



Comparative Study of the Efficacy of Low-Level Laser Therapy and Dexamethasone in Reducing the Severity of Post-Operative Inflammatory Response Following Surgical Extraction of Mandibular Third Molars

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Abstract

Objectives To assess the efficacy of low-level laser therapy (LLLT) over dexamethasone in reducing postoperative edema and trismus following surgical removal of mandibular third molars.

Study design A single-center, parallel group, randomized, prospective, single-blind clinical trial on 50 patients between the age 18–40 years, requiring surgical extraction of mandibular third molars classified as mesioangular, class II and position B impactions, was selected for the study. The selected patients were randomly divided into two groups:

Group 1, n = 25, Soft Tissue Diode laser was applied intra-orally and extra-orally at the insertion of the masseter.

Group 2, n = 25, 8 mg of Dexamethasone was given intravenously preoperatively.

Trismus and edema were calculated preoperatively and on the 1st and 5th postoperative day. The collected data were subjected to statistical analysis using student's t test.

Results Trismus (4.61 ± 0.26 cm [$p = 0.0001$]) in the LLLT group was significantly less than the dexamethasone group (trismus: 3.82 ± 0.73 cm). Edema at different anatomic locations in the LLLT group was also significantly

less than the dexamethasone group (Angle-tragus [$p = 0.0008$], angle-canthus [$p = 0.0021$], angle-ala [$p = 0.0258$], angle-commissure [$p = 0.0168$], angle-mentus [$p = 0.0227$]).

Conclusion This study demonstrates that LLLT was beneficial in reduction in edema and trismus compared to dexamethasone following surgical extraction of third molars.

Keywords Dexamethasone · Low-level laser therapy (LLLT) · Edema · Trismus · Postoperative

Introduction

Surgical extraction of impacted third molar is the most common procedure performed in the oral and maxillofacial surgery office [1]. The local signs of inflammation following routine third molar surgeries such as postoperative edema and trismus disturb the patient much more than the surgical procedure itself. Patients experience a varied range of unnerving symptoms after surgical extraction of third molars. These include pain, trismus, facial edema and functional limitation [2]. Postoperative edema is a sequel of tissue injury, a consequence of reflection of muscular attachments in particular and the surgical procedure in general, and appears as a result of direct insult to blood and lymph vessels. This condition is reflective of fluid accumulation in the interstitial area due to transudation from injured blood vessels and fibrin obstruction of lymph drainage. The size of the edema depends on the magnitude of tissue injury and looseness of the connective tissue. Edema is particularly severe around 12–48 h after surgery, but may completely resolve in 5–7 days [3]. Postoperative trismus is another sequel of third molar surgery, generally

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arising from the inflammation of the muscles of mastication, masseter being the suspect in most of the cases. Several means have been used to prevent the occurrence of postoperative edema and trismus, including drugs, physical procedures (enzymes, steroids, cold packs, etc.), Ultrasonography and Hilotherapy. The administration of local or systemic corticosteroids and nonsteroidal anti-inflammatory drugs is recommended; however, adjunctive techniques like compression, cryotherapy and LLLT in combination with drug therapy are gaining popularity as they help in providing holistic relief without any unwarranted side effects [4,5]. LLLT exhibits anti-inflammatory effects by having a direct effect on lymph vessels (increase in number) and blood vessels (decrease in permeability). Additionally, LLLT increases protein absorption by activation of macrophages, modifying hydrostatic and intracapillary pressure. LLLT induces the absorption of interstitial fluids with a consequent reduction in edema [6,7]. Also, LLLT increases the production of cytochrome oxidase and accelerates conversion of ADP to ATP [6,7]. This in turn aids the healing procedure bringing about resolution of trismus and pain. Although LLLT has been widely used to manage postoperative sequel of third molar surgeries, there still exists ambiguity over its efficacy, as the literature is replete with conflicting studies. A study conducted by **Royesdal** did not find any beneficial effects of LLLT on trismus and edema following surgical extraction of third molars [8]. However, studies such as those conducted **Batinjan** showed marked reduction in edema following the use of laser therapy [9]. Such conflicts are mainly due to different study designs, differing measurement parameters as well as due to different laser types and irradiation parameters [5,6,8,10,11,14]. The aim of this study was to compare the effectiveness of a LLLT and dexamethasone, used locally and systemically, respectively, in minimizing edema (as revealed by facial measurements) and trismus (as revealed by maximum inter-incisal distance) after surgical removal of impacted lower third molars under local anesthesia.

