

Assessing Health-Related Quality of Life with Antimicrobial Photodynamic Therapy (APDT) and Low Level Laser Therapy (LLLT) after Third Molar Removal

Goran Batinjan¹, Irina Filipović Zore¹, Ivana Rupiċ¹, Ivona Bago Juriċ²
Zvonimir Zore³, Dragana Gabriċ Panduriċ¹

¹University of Zagreb, School of Dental Medicine, Department of Oral Surgery, Zagreb, Croatia

²University of Zagreb, School of Dental Medicine, Department of Endodontics and Restorative Dentistry, Zagreb, Croatia

³University Clinical Hospital Center, Sisters of Mercy, Department of Surgical Oncology, Zagreb, Croatia

Abstract:

Introduction: The purpose of this study was to evaluate the antimicrobial photodynamic therapy (APDT) and low level laser therapy (LLLT) on wound healing, pain intensity, swelling problems, halitosis and the postoperative usage of analgesics after surgical removal of lower third molars.

Methods: One hundred and fifty patients, randomly divided into three groups were selected (50 per each group). The P1 group received the APDT after a third molar surgery, the P2 group received the LLLT and the C group (control group) was without any additional therapy after surgery. A photoactive substance was applied in the APDT study group before suturing. After 60 seconds the photosensitive substance was thoroughly washed with saline water and the laser light was applied in two intervals (30 seconds each). The irradiation power was 50 mW while the wavelength was 660 nm. The laser therapy in P2 group was performed before suturing and the laser light was applied also in two intervals (90 seconds each), the irradiation power was 90 mW while the wavelength was the same as in the first group – 660 nm. Postoperative follow-ups were scheduled on the third and the seventh day in patients who received laser therapy.

Results: The results of the postoperative evaluation showed that there was a statistically significant difference in the postoperative wound healing, pain intensity, swelling problems, halitosis and analgesics intake between patients in all three groups ($p < 0.001$). The patients that were subjected to APDT (P1) had the least postoperative problems. After the laser therapy (P1 and P2) wound healing was without any complications, opposite from the patients from the C group ($p < 0.001$). Postoperative application of a laser therapy significantly reduced patient's use of analgesics over the observed period of time ($p < 0.001$).

Conclusion: Both modalities of laser therapy significantly reduced postoperative problems after surgical removal of third lower molars with the best results in both laser groups.

Keywords: low level laser therapy; photodynamic therapy; postoperative complications; diode laser

Please cite this article as follows:

Goran Batinjan, Irina Filipović Zore, Ivana Rupiċ, Ivona Bago Juriċ, Zvonimir Zore, Dragana Gabriċ Panduriċ. Assessing Health-Related Quality of Life with Antimicrobial Photodynamic Therapy (APDT) and Low Level Laser Therapy (LLLT) after Third Molar Removal. *J Lasers Med Sci* 2013; 4(3):120-6

***Corresponding Author:** Dragana Gabriċ Panduriċ, PhD, DMD; University of Zagreb, School of Dental Medicine, Department of Oral Surgery, Gunduliċeva 5, HR- 10000 Zagreb, Croatia; Tel: +385 1 4802 119; Fax: +385 1 4802 108; e-mail: dgabric@sfg.hr

