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Systematic Review

Effect of photo-biomodulation therapy in decreasing postoperative pain after surgical removal of third molars compared to other treatment therapies: a systematic review

Shreya Ganguly*, Asish K. Das, Subhasish Burman, Abhijit Maji, Abhishek Khatua

Department of Oral and Maxillofacial Surgery, Dr. R. Ahmed College and Hospital, Kolkata, West Bengal, India

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***Correspondence:**
Dr. Shreya Ganguly,
E-mail: shreyathomasina1996@gmail.com

ABSTRACT

Post-operative pain, discomfort, and trismus are common postoperative complications after surgical extraction of third molars. Various therapeutic approaches like prescribing analgesic drugs, corticosteroids, and Non-steroidal anti-inflammatory drugs are followed to reduce these complications. Photo-biomodulation therapy (PBMT) utilizes a monochromatic light source that shows effects in all phases of inflammation by reducing edema, redness, heat, and pain. In vivo studies were searched to evaluate postoperative pain levels in patients who underwent photo-biomodulation therapy following extraction of impacted third molars. A comprehensive search was done from January 2023 to July 2023 in PubMed electronic databases. In addition, a manual search of the references mentioned in the studies and gray literature was done. The literature search yielded a total of 157 studies through a search in the electronic database PubMed. Among all the studies, 51 duplicate records were removed. Ninety-seven studies were removed after screening of titles and abstracts. A total of 9 studies were included for full-text reading. Five studies were included (one randomized single-blind study, two randomized double-blind split-mouth studies, and two randomized clinical trials) in the review. Four out of five studies that were included in this review demonstrated a positive impact of PBMT on reducing pain, especially during the post-operative period compared to other non-surgical treatment protocols. Photo-biomodulation therapy demonstrated an overall positive impact on reducing postoperative complications like edema and trismus.

Keywords: Photobiomodulation, Third molar, Post-operative pain

INTRODUCTION

Post-operative pain, discomfort, and trismus are common postoperative complications after surgical extraction of third molars. Post-operative complications are directly related to the degree of invasiveness during third molar removal surgery.[1,2] Various therapeutic approaches like prescribing analgesic drugs, corticosteroids, and non-steroidal anti-inflammatory drugs are followed to reduce these complications.[3] Previous literature reported that pre-operative administration of corticosteroids is also a very good approach to decrease post-operative swelling and pain.[4] However, there is still no standardized protocol present, which frequently causes excessive use of medications leading to renal and gastrointestinal disorders.[5-7]

Photo-biomodulation therapy (PBMT) utilizes a monochromatic light source (laser or Light emitting diode) to evaluate cellular metabolism and for therapeutic purposes.[8-10] Ruby laser (694 nm) was first used in an in-vivo model to treat tumors by Mester et al. The biostimulation principle of the laser was again used during wound healing in rats.[11-13] Recent literature has generated scientific evidence in favor of the red (600–700 nm) and infrared (770-1200 nm) wavelengths of laser that showed beneficial effects in the field of medicine.[14-16]

Apart from wound healing, it has been shown that PBMT activates the immune system and decreases the inflammatory response.[17] PBMT exhibits its effect by activating enzymatic processes which accelerates chemical reactions.[18] Photo-biomodulation therapy (PBMT) shows effects in all phases of inflammation reducing edema, redness, heat, and pain. It inhibits prostaglandin, and bradykinin synthesis and decreases histamine release. Other effects include increased phagocytosis, vasodilatation, blood flow, and lymphatic drainage.[19-21]

Photo-biomodulation therapy gradually becoming a popular treatment option in dentistry. Till now various alternative treatment plans have been used in dentistry to reduce post-operative pain after surgical removal of impacted molars like medications, cryotherapy, and platelet rich fibrin (PRF).[22,23] Although photo-biomodulation therapy might be an appropriate therapy for reducing post-operative complications after tooth removal surgery still enough evidence is not present in the literature regarding the use of PBMT in third molar removal surgery. Therefore, this systematic review aimed to evaluate the potential effect of PBMT to reduce post-operative complications after surgical extraction of impacted third molars.