Material and Methods

Study Sample

A single-center, parallel group, randomized, prospective, single-blind clinical trial was conducted. Fifty patients between the age 18–40 years fulfilling the inclusion criteria were selected for the study between December 2015 to August 2017. The study was submitted to and approved by the ethics committee of the institute (IRB Reference No. 2015/P/0S/35). The patients were randomly designated into two groups by tossing a coin.

The sample size was calculated with an absolute precision of 80% and clinically significance level of 0.05, and a sample size of 20 participants per group was calculated. With a dropout rate of about 20 percent, 25 patients were recruited for each group in the present trial.

Group 1, $n = 25$ (Patients who received Low-Level Laser Therapy). Soft Tissue Diode laser was applied intra-orally and extra-orally on the skin surface at the insertion of the masseter muscle, postoperatively, immediately after the completion of the procedure, before the onset of inflammation [8]. A soft tissue diode laser device (Biolase, model Ezlase 940) with a wavelength of 940 nm was used for the study. The laser probe was used in continuous wave mode, with the probe approximately 1 cm from the target area. The LLLT parameters used in the study are as follows: (Table 1).

Group 2, $n = 25$ (patients who received dexamethasone). A single dose of 8 mg dexamethasone was given intravenously in a 2 cc syringe preoperatively, 30 min prior to the surgery. 8 mg Dexamethasone was used as it has been found to cause greater reduction in edema and trismus as compared to a dosage of 4 mg [21]. Dexamethasone with a half-life of 36–54 h provided a longer of duration of action [22].

Patients with similarly impacted wisdom teeth, that is, mesioangular (Winter's classification), class II and position B impactions (Pell-Gregory classification) between the age group of 18 to 40 years with no comorbidities, having good health status with clinical and radiographic indication for surgical extraction of third molars were selected for the study [20]. Patients above the age of 40 years, with active signs of infection or any systemic disease, periodontally compromised dentition, history of use of steroids and pregnant or lactating females, were excluded from the study.

Table 1 Low-level laser therapy settings

Parameter	Intra-oral	Extra-oral
Wavelength	940 nm	940 nm
Power	0.3 Watts	0.5 Watts
Irradiation time	40 s	50 s
Energy	12 J	25 J
Energy density	4 J/cm ²	8 J/cm ²
Pulse rate	Continuous	Continuous
Mode	Non-contact	Non-contact
Spot Size	3 cm ²	3 cm ²

Intervention

Informed consent was obtained from all the selected patients. The surgical procedures were performed by the same surgeon. All procedures were performed under local anesthesia with infiltration of the anesthetic lignocaine hydrochloride 2% with epinephrine 1:100,000 for inferior alveolar, lingual and buccal nerve blocks. Ward's incision was given to gain access to the teeth, elevation of the flap, and buccal and distal osteotomies were performed. After removal of bone, the teeth were sectioned followed by extraction. The soft tissue was carefully repositioned using interrupted 3.0 vicryl (polyglactin 910) sutures. The patients were prescribed postoperative medications including 625-mg amoxicillin–clavulanic acid tablet every 12 h for 5 days, metronidazole 400 mg tablet thrice daily for four days, a 50 mg diclofenac sodium/potassium tablet every 12 h for 5 days for pain relief and a 40 mg pantoprazole once daily for 5 days to be taken on empty stomach. The patients were asked to use chlorhexidine 0.12% mouthwash twice a day for 5 days. Lukewarm saline solution rinses 4 to 5 times daily were advised in both the groups starting on the day after surgery.

Data Collection

This study was a single-blind study, in which the researcher who analyzed the responses after administration LLLT/dexamethasone was unaware of the treatment received.

