Consequences of 660 nm Diode Laser Following Postsurgical Exodontia in Patients under Contraceptive Pills: A Randomized Double-blinded Clinical Trial

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ABSTRACT

Aim: The photobiomodulation (PBM) effect of 660 nm diode laser in reducing pain, edema, trismus and promote healing subsequently to the transalveolar extraction of mandibular third molars in female patients taking contraceptive pills were evaluated.

Materials and methods: Fifty female patients participated in our study. The 660 nm diode laser was applied immediately on randomly selected patients of the study group ($n = 25$) over the surgical site for 1 minute with continuous laser beam application. For the control group ($n = 25$), the same extraction procedure was performed without the application of 660 nm diode laser. Pain intensity, swelling, trismus, and healing was evaluated before extraction and during recall visits 24 hours, 48 hours, and 7 days postoperatively.

Results: The values of pain, swelling, and trismus were significantly inferior in the study group compared to the control group ($p < 0.05$) at T2 and T3; while the values of the healing index were significantly superior in the study group compared to the control group ($p < 0.001$) at T1, T2, and T3.

Conclusion: Using 660 nm diode laser reduced the postsurgical discomforts (pain, edema, and trismus) and promote healing associated following transalveolar extraction of the lower third molar.

Clinical significance: To develop a framework based on the results regarding the PBM effect of 660 nm diode laser following transalveolar extraction of lower third molar in a female patient taking oral contraceptive pills, which may help to improve the treatment services provided to the community.

Keywords: Contraceptive pills, Photobiomodulation, 660 nm diode laser, Transalveolar extraction.

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INTRODUCTION

Third molar extraction surgery is one of the standard procedures in oral surgery and is known as a standout amongst the most well-known measure performed in maxillofacial outpatient procedures.¹⁻³ It is frequently accompanied with postoperative complications that usually presented with various frequencies and a broad extent of features, extends from slight postoperative discomfort to progressively complexities that necessitate further management with the capability of changeless harm to healing.⁴

Transalveolar extraction frequently accompanied by postoperative pain, swelling, and trismus which reaches its peak postsurgical within the first 5 hours and lasted for 2-3 days and start to subside slowly till the 7th day postoperatively.^{5,6} Moreover, post-surgical edema has high incidence to develop and usually originated from tissue responses to surgical manipulation. Its onset is slow and reaches to its peak after 48 hours postoperatively.⁷ Edema starts to subside at the 4th postoperative day and totally disappear at the 7th postoperative day.⁸

Jaw stiffness also had been that rise and reaches its peak on the 2nd postsurgical day and completely disappears within 1 week.⁹ There is a direct relation between postoperative pain and limitation of mouth opening, supposing that pain might be one of the principle reasons to develop trismus following transalveolar extraction procedures.⁹ Edema, pain, and trismus are reckoned as temporary adverse symptoms that may develop after surgery. Although these complications are temporary they may cause anxiety for the patient.⁸

On some occasions, the succession of typical healing after extraction does not generally, take place, an early blood clot

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may be formed within the extraction socket and followed by premature fibrinolysis of the clot, associated with pain, halitosis,¹⁰ and development of alveolar osteitis (AO) that usually appears at the third postextraction day.⁹

The oral contraceptive pill is one of the main drugs that was connected to the development of AO. It used widely since 1960s and several studies report a significantly higher rate of AO in females taking oral contraceptive pills.¹¹⁻¹³ Estrogen was assumed to significantly cause effect on the fibrinolytic cycle. Estrogen indirectly will stimulate the fibrinolytic cycle (elevating factors II, VII, VIII, X, and plasminogen) and consequently escalates disintegration of the fibrin clot and increasing the possibility of developing AO.¹⁴

Different strategies had been proposed for controlling the immediate inflammatory reactions that might be developed following the transalveolar extraction of the lower third molar in the literature. Some proposed various surgical closure approaches with or without using drains,^{15,16} using medication such as analgesics,¹⁷ corticosteroids,^{18,19} fibrin and platelet glue,^{20,21} antibiotics^{22,23} and other proposed new modalities to include physical therapeutic approaches such as cryotherapy²⁴ and laser application.²⁵