Introduction

Low power diode lasers, also called biostimulators, base their anti-inflammatory effects, accelerated wound healing and reduction of acute and chronic pain on photobiostimulation effects. Anti-inflammatory effect of the laser beam is based on the reduction of prostaglandin (PGE₂) concentration, changing the path of arachidonic acid and reduced effect of tumor necrosis factors (TNF α) in acute inflammatory states¹. Furthermore, the anti-inflammatory effect of laser irradiation is contributed by the change of permeability and the size of lymphatic and blood vessel lumen and collateral growth stimulation which enhances defensive mechanism for fighting infection^{2,3}. Accelerated healing via laser effect is achieved by stimulation of natural biological processes⁴. Cells with low redox-state are acidic, but turn alkaline after laser therapy and its optimal regeneration is achieved. Healthy cells can not significantly increase their redox-states and they will not react to laser energy effects, while cells with low redox-states will be stimulated⁵. The most important effect the laser energy has on the cell is the increase of adenosine triphosphate (ATP)^{6,7}. Analgesic effect mechanism of the laser beam is based on changing neurotransmitter activity, especially serotonin, beta-endorphin and acetylcholinesterase. It is also proven that transient varicosities along neurons are achieved. This way, a transmission signal interference⁸ and inhibition of complex reaction of action potential creation occur⁹. The enhanced effect cannot be achieved by using multiple therapies simultaneously. On the contrary, that would lead to wound healing inhibition (Arndt-Schulz law)¹⁰. Because of that, acute states (oedema and inflammation symptoms) are treated until symptoms are cured, while therapy in chronic states (wounds, paresthesia, chronic pain) should not be applied more than once or twice a week¹¹⁻¹³. The biostimulative effect of laser therapy is increasingly being used for reducing postoperative problems after many operative procedures in the area of the orofacial region and even after third molar removal, one of the most frequent dentoalveolar surgical procedures in oral and maxillofacial surgery¹⁴. The period after alveolectomy is often followed by problems such as pain, halitosis and swelling problems, problems with postoperative healing which greatly impair life quality and cause work incapacity. Such problems are the reason for increased postoperative application of analgesics and antibiotics^{15,16}.

By comparing recent literature on the effects of

different lasers therapy on postoperative problems after the removal of lower third molars, there are some differences between the results. Lopez-Ramirez et al. have proved on a sample of 20 patients after third molar removal on both sides that laser irradiation has positive effects on pain, swelling problems and trismus, although not statistically significant¹⁷. Statistically insignificant effects of laser irradiation on the aforementioned postoperative symptoms have also been proven by Braams et al¹⁸. Wahl et al. have proved that laser irradiation of soft tissue statistically significantly reduced postoperative problems¹⁹. Almost all of that researches used different methodology and different laser irradiation parameters which can be the cause of result discrepancy²⁰.

The aim of this study was to evaluate the effects of anti-microbial photodynamic therapy (APDT) and low level laser therapy (LLLT) on wound healing, pain intensity, swelling problems and halitosis after the removal of lower third molars and postoperative analgesic usage.

Methods

Subjects

This study was approved by the Ethical Committee of the School of Dental Medicine, University of Zagreb, Croatia. The research consisted of 150 participants, 92 (61%) were females and 58 (39%) were men. The participants were separated into four age groups: under 18 (8%), 19 to 24 years (42%), 25 to 30 years (25%) and over 30 years (25%). The exclusion criteria in the present study were systemic diseases, with developing local infections, smokers, pregnant women, breastfeeding mothers and patients using contraception. All participants were patients of the Department of Oral Surgery School of Dental Medicine University of Zagreb with complete indications for removal of the lower third molar. Before the surgery, patients were informed in detail about the laser therapy, its application, effects, indications and side effects and signed a participation agreement in which they accepted laser therapy after surgery. All anamnestic data was collected and inserted into a Patient Questionnaire, in the section "Patient General Information".

Procedures

All surgical procedures were performed under

local anesthesia (UbistesinTM, 3M ESPE, Espe Platz, D-82229 Seefeld, Germany). Local anesthetic quantity in each procedure was two ampoules per patient. Molars were removed using surgical technique of mucoperiosteal flap with osteotomy. In order not to influence the trauma level by surgical experience of the operator, both surgeons performing the operations on all participants had more than 10 years experience. Surgical approach was buccal with the incision of mucoperiosteal flap. The incision was of sufficient size in order to allow good visibility, in order not to place the operative area under tension, to make it vascularized and to rest edges of the operative area on solid bone surface. After removing the bone with drills, tooth removal was performed using elevating instruments (pliers, elevators, MEDIN, a.s., Nové Město na Moravě, Czech Republic) in the appropriate direction.