METHODS

Information source/search strategy

In vivo, studies were searched for the evaluation of postoperative pain levels in patients who underwent photo-biomodulation therapy following extraction of impacted third molars. A comprehensive search was done from January 2023 to July 2023 in PubMed electronic databases. In addition, a manual search of the references mentioned in the studies and gray literature was done. Published articles in English languages and in vivo studies are only included in this review. Keywords used in this study were “photo-biomodulation therapy”, “third molar extraction”, “impacted third molars”, and “postoperative pain”. The following combination of keywords was used to search the literature – photo-biomodulation therapy and third molar extraction, photo-biomodulation therapy and impacted third molars, photo-biomodulation extraction and third molar extraction and post-operative pain. Two independent reviewers (SG and AD) conducted the literature search and any disagreements between reviewers were solved by discussion.

Preferred reporting items for systematic review and meta-analyses (PRISMA) guidelines were used and the following checklist was followed in this systematic review. This review is in the process of being registered in PROSPERO with acknowledgment receipt number 476959.

Population, intervention, control, outcome, study design (PICOS) strategy was followed- P: patients who underwent surgical extraction of impacted third molars, I: photo-biomodulation therapy was used in the postoperative period following surgical extraction of impacted third molars, C: non-surgical treatments (medications and placebo) were used in the post-operative period following surgical extraction of impacted third molars, O: postoperative pain assessment (visual analogue scale), and S: study design.

Focus question

“Does photo-biomodulation therapy decrease postoperative pain after third molar extraction compared to other non-surgical treatment protocols?”

Study design

Study designs used in this review were In-vivo randomized controlled clinical trials, prospective and retrospective studies.

Eligibility criteria

The inclusion criteria were: published articles on photo-biomodulation therapy following surgical extraction of impacted third molars, photo-biomodulation therapy should be used as an interventional procedure following extraction of impacted third molars, postoperative pain assessment should be used as an outcome variable in the study, published articles in the English language, randomized controlled clinical trials, prospective studies, retrospective studies, and in-vivo studies.

The exclusion criteria were: literature reviews, in-vitro studies, and animal studies; studies in non-English language; case reports and case series; and studies with incomplete data.

Data analysis

The data were extracted by two independent reviewers (SG and AD) from all the included studies. Extracted data were filled into a predetermined form, consisting of the following pieces of information: study, year, country, study design, sample description, and interventional procedure. Any disagreements between the reviewers were solved by discussion.

Assessment of risk of bias

Assessment of the risk of bias in the included studies was done according to The recommendations of the consolidated standards of reporting trials statement (CONSORT) by using the Cochrane tool for systematic reviews of interventions.[24] The assessed domains were sequence generation, allocation sequence concealment, blinding, incomplete outcome data, selective outcome reporting, and other sources of bias. Bias scores low, unclear, or high were used to assess the overall risk of bias. The risk of bias for each entry recording was scored as

"no" to indicate a high risk of bias, "yes" to indicate a low risk of bias, and "unclear" to indicate either a lack of information or uncertainty over the potential risk of bias. The extracted data were stratified and tabulated in chronological order in a summary-like format. Overall, the studies were considered 'high' quality if all conditions were met, 'low' quality if ≥1 condition did not meet, or 'unclear' quality if ≥1 condition was partly met.

RESULTS

Study selection

The literature search yielded a total of 157 studies through a search in the electronic database PubMed. Among all the studies, 51 duplicate records were removed. Ninety-seven studies were removed after screening of titles and abstracts. A total of 9 studies were included for full-text reading. Five studies were included (one randomized single-blind study, two randomized double-blind split-mouth studies, and two randomized clinical trials) in the review.[25-29] Four studies were excluded due to various reasons (Table 1).[30-33] The study selection procedure was done by two independent reviewers (SG and AD) and any disagreements between the reviewers were solved by discussion. The study selection procedure is shown in (Figure 1).