The implementation of low-level laser therapy (LLLT) as a successful tool in dentistry reported in the literature for more than three decades.²⁶ Photobiomodulation, likewise known also as LLLT uses the energy of light to initiate biological reactions from the cell and organize the cell function. Several investigations reported that LLLT acts on the mitochondria of the cell, primarily on cytochrome C oxidase enzyme in the electron transfer chain and porphyrins on the cell membrane.^{26,27}

Using PBM postsurgically aimed to reduce the need for analgesics postoperatively and accelerating patient recovery immediately after surgery which effects on patient feedback toward their dental treatment.²⁸

Several studies have exhibited that PMB can significantly reduce pain throughout the healing period, also encourage soft tissue healing, making it a promising treatment tool after surgical procedures.^{29,30}

Low-level laser therapy show more superior results than other modalities and, contingent on the dosage, wavelength, and the context of the irradiated area, it can enhance a wide cellular reaction. Also, it had been utilized with different power densities to reduce tissue damage. Laser energy proved to improve the proliferation of osteoblasts, epithelial cells and fibroblasts, activation of the lymphatic system, increased angiogenesis, and bone mineralization.⁵

Furthermore, some investigators reported the improvement of the ingestion of proteins by enhancing macrophages activity and improving intracapillary hydrostatic pressure that decrease the extracellular fluid, reducing postsurgical edema.^{31,32}

In addition, LLLT has been proved to significantly reduce inflammation through its antiinflammatory action on the initial healing stages; lowering chemical mediators, cytokines, swelling, and migration of inflammatory cells, and enhance growth factors synthesis, which directly play an important role in the tissue recovery process, in addition to its indirect action on the reduction of the inflammation inherent that will boost the repair of the daily damage of tissues.³³

Many investigations proposed also that LLLT has a pain relieving impact as it provides a better-balanced arrangement of the lipid bilayers providing more stabilization of nerve cell membranes, also augment the oxidation–reduction status of the cells and would stimulate the formation of adenosine triphosphate (ATP), promoting the rebuilding of neuronal membranes and reducing transmission of pain.^{34,35}

Several limitations of using laser therapy had been reported and were attributed to its possible biostimulation response on benign and malignant cells. The chance of irradiating the gonads, threatening of eye and thyroid gland irradiation, cardiac pacemaker, epilepsy, pregnancy, local infection, hematological disease patients with a malignant tumor and photosensitive skin or use of medication that causes photosensitivity considered as a contraindication for the use of laser therapy.^{36,37}

To date, there is no report in the English language, literature light on the effect of LLLT in decreasing the possibility of postoperative

complication that may be developed following transalveolar extraction of lower third molars in the female patient taking oral contraceptive pills. The current study will attempt to throw light on the PBM effect of LLLT which increases the perception of the patients toward the dental services provided to them.

MATERIALS AND METHODS

Subjects

Fifty female adult patients with a clinical and radiographically hopeless mandibular third molar indicating for extraction were selected from the outpatient dental clinic of the College of Dentistry, Qassim University. Consents were obtained from all participants after providing detailed information about the laser therapy, its uses, impacts, indications, and expected reactions.

Subjects Inclusion/Exclusion Criteria

The following criteria had been applied in selecting patients participating in this study.

Inclusion Criteria

- Age range from 30 to 45 years with mean 32.3 years.
- All participants were grade I according to American Society of Anesthesiologists (ASA).
- Patients taking oral contraceptive pills.
- Normal hematological values.

Exclusion Criteria

- Patients with ASA grades II, III, and IV.
- Patients with extraoral swelling and cellulitis.
- Patients with temporomandibular joint ankyloses.
- Patients with systemic diseases.
- Local infection related to the lower third mandibular teeth.
- Patients were on antibiotics or analgesics treatment for the last month before extraction.