Patients were divided into three groups using a random selection: P1 group consisted of 50 patients who received APDT, P2 group consisted of 50 patients who received LLLT, and the C group (control group) consisted of 50 patients who did not receive any kind of laser therapy. In all examined groups data had been obtained by using identical questionnaire²¹. The laser HF (Hager and Werken GmbH and Co. Duisburg, Germany, 2009.) was used in the study. In the P1 group, before suturing, a photosensitive substance consisting of toluidine chloride powder (155µg/ml), water, sodium phosphate and hydroxymethyl cellulose (LaserHF Paro - PDT solution, Hager and Werken GmbH and Co., Duisburg) was applied in the postextraction socket. After 60 seconds, the Paro-PDT solution was thoroughly rinsed using saline solution and laser light was applied directly into the surgical site for 60 seconds (2x30 seconds) with constant laser beam irradiation over the surgical area. The laser probe was used in non-contact mode and was set at the distance of approximately 5mm of the bone surface. The irradiation intensity was 50 mW, with the wavelength of 660 nm. The laser therapy in the P2 group was performed in the same manner as in the P1 group before suturing, but without the application of the Paro-PDT solution and it lasted for 180 seconds (2x90 seconds). The irradiation intensity was 90 mW and the wavelength was 660 nm, the same as the P1 group. Laser settings for both therapy modalities were according to the manufacturer's instructions and were not changed arbitrarily. All patients received identical postoperative instructions.

The postoperative follow-ups were scheduled to the third and to the seventh day in laser P1 and P2 groups. Healing and postoperative recovery was assessed by two questionnaires (one for patients and another for surgeons). Patients evaluated their postoperative problems with grades from 1 to 4 (1=no problems, 2=mild problems, 3=medium problems, 4=intensive problems). The following symptoms were assessed: pain, swelling problems and halitosis. Patients also recorded their postoperative analgesics usage using a dichotomous scale (1=yes, 2=no). Surgeons evaluated the type of post-extraction alveolus healing (1=normal, 2=acute inflammation, 3=acute inflammation followed by infected alveolus and 4=alveolar osteitis). Three different surgeons evaluated 20 same patients independently. There was no significant difference considering their assessment ($p<0.01$; one way ANOVA).

Patients were also contacted on the fourteenth day after the procedure via their electronic mail or a telephone for additional questions regarding possible problems and for evaluation of their satisfaction with the results of the surgical procedure.

Statistical methods

Statistical analyses were performed using the SPSS Statistical package (IBM, Chicago, Illinois, USA). A descriptive statistic was made (frequencies, arithmetic means, and standard deviations). The tests used in this research were χ^2 test (Fisher's test in cases when contingency was smaller than 5 samples), independent Student t-test and one-way analysis of variance (ANOVA) with post-hoc Scheffe's tests.

Significance of the differences between participating groups (P1, P2 and C) regarding patient's evaluation of pain, swelling problems and halitosis were tested with one-way variance analysis (post-hoc Scheffe).

Significance of difference in usage of analgesics between participating groups (P1, P2 and C) was tested by χ^2 test (Fisher's test in cases when contingency was smaller than 5 samples). Significance of differences of clinical states between participating groups (P1, P2 and C) for the type of post-extraction alveolus healing was made by χ^2 test (Fisher's test in cases when contingency was smaller than 5 samples).

Results

Results of postoperative healing evaluation showed

there was a statistically significant difference in postoperative wound healing between three groups on third and seventh day after removal of lower third molars (day three $\chi^2 = 26.02$, $p < 0.001$, day seven $\chi^2 = 18.13$, $p < 0.001$, Fisher's exact test).

On the first postoperative day there was a significant difference between the groups regarding pain levels ($F = 6.17$, $p = 0.003$), swelling problems ($F = 8.21$, $p < 0.001$) and halitosis ($F = 4.22$, $p = 0.016$). The post hoc Scheffe's tests showed that significantly less pain and halitosis was experienced by patients in the group P1 compared to other two groups. Moreover, the patients from the group C had significantly larger swelling problems when compared to patients from both laser groups.

On the third postoperative day there was also a significant difference between the groups considering pain intensity ($F = 10.71$, $p < 0.001$), swelling problems ($F = 10.67$, $p < 0.001$) and halitosis ($F = 7.23$, $p = 0.001$). The post hoc Scheffe's tests showed that significantly more pain was experienced by patients in the group C than in the laser groups. The patients in the group P1 experienced significantly less swelling problems and halitosis compared to other two groups.