Quality of the included studies

Qualities of randomized controlled clinical trials were assessed by Cochrane's tool for systematic reviews of interventions.[24] All the included trials mentioned about allocation concealment and adequate sequence generation procedure during randomization. Blinding procedure was clearly mentioned in all the studies. All the studies measured pre-specified outcome criteria and mentioned about attrition and exclusion of patient with proper reason. Overall all the included studies had low risk of bias (Table 2).

Characteristics of the included studies

A total of 5 randomized control trials were included in this systematic review. Although only 5 studies were found to be eligible for inclusion in this systematic review, they were randomized controlled clinical trials, defined by the National Health and Medical Research Council (NHMRC) guidelines as the level of evidence II.[34] Out of five of the included studies, one study reviewed the extraoral application of PBMT, another study reviewed the extraoral and intraoral application of PBMT whereas three other studies reviewed the intraoral application of PBMT. All the included studies used photo-biomodulation as an intervention following surgical extraction of impacted lower third molars. In four of the included studies, the control group received placebo therapy whereas in one study the control group received an intramasseteric injection of methylprednisolone, and its effects were compared with that of PBMT. Characteristics of the included studies are presented in (Table 3) and outcome data has been mentioned (Table 4). Included studies evaluated the results through visual analog scale, mouth opening, and facial distance measurement at various post-operative time intervals. Some of the included studies also evaluated a secondary outcome variable which was the number of analgesics taken in the post-operative period.

Table 1: Excluded studies.

Name of study	Reason for exclusion
Abdel-Alim et al, 2015[30]	Compared the immediate versus delayed application of photo-biomodulation (PBM) therapy following odontectomy of horizontally impacted mandibular third molars.
Tenis et al, 2018[31]	Compare the efficacy of photo-biomodulation with light emitting diode (LED) in the control of pain, facial edema, trismus, and quality of life resulting from the extraction of impacted lower third molars.
Yuksek et al, 2021[32]	This study compared the effects of single and repeated photobiomodulation sessions, applied at two different therapeutic wavelengths within the infrared spectrum, on postoperative inflammatory response after extraction of impacted third molar teeth.
Filho et al, 2022[33]	Compared the effect of photobiomodulation with low-level laser therapy (LLLT) and nimesulide on inflammatory parameters, oxidative stress and inflammation biomarkers, and quality of life after lower third molar surgery

Table 2: Quality of the included studies.

Study	Adequate sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective outcome reporting	Other risk of bias	Overall risk of bias
Fesilhan et al, 2019[25]	Yes	Yes	Yes	Yes	Yes	Yes	Low
Singh et al, 2019[26]	Yes	Yes	Yes	Yes	Yes	Yes	Low
Hadad et al, 2021[27]	Yes	Yes	Yes	Yes	Yes	Yes	Low
Isolan et al, 2021[28]	Yes	Yes	Yes	Yes	Yes	Yes	Low
Nejat et al, 2021[29]	Yes	Yes	Yes	Yes	Yes	Yes	Low

Table 3: Characteristics of the included studies.