Both the groups were evaluated for predictor variables like preoperative inter-incisal mouth opening (in centimeters) and preoperative cheek measurements (in centimeters) from angle of the mandible to the following points:

1. Tragus.
2. Outer canthus of eye.
3. Ala of nose.
4. Commissure of mouth.
5. Mentus. (Figs. 1, 2, 3, 4)

The outcome variables were postoperative inter-incisal opening evaluated by measuring the distance on maximal opening between the maxillary and mandibular central incisor with a metallic scale on the 1st and 5th postoperative day and postoperative cheek measurements (in centimeters) taken with a silk thread and centimeter ruler scale on the 1st and 5th postoperative day.

Statistical Analysis

Normal Distribution of the collected data was evaluated using Kolmogorov–Smirnov Test. Data were expressed in terms of mean \pm standard deviation. Facial Swelling (Edema) and Trismus scores were compared using the



Fig. 1 Facial measurements for edema

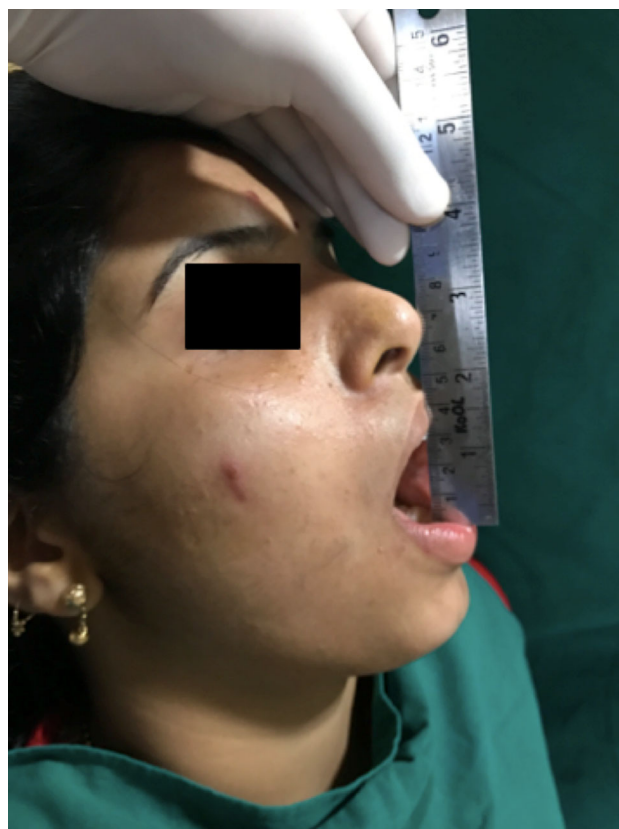


Fig. 2 Mouth opening measurements

Independent ‘*t*’ test. Statistical significance: ‘*p*’ value was calculated using the Paired ‘*t*’ test. $P < 0.05$ was considered significant.



Fig. 3 Laser application at the insertion of masseter muscle

Results

No adverse reactions were noted in the patients undergoing treatment. Duration of the procedure ranged from 15 to 35 min, with an average of 22 min. Fifty patients requiring surgical extraction of third molars were included in the study, 30 were males (60%) and 20 females (40%), with a mean age of 28.36 years. Trismus on the first postoperative day (4.27 ± 0.27 cm [$p = 0.0001$]) and on the fifth postoperative day (4.61 ± 0.26 cm [$p = 0.0001$]) was significantly less in the dexamethasone group (trismus: first postoperative day 3.02 ± 0.80 cm, fifth postoperative day: 3.82 ± 0.73 cm). Postoperative mouth opening exhibited a reduction of 3.60% in the laser group, where LLLT irradiation was done. The postoperative reduction in the mouth opening in the dexamethasone group was much larger, around 17.96%. Therefore, statistical analysis of the results exhibited a significant difference between the two study groups (Table 2). Postoperative edema at different anatomic locations in the LLLT group was also significantly less than the dexamethasone group. Statistically significant difference was found between the two study groups: angle-tragus (laser: 0.15 ± 0.16 cm, dexamethasone: 0.66 ± 0.70 [$p = 0.0008$]), angle-canthus (laser: 0.13 ± 0.11 cm, dexamethasone: 0.39 ± 0.38