On the seventh postoperative day there was still a significant difference between the groups in pain intensity ($F = 12.41$, $p < 0.001$), swelling problems ($F = 11.62$, $p < 0.001$) and halitosis ($F = 17.37$, $p < 0.001$). The post hoc Scheffe's tests showed that significantly more pain and halitosis was experienced by patients in the group C compared to laser groups. The patients in the group P1 and P2 experienced significantly less swelling problems compared to the group C.

On the fourteenth postoperative day, there was a significant difference between the groups regarding pain intensity ($F = 7.01$, $p = 0.001$), swelling problems ($F = 6.13$, $p = 0.003$) and halitosis ($F = 8.02$, $p < 0.001$). The post hoc Scheffe's test showed that C group had significantly higher pain intensity, swelling problems and halitosis than laser groups. Average grade of postoperative pain intensity (Figure 1), swelling problems (Figure 2) and halitosis (Figure 3) evaluated on the first, third, seventh and fourteenth day was the highest in the control group.

Discussion

The results of the present study showed positive

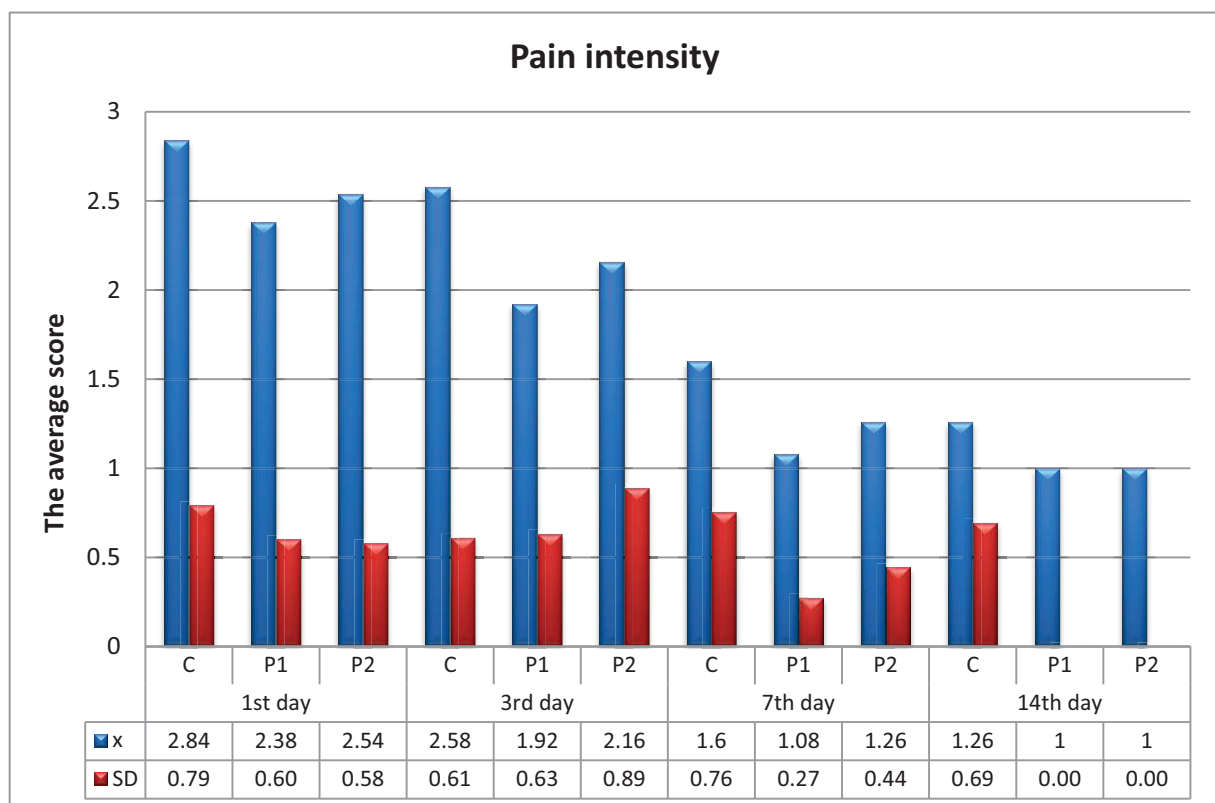


Figure 1. The distribution of pain intensity between groups: C= control group, P1= APDT group, P2= LLLT group

