therapy for treatment of diabetic foot ulcer. *Wound Repair Regen.* 2016; 24 (2): 418-426.
19. Wang W., Jiang W., Tang C., Zhang X., Xiang J. Clinical efficacy of low-level laser therapy in plantar fasciitis: a systematic review and meta-analysis. *Medicine.* 2019; 98 (3): 140.
20. Hersant B., SidAhmed-Mezi, M., Bosc R., Meningaud J.P. Current indications of low-level laser therapy in plastic surgery: a review. *Photomed Laser Surg.* 2015; 33 (5): 283-297.
21. Enwemeka C.S., Parker J.C., Dowdy D.S., Harkness E.E., Sanford L.E., Woodruff L.D. The efficacy of low-power lasers in tissue repair and pain control: a meta-analysis study. *Photomed Laser Therapy.* 2004; 22 (4): 323-329
22. Salehpour F., Gholipour-Khalili S., Farajdokht F., Kamari F., Walski T., Hamblin M.R., DiDuro J.O., Cassano P. Therapeutic potential of intranasal photobiomodulation therapy for neurological and neuropsychiatric disorders: a narrative review. *Rev Neurosci.* 2020; 31 (3): 269-286.
23. Hennessy M., Hamblin M.R. Photobiomodulation and the brain: a new paradigm. *J. Opt.* 2016; 19.
24. Liu T.C.Y., Wu D.F., Gu Z.Q., Wu M. Applications of intranasal low intensity laser therapy in sports medicine. *J Innov Opt Health Sci.* 2010; 3: 1-16.
25. Liu T.C.Y., Cheng L., Su W.J., Zhang Y.W., Shi Y., Liu A.H., Zhang L.L., Qian Z.Y. Randomized, double-blind, and placebo-controlled clinic report of intranasal low-intensity laser therapy on vascular diseases. *Int J Photoenergy.* 2012; 1-5.
26. Gao X., Zhi P., Wu X. Low-energy semiconductor laser intranasal irradiation of the blood improves blood coagulation status in normal pregnancy at term. *Nan Fang Yi Ke Da Xue Xue Bao.* 2008; 28: 1400-1401.
27. Gao Z.S., Zhang L., Qin C.I. The relationship between hemorheological changes and the anxiety and depression symptoms in schizophrenia. *Chin J Hemorheol.* 2004; 1.
28. Elwood P.C., Pickering J., Gallacher J.E. Cognitive function and blood rheology: results from the Caerphilly cohort of older men. *Age Ageing.* 2001; 30: 135-139.
29. Bersani I., Piersigilli F., Gazzolo D., Campi F., Savarese I., Dotta A., Tamborrino P.P., Auriti C., Di Mambro C. Heart rate variability as possible marker of brain damage in neonates with hypoxic ischemic encephalopathy: a systematic review. *European Journal of Pediatrics.* 2020; 27: 1-11.
30. Celiker M., Cicek Y., Tezi S., Ozgur A., Polat H.B., Dursun E. Effect of Septoplasty on the Heart Rate Variability in Patients with Nasal Septum Deviation. *J Craniofac Surg.* 2018; 29 (2): 445-448.
31. Kastyro I.V., Reshetov I.V., Khamidulin G.V., Shmaevsky P.E., Karpukhina O.V., Inozemtsev A.N., Torshin V.I., Ermakova N.V., Poadyuk V.I. The Effect of Surgical Trauma in the Nasal Cavity on the Behavior in the Open Field and the Autonomic Nervous System of Rats. *Doklady Biochemistry and Biophysics.* 2020; 492: 121-123.
32. Dolgalev A.A., Svyatoslavov D.S., Pout V.A., Reshetov I.V., Kastyro I.V. Effectiveness of the Sequential Use of Plastic and Titanium Implants for Experimental Replacement of the Mandibular Defect in Animals using Preliminary Digital Design. *Doklady Biochemistry and Biophysics.* 2021; 496: 36-39.
33. Xiao X., Guo Y., Chu X., Jia S., Zheng X., Zhou C. Effects of low power laser irradiation in nasal cavity on cerebral blood flow perfusion of patients with brain infarction. *Chin J Phys Med.* 2005; 27: 418-420.
34. Caldieraro M.A., Sani G., Bui E., Cassano P. Long-term near-infrared photobiomodulation for anxious depression complicated by Takotsubo cardiomyopathy. *J Clin Psychopharmacol.* 2018; 38: 268-270.
35. Dou Z., Xiquan H., Zhu H. The effects of two kinds of laser irradiation on patients with brain lesion. *Chin. J Phys Med Rehabil.* 2003; 2: 38-43.