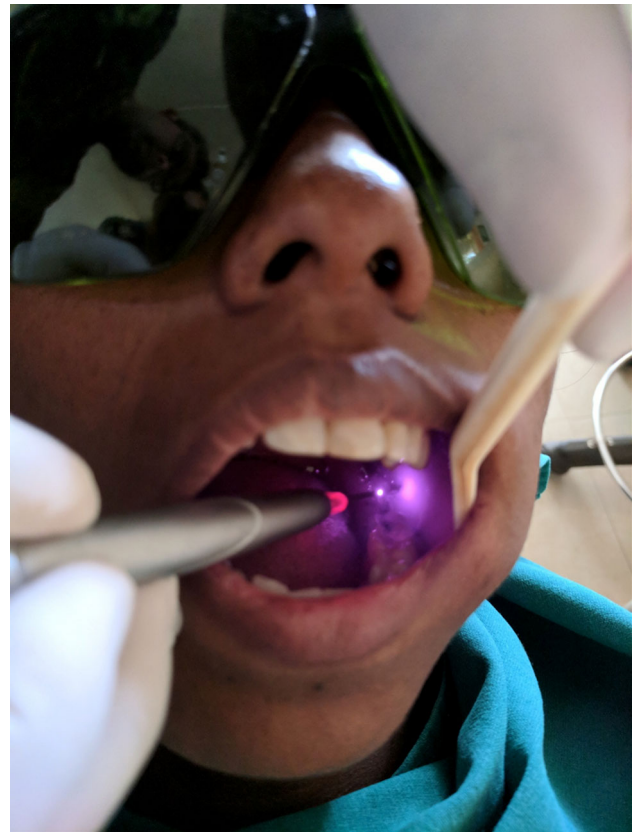


Fig. 4 Intra-oral laser application

[$p = 0.0021$]), angle-ala (laser: 0.16 ± 0.13 cm dexamethasone: 0.54 ± 0.82 [$p = 0.0258$]), angle-commissure (laser: 0.15 ± 0.11 cm, dexamethasone: 0.54 ± 0.82 [$p = 0.0168$]), angle-mentus (laser: 0.12 ± 0.13 cm, dexamethasone: 0.40 ± 0.58 [$p = 0.0227$]) (Table 3).

Therefore, this study found that LLLT was far more beneficial in reduction in edema and trismus compared to parenteral administration of dexamethasone following surgical extraction of third molars.

Discussion

Surgical removal of mandibular third molar in the present generation of well aware patients makes it imperative for the maxillofacial surgeon to carry out an impeccable procedure with minimum postoperative discomfort to the patient. In such a scenario, LLLT is an effective tool in dealing with the postoperative edema and trismus following surgical extraction of impacted third molars. The anti-inflammatory effects of LLLT have been proved both experimentally and clinically [3,15–17]. However, there is still ambiguity over the role of LLLT due to conflicting results seen in different studies. Such conflicts are mainly due to different study designs, differing measurement

Table 2 Comparison of Pre-op, Day 1 and Day 5 time points with respect to mouth opening scores in laser group and dexamethasone group

Time points	Laser group			Dexamethasone group			<i>t</i> value	<i>P</i> value
	Mean	SD	SE	Mean	SD	SE		
Pre-op	4.78	0.31	0.06	4.66	0.47	0.09	1.1362	0.2615
Day 1	4.27	0.27	0.05	3.02	0.80	0.16	7.4494	0.0001*
Day 5	4.61	0.26	0.05	3.82	0.73	0.15	5.0971	0.0001*
Pre-op Day1	0.52	0.22	0.04	1.64	0.73	0.15	− 7.3971	0.0001*
Pre-op Day5	0.17	0.09	0.02	0.84	0.56	0.11	− 5.8813	0.0001*
Day 1–Day 5	− 0.34	0.19	0.04	− 0.80	0.61	0.12	3.5827	0.0008*

p* < 0.05Table 3** The comparison of edema level over 5 days in the laser and dexamethasone groups