Study Design

The research was a randomized, double-blinded, controlled clinical trial conducted on female patients following transalveolar extraction of the mandibular third molar. Participants were randomly divided into two groups, the study group ($n = 25$) received 660 nm diode laser ($n = 25$) and the control group ($n = 25$) who did not receive diode laser. All surgical procedures were performed by the same investigator; while the assessment was performed by a different one.

Pretreatment Assessment

History

A detailed patient history was obtained from the selected patients including name, age, medical and medication history.

Treatment Protocol

All surgical procedures were carried out after effectively anesthetized the region of concern using inferior alveolar nerve block and long buccal nerve block techniques with OCTOCAINE 100 "Lidocaine HCl and 2% and Epinephrine 1:100,000" (Novocol Pharmaceutical of Canada, Inc., Ontario, Canada).

The difficulty of the surgical procedures was evaluated postoperatively using the parent scale modified by Garcia Garcia et al.³⁸ (Table 1).

Table 1: Parent surgical difficulty scale modified by Garcia Garcia

Type	Technique
I	Simple extraction
II	Extraction requiring osteotomy
III	Extraction requiring osteotomy and coronal section
IV	Complex extraction (root section)

Fig. 1: SIRO laser 660 nm

A LLLT (SIRO Laser, Sirona Dental Systems GmbH, Bensheim, Germany Fig. 1) was utilized in the investigation. All participants were not informed if they had received laser therapy or not. In the study group, the laser intensity was adjusted 25 mW, with a wavelength of 660 nm. The diode laser MultiTip (SIRO Laser, Sirona Dental Systems GmbH, Bensheim, Germany) was used in noncontact mode and was set at a distance of 1 cm from the tissue surface. The laser device was activated and the diode red light was applied with constant laser beam illumination for 60 seconds over the surgical area (Fig. 2). In the control group, the diode laser MultiTip was placed over the surgical area, but without any illumination.

Normal saline mouth wash had been prescribed for all participants and the sutures were removed on the 7th day postoperatively.

Postoperative instructions, including soft dietary intake on the first 48 hours after surgery, and no tooth brushing, rinsing or spitting on the day of surgery. Also, they were advised to start regular tooth brushing on the second day after surgical procedure, taking into consideration to avoid tooth brushing near the site of surgical for 72 hours.

Treatment Sequence

Before starting the procedures (baseline; T0) and during recall visit, (24 hours postsurgical; T1, 48 hours postsurgical; T2, and 7 days postsurgical; T3) a schedule was followed. The reasons for this schedule were to achieve patient compliance and to achieve effective numbers of application of the treatment. The application of diode laser, evaluating posttreatment results, and collecting data were carried out by different examiner.

Posttreatment Evaluation

Subjective and objective assessments were recorded for each patient.

Fig. 2: SIRO laser 660 nm in use

Subjective Evaluation

Universal pain assessment tool (UPAT) had been used for subjective evaluation (Fig. 3). Using UPAT assess the level of pain using faces or behavioral expressions to interpret pain if patients are unable to identify the severity of their pain. It consisted of a 10 cm printed chart marked from 0 to 10 (0; no pain, 1–3; minor pain experienced, 4–6; moderate pain experienced and 7–10; severe pain experienced) and was measured at four points of the treatment sequence.³⁹

Objective Evaluation

The postsurgical edema was measured immediately after 24 hours of the surgical procedure (the baseline level was set before surgery). The distance from the chin tip to the lower part of the auricle lobe was measured at four points of the treatment sequence, and the edema coefficient (E_c) was calculated using the modified equation of Carrillo.⁴⁰

$$E_c = \frac{\text{postoperative distance} - \text{preoperative distance}}{\text{preoperative distance}} \times 100$$

Limitation of mouth opening or trismus was evaluated at the four points of the treatment sequence by measuring the maximum interincisal opening with a ruler.⁴⁰ Participants who have a 10 mm at T2 and T3 should be considered with trismus.⁴¹

The wound and soft tissue healing evaluation was performed using the Landry and Turnbull index⁴² (Table 2).