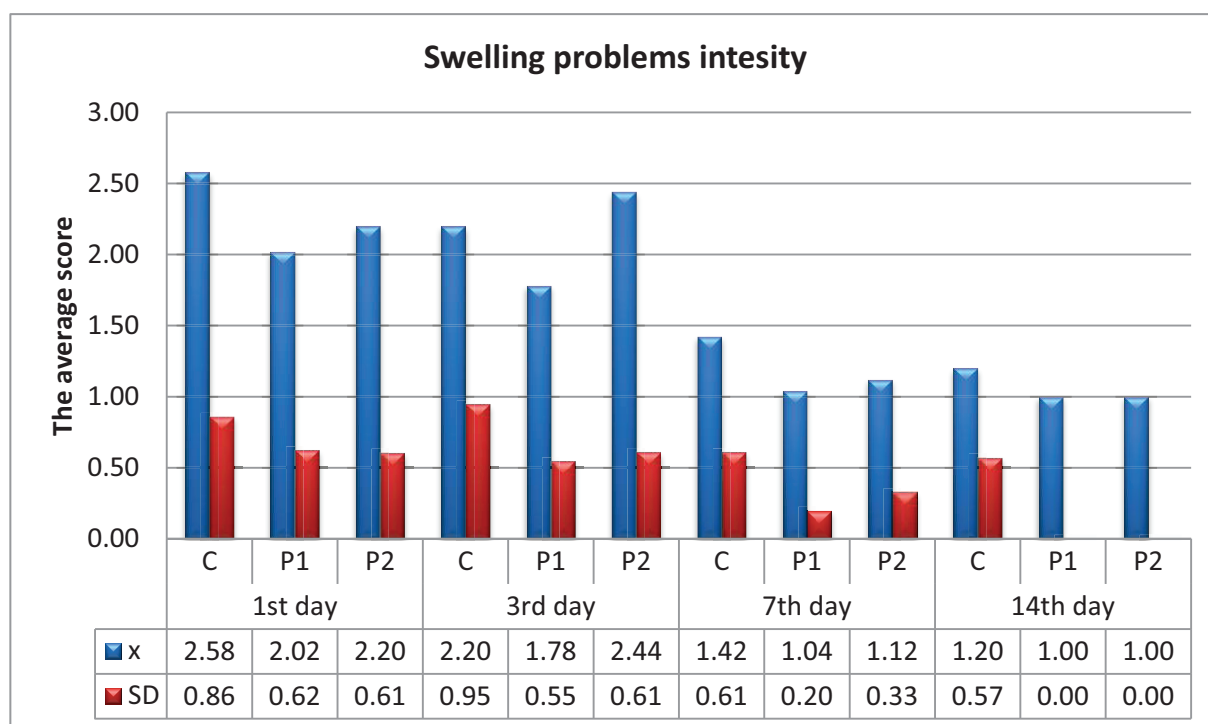


Figure 2. The distribution of swelling problems intensity in three examined groups: C= control group, P1= APDT group, P2= LLLT group

