ORIGINAL ARTICLE

PAIN, OEDEMA AND TRISMUS RESPONSES FOLLOWING PHOTOBIOMODULATION THERAPY IMMEDIATELY AFTER LOWER THIRD MOLAR EXTRACTION: RESULTS OF A RANDOMIZED, DOBLE-BLIND AND SPLIT MOUTH CLINICAL TRIAL

GISELA CRISTINA VIANNA CAMOLESI[a,b], AHMED SAMIR EL KATTAN[c], JOSÉ LOPEZ-LOPEZ[d,e], ANDRÉS BLANCO-CARRIÓN[a,b], ABEL GARCÍA-GARCÍA[a,b], PILAR GÁNDARA-VILA[a,b], AND MARIO PÉREZ-SAYÁNS[a,b,f]

[a]Oral Medicine, Oral Surgery, and Implantology Unit (MedOralRes), Faculty of Medicine and Dentistry, Universidade de Santiago de Compostela (USC). Calle Entrerríos s/n., Santiago de Compostela, Galicia, Spain
[b]Foundation Health Research Institute of Santiago de Compostela (FIDIS). Av. Choupana s/n., Santiago de Compostela, Galicia, Spain
[c]Mastership Laser Therapy in Dentistry, RWTH AACHEN University, Aachen, Germany
[d]Oral Health and Masticatory System Group, Bellvitge Biomedical Research Institute, IDIBELL, University of Barcelona, Barcelona, Cataluña, Spain
[e]Department of Odontostomatology, Faculty of Medicine and Health Sciences (Dentistry), Barcelona University Dental Hospital, University of Barcelona, Barcelona, Cataluña, Spain
[f]Materials Institute of Santiago de Compostela (iMATUS), Santiago de Compostela, Galicia, Spain

ABSTRACT

Objectives
To assess the impact of photobiomodulation therapy in pain, facial oedema, and trismus mitigation in the postoperative period after lower third molar extractions.

Methods
We conducted a comparison between active photobiomodulation and simulated photobiomodulation after both lower third molars extraction in the same patients, within a double-center clinical trial. The role of photobiomodulation was evaluated based on pain, measured using the VAS scale. Oedema and trismus, assessed through millimetric measurements. Additionally, analgesic consumption was monitored during the 7-day's postoperative period. The study adhered to the CONSORT checklist and was registered on the ClinicalTrials (NCT05255731). The Levene test was used to assess precision (α=0.05), and statistical analysis was performed using Jamovi software. Paired t-tests or the Wilcoxon test were employed to analyze the primary and secondary outcomes.

Results
The study included 83 patients and 166 randomization units. The study group showed a significant reduction in pain at all evaluation times ($P < .01$), as well as reductions in facial oedema and trismus on postoperative days 2 and 7 ($P < .01$). A significant difference in analgesic use was observed on all days, except on the seventh postoperative day.

Conclusion
The photobiomodulation protocol, using an 808 nm, 100 mW Ga-Al-As diode laser, applied both intraorally and extraorally in a single 30 seconds (3 Joules/per point) postoperative session, significantly reduced pain, oedema, and trismus following mandibular third molar extraction, particularly on postoperative days 2 and 7.

CORRESPONDING AUTHOR: Pilar Gándara-Vila
E-mail: pilar.gandara@usc.es

KEYWORDS

Photobiomodulation therapy, Pain management, Postoperative facial oedema, Trismus reduction, Lower third molar extraction

Source of Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Received 21 September 2024; revised 15 November 2024; accepted 4 December 2024

J Evid Base Dent Pract 2025: [102080]

1532-3382/$36.00

doi: https://doi.org/10.1016/j.jebdp.2024.102080

Clinical Significance
Photobiomodulation can be an effective complementary therapy for reducing pain, facial oedema, and trismus in patients after lower third molar extraction.