Marking	Group	Preoperative mean	Postoperative Day 1 mean	Postoperative day 5 mean	Standard deviation	<i>P</i> value
Angle-Tragus	Laser	7.03	7.17	7.18	0.16	0.0008*
	Dexamethasone	6.75	7.61	7.41	0.70	
Angle-Canthus	Laser	10.43	10.58	10.56	0.11	0.0021*
	Dexamethasone	10.27	10.86	10.66	0.38	
Angle-Ala	Laser	11.66	11.89	11.82	0.13	0.0258*
	Dexamethasone	12.02	12.69	12.56	0.82	
Angle-Commissure	Laser	10.26	10.43	10.41	0.11	0.0168*
	Dexamethasone	9.76	10.58	10.32	0.82	
Angle-Mentus	Laser	11.16	11.34	11.28	0.13	0.0227*
	Dexamethasone	10.78	11.19	11.18	0.58	

**p* < 0.05

parameters as well as to different laser types and irradiation parameters [5,6,8,10,11,14].

Roynesdal et al. evaluated the effect of LLLT on postoperative swelling and trismus, following third molar surgery in patients with symmetrical impactions of mandibular third molars, who underwent two separate procedures. Subjects were irradiated unilaterally with a 6-J semiconductor laser. The clinical trial exhibited pain reduction with decrease in swelling and trismus, nine hours postoperatively. However, benefits were not found to be statistically significant [8]. Fernando et al. investigated the effect of LLLT on postoperative swelling by performing extraction of impacted lower third molars in patients with symmetrical impactions of mandibular third molars. Laser with a wavelength of 830 nm, 30 mW, was applied intra-orally at 4 J, at the surgical site. Data analysis exhibited statistically insignificant difference in pain and swelling on the third postoperative day between laser and placebo sides. Also, no difference in the healing pattern of the two sides was noted on the seventh postoperative day [10].

Ramirez et al. conducted a prospective, randomized, double-blind clinical trial undertaken to evaluate the

analgesic and anti-inflammatory effects of a low-level laser therapy following removal of impacted mandibular third molars in patients having symmetrical impactions. The subjects were irradiated with a laser having 5 J/cm² of energy density, wavelength of 810 nm, and an output power of 0.5 W. Edema and trismus data obtained after 2nd and 7th postoperative days did not exhibit any statistically significant changes. Thus, all of these authors concluded that LLLT had no beneficial effect on postoperative edema and trismus [11].

In all these studies, the laser dosage used was much lower, which the authors feel would be inadequate to bring about any tangible benefits. The studies conducted by both Roynesdal et al. and Fernando et al. do not talk about the fluence of the laser. Therefore, we do not know the energy density delivered to the patient. Therefore, there are chances that inadequate laser dosage was delivered to the patients. All these studies applied laser intra-orally with no laser irradiation extra-orally. Surgical extraction of impacted third molars might result in spasm of the masseter muscle, which would not be addressed by intra-oral laser irradiation alone.

However, in complete incongruity Markovic and Todorovic reported that LLLT significantly reduced postoperative swelling following third molar surgery. One hundred and twenty patients were randomly divided into four groups, Group 1 received LLLT irradiation immediately after the surgical procedure, Group 2 was administered intramuscular injection of 4 mg dexamethasone into the internal pterygoid muscle, group 3 received LLLT irradiation supplemented by systemic dexamethasone 4 mg intramuscular injection into the deltoid region, followed by 4 mg of dexamethasone intra-orally six hours postoperatively, and Group 4 served as the control with administration of usual postoperative medications and local measures such as ice pack. Data evaluation showed considerable reduction in edema in all the groups that received LLLT in comparison with the control group, with the group receiving LLLT along with simultaneous administration local steroid showing the foremost results [6].

Landucci et al. reported significant reduction in percentage trismus and edema in the laser group in comparison with the placebo group on the 2nd and 7th postoperative day. They demonstrated that both intra-oral and extra-oral application of LLLT was more beneficial in significantly reducing postoperative edema [12]. Aras et al. studied two groups that underwent extraction of impacted third molars, applying low-level laser irradiation, both intra-orally and extra-orally. Statistical evaluation revealed significant reduction in postoperative edema and trismus in comparison with the control group [14].