Study	Study design	Country	Sample description	Interventional procedure
Feslihan et al, 2019[25]	A randomized, single-blind study design	Turkey	Number of patients- 30; 22 patients (73.3%) were female and 8 (26.7%) were male; mean age-21.3±2.69 years (range-18–27 years).	Interventional group – PBMT was applied extraorally and the insertion point was masseter muscle. Therapy was applied for 60 seconds with an output power of 0.3 W and an energy density of 6 J/cm^2. Therapy was repeated on postoperative days 1 and 2. Control group – 40 mg^2/ml methylprednisolone sodium succinate was injected postoperatively into the masseter muscle through an intrabuccal approach. On postoperative day 1, methylprednisolone injection (20 mg/1 ml) was repeated.
Singh et al, 2019[26]	A randomized, double-blinded, split-mouth pilot study design	India	Number of patients – 25, (56% of the patients were males), mean age- 22.16±4.60 years.	A diode laser of low power was used to irradiate 2 areas intraorally (buccal aspect of the socket and distolingually near to the pterygomandibular raphe) for 45 seconds each. The laser device was composed of a solid-state (Ga-As-Al) laser with a wavelength of 830 nm with 30 mW power at continuous wave mode. The intraoral irradiation was not repeated any further in the postoperative period. Extraorally, the same laser was applied on the skin surface along the masseter muscle, two on the origin of muscle, two on the insertion of muscle, and two on the median length of the masseter; each set of points was around 1 cm away from the others. The irradiation from the infrared laser was repeated on the 2nd, 4th, and 7th postoperative days. On the control (placebo) side, the treatment protocol was similar to that for the laser side with the device turned off.
Hadad et al, 2021[27]	Split-mouth, double-blind, randomized clinical trial	Brazil	Number of patients – 13, (61.77% male and 38.63% female), mean age- 24.16±2.06 years	Interventional and control procedure – intraoral application of photobiomodulation (PBM) therapy was done at 4 points with a diode laser at 810 nm wavelength, 6 J (100 mW, 60 seconds/point) on one side in all the patients and laser irradiation simulation was given on the other side in all the patients.
Isolan et al, 2021[28]	A double-blind randomized clinical trial	Brazil	Number of patients – 44, mean age- 28 years (SD±11.54).	Control group – the tooth extraction was performed according to the specificities of each clinical case. After tooth removal, the surgical area was cleansed with 0.9% saline solution and sutures were performed. Interventional group - PBMT therapy [Gallium aluminum arsenide diode (GaAlAs)] with a wavelength of 808 nm was applied in continuous mode was applied in six points (two points in the labial region (apical and cervical); two points in the lingual region (apical and cervical); and two points in the previous occlusal direction) in contact with the soft tissue after the sutures.
Nejat et al, 2021[29]	A double-blind randomized clinical trial	Iran	Number of patients – 80, (51 females and 29 males), mean age –24.22±4.08 years	Patients having bilateral impacted mandibular third molars were included one socket was randomly assigned to receive photobiomodulation treatment (660 nm 200 mW, CW applied at a distance of 1cm to 4 points on the occlusal area of extraction socket, also, 810 nm 200 mW CW was applied at tissue surface at three points on the buccal and three points on the lingual gingiva, for 15 seconds), the other socket received sham (placebo) treatment.

Table 4: Outcome data of the included studies.

Study	Pre-operative pain		Post-operative pain		Pre-operative mouth opening		Post-operative mouth opening		Post-operative oedema	
	Contr-ol group	Interv-entional group	Control group	Interv-entional group	Control group	Interventional group	Control group	Interv-entional group	Control group	Interv-entional group
Feslihan et al, 2019[25]	-	-	Day 1: 2.97±2.08; day 2: 1.63±1.99; day 7: 0.30±0.84	Day 1: 3.53±2.01; day 2: 1.73±1.57; day 7: 0.20±0.48	-	-	Day 1: 45.97±6.11; day 2: 39.27±8.80; day 7: 44.43±6.37	Day 1: 47.20 ±6.34; day 2: 35.47±9.98; day 7: 43.93±7.22	Day 1: 102.6±4.31; day 2: 105.50 ±4.06; day 7: 103.03±4.13	Day 1: 100.73 ±4.75; day 2: 104.57±4.04; day 7: 101.33±4.67
Singh et al, 2019[26]	VAS score: 1.04±2.54	VAS score: 0.96±2.54	Day 0: 0.0±0.0; day 2: 6±1.44; day 4: 4.36±1.55; day 7: 1.28±1.68	Day 0: 0.16±0.47; day 2: 4.96±1.43; day 4: 2.36±2.06; day 7: 0.48±1.08	39.44 ±5.44 mm	39.40 ±7.42 mm	Day 0: 40.08±5.41; day 2: 27.44±6.15; day 4: 32.92±7.50; day 7: 38.48±5.84	Day 0: 39.96±7.62; day 2: 28.36±8.15; day 4: 35.16±7.56; day 7: 39.92±7.15	Day 0: 2.30±3.63; day 2:9.01±4.52; day 4-6.90±4.08; day 7: 4.44±2.67	Day 0:2.02±3.57; day 2: 6.40±3.74; day 4: 3.44 ±2.44; day 7: 1.34±1.32
Hadad et al, 2021[27]	-	-	24 hours VAS score: 32.25±22.78; 48 hours: 39.87±4.21	24 hours VAS score: 7.56±6.25; 48 hours: 19.47±9.27	-	-	-	-	24 hours: 32.38±15.28; 48 hours: 39.87±22.77	24 hours: 19.7±13.27 mm; 48 hours: 19.47±13.11 mm
Isolan et al, 2021[28]	-	-	6 hours Mean VAS score =2.5; CI: 2.1–2.88 24 hours; mean VAS score =2.86; C.I: 2.40–3.31	6 hours Mean VAS=0.9; CI: 0.63–1.16 24 hours; mean VAS score=0.72; C.I: 0.51–0.93	-	-	-	-	-	-
			48 hours Mean VAS=2.86; C.I: 2.37–3.34	48 hours Mean VAS=0.64; C.I: 0.36–0.92						
Nejat et al, 2021[29]	-	-	Day 1: 52.25±10.32; day 7: 6.47±6.23	Day 1: 53.11±10.65; day 7: 5.75 ±3.52	-	-	-	-	-	-