INTRODUCTION

Lower third molar extraction is 1 of the most common oral surgical procedures.[1] This operation is frequently indicated to prevent or treat issues such as dental impaction, recurrent infections like pericoronitis, dental caries in inaccessible areas that hinder proper oral hygiene, cysts, or even mandibular fractures.[2,3] The complications and adverse effects resulting from wisdom tooth extraction are a concern, as they can significantly impact the patient's quality of life during the postoperative period.[4] Among the main adverse effects that may occur following the procedure are pain, oedema, trismus, paresthesia, and postoperative infections.[1,4]

Postoperative pain and facial oedema are the most prevalent adverse effects following surgery.[4] Both represents a natural inflammatory response of the body to surgical trauma.[5] While the onset and severity can vary, these symptoms typically peak within the first 24-48 hours and may persist for several days. Factors influencing the intensity of pain and the severity of oedema include the complexity of the extraction, the surgical technique employed, the patientś individual characteristics, and the increase of the procedure.[6] Another significant adverse effect is the limitation of mouth opening, or trismus. This condition, which may result from inflammation and muscle spasm induced by the surgery, can hinder eating, oral hygiene, and verbal communication.[4]

These complications are temporary and tend resolve over time. In general, treatment typically involves prescribing antibiotics, anti-inflammatories, analgesics, corticosteroids. In some cases, jaw physiotherapy exercises may also be recommended.[7,8] Complementary therapies like acupuncture, transcutaneous electrical nerve stimulation (TENS), cryotherapy, lymphatic drainage, and photo-biomodulation (PBM), have been suggested as ways to reduce the need for medication.[9-11] In this context, infrared laser PBM is emerging as a promising complementary therapy, as it plays a key role in speeding up cellular repair, modulating inflammation, and alleviating pain.[12]

Our aim is to verify through a doble-center study, using a protocol based on previous studies that have reported significant results, whether the application of infrared laser PBM in the immediate postoperative period is effective in reducing adverse effects such as pain, oedema, and trismus following the extraction of lower third molars.

MATERIALS AND METHODS

Study Design and Sample Size

A randomized, split-mouth, double-center, double-blind design was implemented . In this study design, each participant takes part in both the study group (SG), which receives active PBM, and the control group (CG), which receives simulated PBM, thereby serving as their own control. It included all patients attending at the Masterś program in Oral Medicine, Oral Surgery, and Implantology at the University of Santiago de Compostela, or the Masterś in Oral Medicine, Surgery, and Implantology at the University of Barcelona, between February 2022 and the end of November 2023, who met the specific inclusion criteria and signed the informed consent form. The study received the ethical approval from the Regional Research Ethics Committee of Santiago- Lugo (Ref. 2021/277) and is registered in the International Clinical Trials Registry Platform (ClinicalTrials.com) under the identifier NCT05255731. It adheres to the ethical principles outlined in the Declaration of Helsinki and follows CONSORT checklist.[13,14]

Inclusion and Exclusion Criteria

The inclusion criteria were as follows:[1] participants aged 18 years or older;[2] a clear indication for the extraction of bilateral lower third molars[38] and [48] with a similar pattern of impaction and positioning, assessed according to Winter's[15] and Pell & Gregory[16] classification. Exclusion criteria included:[1] patients with uncontrolled systemic disease (ASA ≥ III);[2] pregnant or breastfeeding women, as the effects of laser therapy in these populations have not been studied;[3] individual who smoke of more than 5 cigarettes per day;[4] patients with local conditions such as presence of pericoronitis at the time of extraction, cysts, or odontogenic tumors related to the third molars, or any presence of infection;[5] surgical procedure lasting over 90 minutes;[6] failure to complete the second surgery within the study period;[7] patients who refused or did not sign the consent form.

Sample Size Calculation

The minimum sample size was calculated based on a previous study,[17] and using the website (http://estatistica.bauru.usp.br/calculoamostral/ta_diferenca_media_dependente.php) [17/09/2024]. To achieve 90% statistical significance, considering a standard deviation of 2.0, an alpha error of 0.05, and an estimated 10% dropout rate. After meeting these criteria, a variance test for independent samples was

performed, which indicated that a sample size of 43 patients was required.