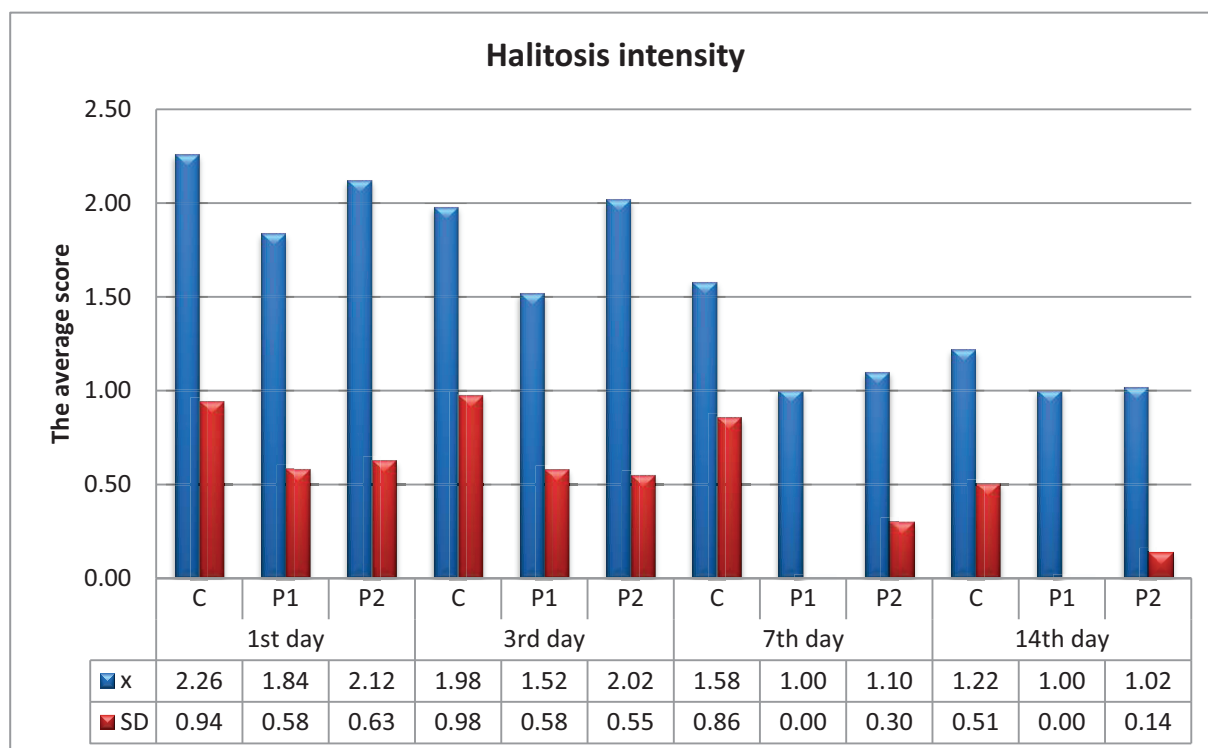


Figure 3. The distribution of halitosis intensity between groups: C= control group, P1= APDT group, P2= LLLT group

effects of low power diode laser therapy for all postoperative problems after the removal of lower third molars. The absence of complications in postoperative

healing of patients in both laser groups, opposite to the control group, indicated the anti-inflammatory effect and enhanced defensive cell reaction of that

treatment. Postoperative healing complications were seen in 36% of cases in the control group, most of which was attributed to alveolar osteitis. Gbotolorun et al. also showed that alveolar osteitis was the most frequent complication seen in 14.2% of their patients²². Average grades for pain, swelling problems and halitosis decreased exponentially through 14 days of postoperative monitoring in all three groups, which was previously expected. But the group with the highest average grade drop, and with the lowest postoperative pain, swelling problems and halitosis intensity, was the P1 group. Such results, apart from many positive effects of laser therapy, could be explained by the anti-microbial effect of the Paro-PDT solution in combination with laser light used in group P1 therapy. The ability to destroy microorganisms by implementing the Paro-PDT solution into the cell wall and consequent creation of free radicals has led to a strong anti-bacterial effect even in hard reachable places. Mattiell et al. showed in their study the anti-microbial effect of Paro-PDT solution and efficiency of photodynamic therapy on *Aggregatibacter actinomycetemcomitans* (Aa) and *Streptococcus sanguinis* (Ss). Photodynamic therapy has displayed statistically significant reduction of Aa and Ss occurrences with *in vitro* samples when compared with the control group²³. P2 group patients had not exhibited significantly lower levels of pain, swelling problems and halitosis on the first and third postoperative days when compared with the control group. On the seventh and fourteenth postoperative day, the intensity of the problems was reduced and equalled the intensity of postoperative problems reported by P1 group patients, which are significantly better results when compared with the results obtained from group C patients on the same days. Such results may be explained by the cumulative effect of laser therapy¹⁰ by which every newly applied postoperative dosage stays in the tissue. That way each new dosage had stronger effect on the tissue. Considering this, future research should be performed using everyday postoperative LLLT laser therapy. Cumulative effect would be increased and postoperative problems would be reduced. While doing so, it is mandatory to follow manufacturer's instructions which stated that laser therapy for treating acute problems can be used until problems disappear, while it should not be used for longer than fourteen days postoperatively in case of chronic problems¹⁰). Significantly lower pain intensity and reduced postoperative analgesics usage in laser therapy proved its complex analgesic

effect. These results cannot be compared with results presented by other authors since most authors in most recent literature evaluated the effect of analgesics as premedication or their influence on long-lasting local anesthetics on postoperative problems²⁴.