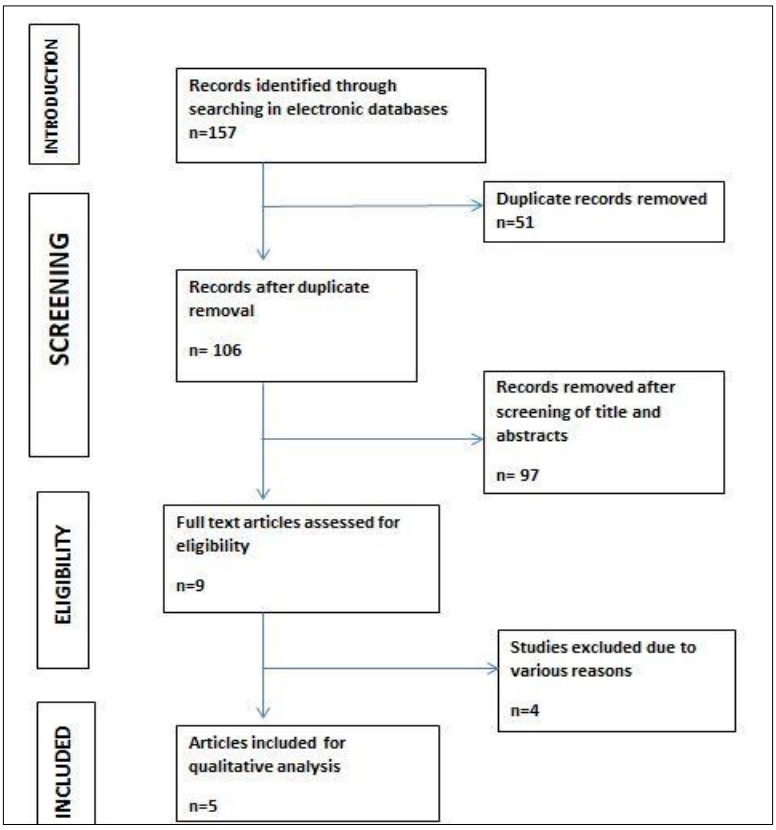

Figure 1: Study design of the systematic review.