Study Variables and Measurement of Primary and Secondary Outcomes

Demographic data were collected, including sex, age, habits, tobacco use, alcohol consumption, and oral hygiene level. Each participants underwent a through clinical and oral examination, including a panoramic dental radiograph, which was used to classify the position of the teeth.[15,16] Primary outcomes are included pain, oedema, and trismus. Secondary outcomes were the number of analgesics taken for pain relief and the overall comfort of PBM application in both groups.

Randomization

In a split-mouth study, the unit of randomization can be at the quadrant level.[18] In this study, each patient served twice as an experimental unit, with 1 quadrant randomly assigned to the active PBM study group (SG), and the other to stimulated PBM, control group (CG). There was a minimum interval of 21 days between extraction of the left and the right lower third molars.

Blinding

The randomization process, as well as the assessments of oedema and trismus, were conducted by investigators who were blinded to the group to which the wisdom tooth was assigned.

Surgical Procedures and Interventions

No preoperative medication was administered to the patients. Prior to the surgical procedure, extraoral antisepsis was performed with 2% chlorhexidine topical solution, and intraoral antisepsis was conducted with a 1-minute mouthwash of a 0.12% chlorhexidine digluconate solution (Laboratorios Lacer S.A., Barcelona, Spain). Initially, patients underwent local nerve block anesthesia for inferior alveolar nerve and infiltrative for buccal and lingual nerves by administering 4% articaine with epinephrine 1:100,000 (INIBSA, Barcelona, Spain). Local anesthesia usage and total surgical time were monitored in all procedures to minimize additional tissue trauma that could influence the outcomes. The surgical procedures were performed by different surgeons, but the same surgeon operated on each patient in both surgeries. PBM therapy or its simulation was administered by a single operator at each center (GCVC, ASK), and patients were not informed about their assigned group.

After extraction, sutures were placed using with 3-0 seda thread (INIBSA, Barcelona, Spain). Patients in both groups received the standard postoperative care, which included rinsing 0.12% chlorhexidine mouthwash, (3 times a day for 1 minute), rescue medication for sever pain, and 7-days course of antibiotics. Patients were given verbal instruction and an information guideline for postoperative care, which included local hemostatic measures, resting for 24 h, maintaining proper oral hygiene, and following appropriate dietary habits.

Postoperative pain was self-reported by the patients immediately after PBM application in the postoperative period. They were given a form with a visual analogue scale (VAS), ranging from 0 to 10, where at represented no pain and at the other end, unbearable, 10 indicated unbearable pain.[19] Patients were instructed to mark a point on the line corresponding to their pain level immediately after surgery (baseline), at 12, 24, 36, and 48 hours, and then every 24 hours up to the seventh postoperative day. On the same form, patients also recorded the number of rescue medication consumed during the 7-day's period.

Oedema and mouth opening were measured in millimeters (mm) and recorded at 3 time points: before surgery (baseline), at 48 hours postsurgery (by the patient themselves), and at 7 days postsurgery (when sutures were removed). For oedema, measurements were taken from the mandibular angle to the corner of the eye (M1), and from the tragus to the corner of the mouth (M2) using a measuring tape. The patient was in maximum intercuspation, with lips at rest, and measurements were repeated 3 times to ensure accuracy. Mouth opening (trismus) was assessed by measuring the interincisal distance between the upper and lower incisors using a calliper, with the patient in maximum spontaneous mouth opening.

The overall comfort of PBM application was assessed using a 0 to 10 scale, completed by patients immediately after each PBM session in both groups. The evaluation considered 5 factors: whether the device caused discomfort, whether the patient felt uncomfortable during the session, if the session felt too long, whether they would undergo the treatment again, and if they would recommend it to a friend or family member. A score of 0 indicated the worst experience, while 10 represented the best possible experience.