Statistical Analysis

The results were statistically analyzed using the Statistical Package for Social Sciences (SPSS for Windows, release 17 Chicago, IL). The statistical test used as follows:

- Number and percent of each category.
- Mean and standard deviation (SD) for numerical data.
- Student *t* test: for statistically analyzing the difference between the two groups during the follow-up evaluation periods.

RESULTS

In a total of 80 patients, 30 patients were excluded from the study either due to improperly filling the UPAT or did not follow the treatment and others for not fulfilling the study criteria.

No significant differences were reported between the two groups regarding the duration or difficulty of the surgical procedure

0 Pain free	1 Very mild	2 Discomforting	3 Tolerable	4 Distressing	5 Vary distressing	6 Intense	7 Very intense	8 Utterly horrible	9 Excruciating unbearable	10 Unimaginable unspeakable
No pain	Minor pain			Moderate pain			Severe pain			
Feeling perfectly normal	Nagging, annoying, but does not interfere with most daily living activities. Patient able to adapt to pain psychologically and with medication or devices such as cushions			Interferes significantly with daily living activities. Requires lifestyle changes but patient remain independent. Patient unable to adapt pain.			Disabling; unable to perform daily living activities. Unable to engage in normal activities. Patient is disabled and unable to function independently			

Fig. 3: Universal pain assessment tool

Table 2: The Landry and Turnbull index for wound and soft tissue healing

Score	Clinical signs
Healing index 1: Very poor	Tissue color: $\geq 50\%$ of gingiva red Response to palpation: bleeding Granulation tissue: present Incision margin: not epithelialized with loss of epithelium beyond incision margin Suppuration: present
Healing index 2: Poor	Tissue color: $\geq 50\%$ of gingiva red Response to palpation: bleeding Granulation tissue: present Incision margin: not epithelialized with connective tissue exposed
Healing index 3: Good	Tissue color: $\geq 25\%$ and $< 50\%$ of gingiva red Response to palpation: no bleeding Granulation tissue: none Incision margin: no connective tissue exposed
Healing index 4: Very good	Tissue color: $< 25\%$ of gingiva red Response to palpation: no bleeding Granulation tissue: none Incision margin: no connective tissue exposed
Healing index 5: Excellent	Tissue color: all tissues pink Response to palpation: no bleeding Granulation tissue: none Incision margin: no connective tissue exposed

either in the amount of anesthetic vial used for the surgical procedure (Table 3).

The results show a statistically significant difference between the study and control groups with lower values of pain, swelling, and trismus at T2 and T3 of the follow-up period and higher values of the healing index at T1, T2, and T3 of the follow-up period among the participants of the study group (Table 4).

Table 3: Demographic and surgical data

	Study group ($n_1 = 25$)	Control group ($n_2 = 25$)
Mean age in years	40.1 ± 7.8	41.4 ± 7.6
Surgical difficulty grade: I/II/III/IV*	6/10/9/0	5/9/11/0
Mean duration of surgery in min	28.4 ± 8.4	30.3 ± 6.3
Mean number of anesthetic vials	2.40 ± 1.4	2.40 ± 1.2

*Surgical difficulty grade by parent scale modified by Garcia Garcia et al.

Pain

Evaluation of pain at T1 of postoperative periods shows a mean score of 0.49, in the study group and 0.54 in the control group with a p value of 0.669 which is statistically insignificant. On the other hand, at T2 and T3 of postoperative period evaluation shows a mean score of 2.22 and 0.55 in the study group and 3.81 and 1.36 in control group, respectively with a p value < 0.05 which is statistically significant (Fig. 4).

Edema

Evaluation of edema at T1 of postoperative periods shows a mean score of 0.96, in the study group and 1.78 in the control group with a p value of 0.10 which is statistically insignificant. On the other hand, at T2 and T3 of postoperative period evaluation shows a mean score of 2.64 and 0.00 in the study group and 5.78 and 0.94 in the control group, respectively with a p value < 0.05 which is statistically significant (Fig. 5).