DISCUSSION

PBMT stimulates the synthesis of endorphins, raises the threshold of pain, and blocks nerve conduction resulting in less neural discharge. Moreover, increased lymphatic drainage, reduced permeability of blood vessels, and reduced inflammatory mediators result in decreased inflammation.[35] The radiation emitted by the low-power laser is a monochromatic beam of light that has the capability of penetrating structures, depending on the wavelength used. PBM therapy causes cellular changes that promote cell viability, proliferation, and tissue healing.[35]

Markovic et al and Amarillas et al in their study showed the effectiveness of low-level laser therapy (LLLT) in reducing swelling after mandibular third molar extraction surgery.[36,37] In a systematic review and meta-analysis conducted by WL He et al, they found that LLLT has a positive outcome in the reduction of postoperative swelling following mandibular third molar surgery.[38] Another study conducted by Aras and Güngörmüs in 2010, found that the diode laser was more effective in reducing swelling and trismus when the laser was irradiated extra-orally than when it was used intraorally.[39] According to these authors, there may be spasms of certain muscles, especially the masseter muscle due to the surgical procedures; therefore, intraoral application of laser would not act directly on this muscle.[39]

Feslihan et al in a randomized single-blind study compared the efficacy of PBMT and methylprednisolone in terms of decreasing pain, edema, and trismus after surgical extraction of impacted third molars.[25] The difference in VAS scores of pains, mouth opening, and post-operative facial distance between the intervention and control group was not statistically significant on postoperative day 1, day 2, and day 7. However, methylprednisolone was found to be more efficacious in alleviating pain and trismus and PBMT helped to relieve edema. However, as the study was a split-mouth study the teeth were not extracted in the same session, pain threshold of the participants changed based on their previous surgical experience. Moreover, tape measurement method was used for the assessment of edema instead of more sensitive measurement methods which might have been the reason for the lack of significant difference between the edema coefficients of the study groups.

Singh et al found a statistically significant difference in edema coefficients between the intervention and control group except in the immediate postoperative period.[26] The difference in mouth opening between the groups was not statistically significant. The pain in the interventional group was significantly lower as compared to the control group at all-time points except immediate post-operatively. As the study was a split-mouth study certain confounding factors were eliminated such as the position of the impacted teeth, age, gender, and pain perception level of the participants. The study used the combined

effect of intraoral and extraoral application of photo-biomodulation at multiple times thereby reducing the post-operative side effects more effectively.

Hadad et al conducted a split-mouth, double-blind, randomized clinical trial (RCT) and found statistically significant differences in terms of VAS score between the groups at 24 and 48 hours ($p<0.001$ and 0.011 respectively).[27] There was no statistically significant difference in facial measurements between the PBMT and control group although the PBMT group showed less swelling postoperatively. Trismus was not included as an outcome criterion in the participants of this study.

Isolan et al in the randomized controlled trial found the PBMT showed statistically significant differences at different post-operative intervals (6^{th} hour, 24^{th} hour, and 48^{th} hour) and at each position (Pell and Gregory position A, position B, and position C).[28]

Nejat et al aimed to evaluate the effectiveness of PBMT for the prevention of alveolar osteitis (AO) and post-operative pain following third molar surgery.[29] AO frequency, VAS score, and the mean numbers of analgesics consumed in the postoperative period were significantly lower in the PBMT group in comparison with the control group.

Limitations of the present review were less number of randomized clinical trials in accordance with the inclusion and exclusion criteria and the selected articles were only in English language. Although only five studies were found to be eligible for inclusion in this systematic review, they were randomized controlled clinical trials, defined by the National Health and Medical Research Council (NHMRC) guidelines as level of evidence II.[34] The heterogeneity of data and difference in VAS score measurement methods in between the studies limited the scope of the meta-analysis of these articles.

CONCLUSION

In this systematic review, PBMT was used for the treatment of postoperative complications such as pain, edema, and trismus following extraction of impacted third molar teeth in five studies. Four out of five studies that were included in this review demonstrated a positive impact of PBMT on reducing pain, especially during the post-operative period compared to other non-surgical treatment protocols. PBMT demonstrated an overall positive impact on reducing postoperative complications like edema and trismus. Data from the included studies did not support the acceptance of the null hypothesis of no difference in reducing postoperative complications between PBMT and other non-surgical treatment therapies.

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