PBM Application Protocol

The SG received PBM with infrared laser applied both intraorally and extraorally; 3 intraoral points around the extracted tooth, and 7 extraoral points, including 4 on the masseter muscle and 1 in each lymph node, parotid, submandibular and sublingual. This protocol was based on previously studies that showed significative results.[17,20-24] The laser parameters are described in the Table 1, based on previous recommendation.[25,26] The control group (CG) underwent a simulated PBM session, where participants heard the characteristic sound of the equipment, and the device was positioned at the same intraoral and extraoral points, but no irradiation

Table 1. PBM treatment parameters. Is recommended that all the following PBM parameters must be provided in the methods section.

Parameter	Unit	Additional notes
Emitter type	GaA1As and InGaAlP	
Wavelength	808 nm	Infrared laser
Operating mode	continuous	Punctual, in contact
Power	0.1 W	
Spot size	0.03 cm²	
Power density	3.33 W/cm²	Per point
Exposure duration	30 s	Per point
Energy dose	99.99 J/cm²	Per point
Energy	3 J	Per point
Treatment description	10 points	1 post operatory session
Accumulated energy	30 J	

cm, centimeters; J, Joules; nm, nanometers; PBM, Photobiomodulation; s, seconds; W, Watts.

was performed. Both groups received a single session in the immediate postoperative period.

Statistical Analysis

Descriptive statistics for the patients were calculated using the t-test. The evaluation of PBM effects was performed through comparative analyses facial oedema, limited mouth opening, pain, and use of rescue medication, as well as surgical time and overall comfort of PBM application between the SG and the CG. First, the Kruskal–Wallis test was applied to check for data normality, followed by either the paired t-test or the Wilcoxon test, its nonparametric equivalent. A $P < 0.05$ was considered statistically significant for all tests. The data were analyzed using Jamovi Project Software (Version.2.3).

RESULTS

The final sample included a total to 83 patients, 55 from USC and 28 from UB (Figure 1), with 51.8 % being women, and an age range of 47 (18–65). A complete demographic and descriptive analysis of the sample can be found in the Table 2.

Pain

The results of the subjective analysis using the visual analogue pain scale (VAS) are presented in the Table 3. The Wilcoxon test was performed as the data did not follow a normal distribution. A statistically significant result was observed between the groups, with $P < .01$ at all evaluation times.

Facial Oedema and Mouth Opening Evaluation

A comparative analysis using the paired t-test for both variables revealed statistically significant differences between the SG and CG, with a $P < .01$ on both second and seventh postoperative days (Table 4), for both oedema and mouth opening. The gross facial measurements in millimeters (mm) M1 and M2 are shown in Supplementary 1.