Trismus

There was an improvement of the mouth opening in the study group when comparing it to the control group; the difference between the two groups were not significant at T1 while it was significant at T2 and T3 with a p value < 0.05 . Most of the participants attained their preoperative interincisal mouth openings at T3 of the postoperative period with superior privilege in the study group in comparison to the control group (Fig. 6).

Wound and Soft Tissue Healing

A higher proportion of individuals in the study group had better healing index when compared to the control group. This difference was statistically significant at T1, T2 and T3 of postoperative healing with a p value < 0.001 (Fig. 7).

Table 4: Mean and *p* values of pain, swelling, trismus, and healing index during the follow-up period

	T0		T1		T2		T3		
	Study group	Control group	Study group	Control group	Study group	Control group	Study group	Control group	<i>p</i> value
Pain	0.16 ± 0.1	0.29 ± 0.12	0.49 ± 0.24	0.54 ± 0.23	2.22 ± 1.3	3.81 ± 1.9	0.55 ± 0.2	1.36 ± 0.8	0.61/0.669/0.001* /0.04*
Edema	0.00	0.00	0.96 ± 0.45	1.78 ± 0.93	2.64 ± 0.54	5.78 ± 3.54	0.00	0.94 ± 0.63	0.00/0.10/<0.001* /0.008*
Trismus	5.20 ± 3.4	4.90 ± 3.1	4.70 ± 2.75	4.60 ± 2.9	4.00 ± 1.97	3.70 ± 1.62	4.80 ± 2.34	4.20 ± 2.64	7.84/0.63/<0.001* /0.007*
Healing	0	0	3.8 ± 2.5	2.7 ± 2.1	4 ± 1.78	3.6 ± 1.21	4.8 ± 2.92	4.0 ± 2.43	0.00/0.002*/0.005* /0.638

Student's *t* test, *p* < 0.05 (pain/swelling/trismus); *p* < 0.001 (healing)

Fig. 4: Difference in pain between two groups during follow-up periods **Fig. 5:** Difference in edema between two groups during follow-up periods

Fig. 6: Difference in trismus between two groups during follow-up periods

Fig. 7: Difference in healing between two groups during follow-up periods

DISCUSSION

Extraction of the third molar can be considered as a routine measure that applied daily in oral surgery practice, several complications were advocated third molar surgical extractions. Alveolar osteitis is one of these complications with incidence rate varies between 1% and 4% in normal extractions and increased to 5–30% transalveolar extraction.⁴³

One of the risk factors in developing AO is oral contraceptive (OC) drugs which enhance the fibrinolysis cycle within the extraction socket resulting in disintegration of the clot and consequently the development of AO.^{43,44}

The participants in this study were selected to be female patients on oral contraceptive pills. Several investigations proposed that oral contraceptives can be correlated positively with the incidence of AO.^{13,14,45} In our study, although none of the participants in the study or the control groups develop AO, the PBM

effect of LLLT resulted in better findings in the study group when comparing to the control group.

Surgical durations were similar between the two groups. No significant difference in the amount of anesthetic used in both groups was reported. To minimize bias all surgical procedures were performed by the same investigator.

Different strategies in the literature were proposed to reduce pain, edema, trismus and the risk of developing AO that may follow the transalveolar extraction of the lower third molar.^{15,24}

Recently, the implementation of LLLT in dentistry is gaining significant concern. Low-level laser therapy reduces the immediate inflammatory reactions and accelerates hard and soft tissue healing with minimizing the risk of developing potential postoperative complications.²⁵

Low-level laser therapy is constrained by the difficulties related to the calibration of the laser type, its wavelength output power, mode and time of the application, and the procedure utilized.^{19,46}