The results of our clinical trial were akin with the observations made by **Aras and Güngörmüş**, who advocated extra-oral laser irradiation to relieve spasm of the masseter muscle. However, in our study we obtained favorable results by combining extra-oral with intra-oral laser irradiation, which resulted in better reduction in trismus and edema [8,12,13]. We suggest, a cumulative effect of intra- and extra-oral irradiation (intra-oral: 4 J/cm², extra-oral: 8 J/cm²) resulted in better healing around the surgical site and relaxation of masseter muscle both qualitatively and quantitatively resulting in improved mouth opening in the postoperative period. The anti-edematous effects of LLLT seem to be dose dependent. LLLT dose less than 4 J/cm² does not seem to have any tangible benefits. In our study, the therapeutic dosage was 4 J/cm² (940 nm wavelength, 0.3 W) intra-orally and 8 J/cm² (940 nm wavelength, 0.5 W) extra-orally. The wavelength of LLLT used lies within the optical window (600–1070 nm), which ensured maximum penetration of deeper-seated tissues, relating to multiple peaks of cytochrome c oxidase within that range [18]. The authors feel a higher single dose postoperatively over a time period of 30 s to 1 min is adequate to provide dosage of 4–8 J/cm² to achieve optimal anti-edematous effects rather than giving

multiple doses. This treatment is completely noninvasive with potential adverse effects similar to other devices used in clinical trials.

The findings of our study were in tandem with the work of **Pryor**, who described the possible anti-edematous activity of LLLT, based on a direct effect on lymph vessels (increase in number) and blood vessels (decrease in permeability) in conjunction with increased protein absorption by macrophage activation, modification of hydrostatic and intra-capillary pressure, with resultant absorption of interstitial fluids. There is evidence that LLLT has significant neuropharmacological effects on the synthesis, release and metabolism of such neurochemicals as serotonin and acetylcholine at the central level and histamine and prostaglandin at the peripheral level. This anti-inflammatory effect can be explained with the effect of LLLT on the synthesis of endorphin and the decrease in the activity of bradykinin on C fibers [6,7].

A plausible explanation for the beneficial effects of LLLT can be inferred from the molecular level trials of **Fujimaki and Shimoyama**, which demonstrated attenuation of Reactive Oxygen Species following irradiation of extracted neutrophils with LLLT. The reduction in the levels of Reactive Oxygen Species exhibited notable decrease in the inflammatory process coupled with enhanced wound healing. Wound healing was further aided by the increased production of mitochondrial Cytochrome C oxidase, resulting in accelerated ADP to ATP conversion [15]. Laser biostimulation has a stimulatory effect on the antenna pigments of the respiratory chain which brings about immediate cell vitalization by increased mitochondrial production of adenosine triphosphate (ATP) brought about by electron transfer in the inner membrane of mitochondria. Laser enhanced biostimulation induces intracellular metabolic changes, resulting in rapid cell division, increased proliferation and migration of fibroblasts along with rapid matrix production [19,23]. **Boschi et al.** reported anti-inflammatory properties of LLLT brought about by inhibition of IL-6, TNF- α , IL-10 and MCP-1 [17]. These findings were further corroborated by the meta-analysis conducted by **Lynda Woodruff et al.** to ascertain the beneficial effects of LLLT on reduction in inflammatory markers and enhanced wound healing [16].

The strengths of the study include symmetrical mandibular third molars, which eliminated any variations in the context of difficulty index variation. The study also combined the beneficial effects of intra-oral and extra-oral laser application as well as single session of LLLT application saved time and labor of both the doctor and the patient.

This study establishes a direct link between LLLT and alleviation of postoperative symptoms of trismus and edema. Patients treated with LLLT showed larger clinical

reduction in edema and trismus. These effects result in reduction in patient discomfort following surgical removal of impacted third molars. LLLT brings about greater relaxation of masseter muscle and accelerates healing as a result of deep penetration into the tissues. However, multicenter studies with larger sample size are required to definitively identify the beneficial effects of LLLT. To conclude, LLLT is an effective adjunctive modality to improve the quality of patient care by reducing postoperative trismus and edema.

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Declaration

Conflict of interest All authors declare that they have no conflict of interest.

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