Expert literature is expanding every day and various new data on the effect of various laser therapies on postoperative problems after the removal of lower third molars is constantly added. The difference in reports can be caused by the type of the laser used, laser beam wave length, radiation dosage and time of exposure²⁰. It was shown that laser radiation applied extraorally better reduces postoperative problems when compared with intraorally applied therapy²⁵.

Marković et al. showed that better postoperative swelling problems reduction after surgical removal of lower third molars is accomplished by a combination of laser therapy and local intramuscular application of dexamethasone, while the combination of laser therapy and systematic dexamethasone application did not show statistically significant effects compared with laser therapy²⁶. In the future, a standard laser therapy should be determined, a therapy in which numerous proved positive effects of diode laser on soft tissue should be applied, while all other variations of the standard therapy that would include medicament usage or other variation regarding therapy application should be proven in future researches.

Conclusion

The present study has approved the diode laser usage for significant enhancement of patient's postoperative problems after third molar surgery. Both laser therapy modalities significantly reduced postoperative pain, swelling problems, halitosis and analgesic usage. The least postoperative problems were present in the group which received antimicrobial photodynamic (APDT) and low level laser therapy (LLLT).

Conflicts of Interest

The authors deny any conflicts of interest.

Acknowledgments

The authors would like to thank Professor Asja Čelebić for her selfless help with statistical analysis, support and guidance.