In our study group, the laser beam was administrated precisely over the surgical site for 60 seconds with constant irradiation. The MultiTip 8 mm was set at a distance of 1 cm in noncontact mode from the tissue surface. The power was adjusted to 25 mW, with a 660 nm wavelength. In 2005, Marković and coworker propose using energy output 4 J/cm² with a constant power density of 50 mW, wavelength 637 nm to assess the effectiveness of dexamethasone and low-power laser in minimizing edema after third molar surgery.⁵

On the other hand, Landucci et al. in 2015 propose using one dosage of 7.5 J/cm² at 10 mW, with an infrared 780 nm wavelength to assess the effectiveness of a single dose of LLLT in decreasing the postsurgical complications correlated to surgical extraction of the third molar.⁴⁷

In this study the values of pain, edema, and trismus were significantly lower in the study group compared to the control group ($p < 0.05$) at T2 and T3 of the follow-up periods.

Several studies did not succeed to record any favorable effects of LLLT in decreasing pain and edema associated with mandibular third molar extraction. Also, Taube et al. not able to report an advantageous result of using a single dose of LLLT in minimizing the postoperative pain following surgical extraction of the third molar.^{44,46}

On the other hand, Roynesdal et al.⁴⁸ reported lower values of pain, edema, and trismus at 9 hours after applying LLLT following third molar extraction surgery. Unfortunately, they were not able to confirm their findings statistically which may be attributed to the low irradiation dose they apply and short assessment period.

The impact of LLLT on severe pain following trauma proposed to be attributed to a decrease in edema, hemorrhage, neutrophil infiltration, and enzyme.⁴⁹ Saber et al. reported a reduction of pain at 48 hours postoperatively following the application of LLLT; however, no significant effects on the duration of pain were observed 7 days postoperatively.⁵⁰ Wathier et al. also reported a statistically significant reduction of pain at 1–5 days of postoperatively following the application of LLLT.⁵¹

On the other hand, Aras and Güngörmüş,⁵² and Carrillo et al.⁴⁰ observed a significant reduction in pain and trismus only after 7 postoperative days following an administration of intraoral LLLT. Also, Roynesdal et al.⁴⁸ and Fernando et al.,⁵³ reported that no clinical efficacious of LLLT was observed on lowering the postoperative complications associated with third molar surgery.

In 2015, Landucci et al. were evaluating the efficacy of a single dose of LLLT in reducing pain, edema, and trismus following third molar extraction surgery, and they reported that using 780 nm wavelength LLLT will reduce pain, trismus, and edema because it penetrates deep into tissues.⁴⁷

In our study, the healing index in the study group was superior then in the control group and the difference was statistically significant at T1, T2, and T3; of the postoperative period.^{54,55} This may be related to the fact that LLLT is not only capable to reduce pain and inflammation, but also can increase the rate and quality of wound healing through multiple processes involving increased proliferation of fibroblasts,⁵⁶ promoted epithelization,⁵⁷ enhanced organization and maturation of collagen fibers⁵⁸ and increased matrix synthesis and angiogenesis.⁵⁴

The clinical action of LLLT can be linked to the expression of antiapoptosis and prosurvival genes responsive to nuclear factor kappa B (NF- κ B). Low-level laser therapy can also promote mitochondrial respiration and stimulates redox-sensitive NF- κ B signaling via the production of reactive oxygen species (ROS).⁵⁹

Moreover, the effect of LLLT on cell membranes trigger the cellular response that induces multiple biochemical reactions and modifies the physiological processes in addition to enhance and promote secondary or indirect actions, and increase blood flow and lymphatic drainage result in the acceleration of the healing process.³¹

CONCLUSION

Although both group showed a reduction of postoperative complications following transalveolar extraction of the mandibular third molar, but using single-dose LLLT with a wavelength 660 nm, demonstrated a reduction of postoperative complication, and promoting soft and hard tissue healing when compared to the control group, that resulted in more patient satisfaction toward the dental service provided to them.

CONSENT

All authors declare that written informed consent was obtained from the patient prior conducting this research.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee (Code#: ST/50/2018) and have therefore been performed in accordance with the ethical standards laid down in the 1964 declaration of Helsinki.

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