References

1. Aimbire F, Albertini R, Pacheco MT, Castro-Faria-Neto HC, Leonardo PS, Iversen VV, et al. Low-level laser therapy induces dose-dependent reduction of TNF α levels in acute inflammation. *Photomed Laser Surg* 2006;24(1):33-7.
2. Lievens PC. The effect of a combined HeNe and IR laser treatment on the regeneration of the lymphatic system during the process of wound healing. *Lasers Med Sci* 1991; 6:193-9.
3. Meneguzzo DT, Pallotta RC, Marco RL, Penna SC, Ramos L, Teixeira SA et al. Near infrared laser therapy (810 nm) on lymph nodes: effects on acute inflammatory process. *Photomed Laser Surg*. 2009; 27(1):157.
4. Aras MH, Güngörmüş M. The effect of low-level laser therapy on trismus and facial swelling following surgical extraction of a lower third molar. *Photomed Laser Surg*. 2009;27(1):21-4.
5. Yamamoto Y, Kono T, Kotani H, Kasai S, Mito M, et al. Effect of low-power laser irradiation on procollagen synthesis in human fibroblasts. *J Clin Laser Med Surg*. 1996; 14(3):129-32.
6. Amat A, Rigau J, Nicolau R, Aalders M, Fenoll MR, van Gemert M, et al. Effect of red and near-infrared laser light on adenosine triphosphate (ATP) in the luciferine-luciferase reaction. *J Photochem Photobiol A Chem*. 2004;168(1-2):59-65.
7. Huang YY, Chen AC, Carroll JD, Hamblin MR. Biphasic dose response in low level laser therapy. *Dose Response*. 2009; 7(4):358-83.
8. Chow RT, David MA, Armati PJ. 830 nm laser irradiation induces varicosity formation, reduces mitochondrial membrane potential and blocks fast axonal flow in small and medium diameter rat dorsal root ganglion neurons: implications for the analgesic effects of 830 nm laser. *J Peripher Nerv Syst*. 2007; 12(1):28-39.
9. Montesinos M, et al. Experimental effects of low power laser in enkephalin and endorphin synthesis. *J Eur Med Laser Assoc*. 1988;1(3):2-6.
10. Robert A. Principles and Practice of Laser dentistry. New York: Hospital Queens, Private Practice. 2010.
11. Karu TI, Ryabykh TP, Antonov SN. Different sensitivity of cells from tumor-bearing organisms to continuous-wave and pulsed laser radiation (632.8 nm) evaluated by chemiluminescence test. I. Comparison of responses of murine splenocytes: intact mice and mice with transplanted leukemia EL-4. *Lasers Life Sci*. 1996; 7(2):91-8.
12. Karu TI, Ryabykh TP, Antonov SN. Different sensitivity of cells from tumor-bearing organisms to continuous-wave and pulsed laser radiation (632.8 nm) evaluated by chemiluminescence test. II. Comparison of responses of human blood: healthy persons and patients with colon cancer. *Lasers Life Sci*. 1996; 7(2):99-106.
13. Karu TI, Ryabykh TP, Letokhov VS. Different sensitivity of cells from tumor-bearing organisms to continuous-wave and pulsed laser radiation (632.8 nm) evaluated by chemiluminescence test. III. Effect of dark period between pulses. *Lasers Life Sci*. 1997; 7(3):141-56.
14. Poeschl PW, Eckel D, Poeschl E. Postoperative prophylactic antibiotic treatment in third molar surgery – a necessity? *J Oral Maxillofac Surg*. 2004;62(1):3-8.
15. Savin J, Ogden GR. Third molar surgery – a preliminary report on aspects affecting quality of life in the early postoperative period. *Br J Oral Maxillofac Surg*. 1997;35(4):246-53.
16. McGrath C, Comfort MB, Lo EC, Luo Y. Changes in life quality following third molar surgery – the immediate postoperative period. *Br Dent J*. 2003;194(5):265-8.
17. López-Ramírez M, Vilchez-Pérez MA, Gargallo-Albiol J, Arnabat-Domínguez J, Gay-Escoda C. Efficacy of low-level laser therapy in the management of pain, facial swelling, and postoperative trismus after a lower third molar extraction. A preliminary study. *Lasers Med Sci*. 2012;27(3):559-66.
18. Braams JW, Stegenga B, Raghoobar GM, Roodenburg JL, van der Weele LT. Treatment with soft laser. [The effect on complaints after the removal of wisdom teeth in the mandible]. *Ned Tijdschr Tandheelkd*. 1994;101(3):100-3.Dutch.
19. Wahl G, Bastänier S. [Soft laser in postoperative care in dentoalveolar treatment]. *ZWR*. 1991;100(8):512-5. German.
20. Tunér J, Hode L. It's all in the parameters: a critical analysis of some well-known negative studies on low-level laser therapy. *J Clin Laser Med Surg*. 1998;16(5):245-8.
21. Pandurić DG, Brozović J, Sušić M, Katanec D, Bego K, Kobler P. Assessing health-related quality of life outcomes after the surgical removal of a mandibular third molar. *Coll Antropol*. 2009; 33(2):437-47.
22. Gbotolorun OM, Olojede AC, Arotiba GT, Ladeinde AL, Akinwande JA, Bamgbose BO. Impacted mandibular third molars: presentation and postoperative complications at the Lagos University Teaching Hospital. *Nig Q J Hosp Med*. 2007;17(1):26-9.
23. Mattiello FD, Coelho AA, Martins OP, Mattiello RD, Ferrão Júnior JP. In vitro effect of photodynamic therapy on aggregatibacter actinomycetemcomitans and Streptococcus sanguinis. *Braz Dent J*. 2011; 22(5):398-403.
24. Marković AB, Todorović L. Postoperative analgesia after lower third molar surgery: contribution of the use of long-acting local anesthetics, low-power laser, and diclofenac. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2006; 102(5):e4-8.
25. Aras MH, Güngörmüş M. Placebo-controlled randomized clinical trial of the effect two different low-level laser therapies (LLLT)-intraoral and extraoral-on trismus and facial swelling following surgical extraction of the lower third molar. *Lasers Med Sci*. 2010; 25(5):641-5.
26. Markovic A, Todorovic Lj. Effectiveness of dexamethasone and low-power laser in minimizing oedema after third molar surgery: a clinical trial. *Int J Oral Maxillofac Surg*. 2007; 36(3):226-9.