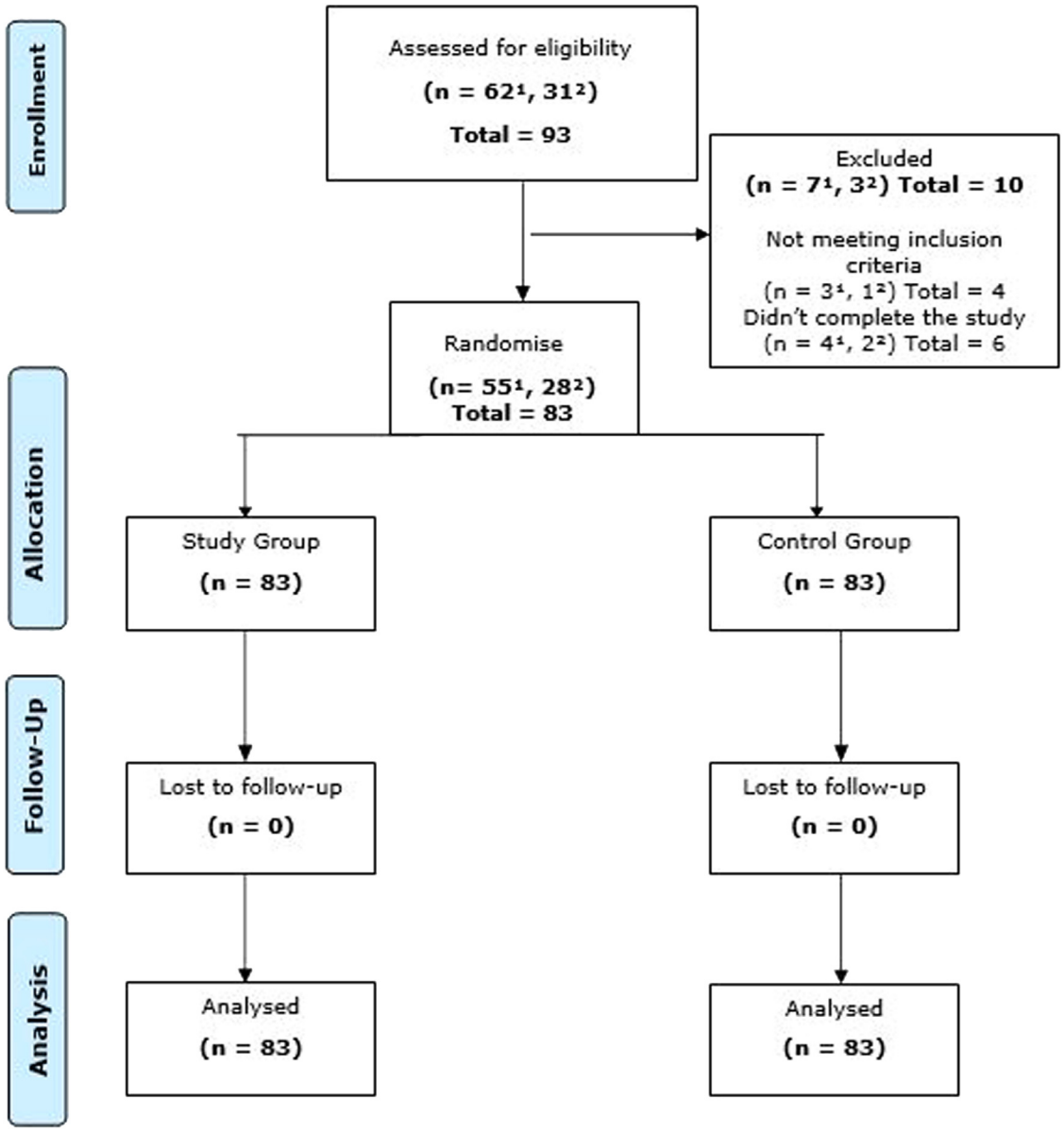
Secondary Outcomes

The evaluation of rescue medication and overall comfort was conducted only for the 55 patients treated at the USC. Statistical analysis found a significant difference in the number of analgesics used on all days except the seventh postoperative day (Table 3). No statistically significant differences were found between both groups about the analgesics used or overall comfort (Table 2).

DISCUSSION

A recent systematic review and meta-analysis concluded that infrared laser PBM, with both intraoral and extraoral applications in a single session during the immediate postoperative period, is effective as a complementary method to routine care for reducing pain and oedema following third molar extraction.[12] Based on parameters and protocols including, application area, number of sessions, laser frequency,

Figure 1. CONSORT flow chart.
Centre Universidade de Santiago de Compostela = USC*, Centre Universidad de Barcelona = UB=
From Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. Lancet 2001; 357(9263):1191–1194.
For more information, visit www.consort-statement.org.



wavelength, and energy per point, that have described successful in previous studies, for reducing pain,[17,20-22,24] oedema,[17,20-22,24] and trismus[17,20-22] we developed the protocol used in the present study (Table 1).

To effectively stimulate biological processes, an optimal dose of energy is required[27] . It has been observed that lower levels of doses are more effective for tissue repair, while higher levels are better suited for modulating inflammation and controlling pain.[27,28] With appropriate protocols, PBM regulates COX-2 activity,[29] and consequently inhibits the production of prostaglandin E2.[30] It also modulates pro-inflammatory cytokines (IL-6, IL-1β, and TNF-α) and

Table 2. Clinical features and descriptive statistics comparison Control Group (CG) vs Study Group (SG).

Variable		Group	N (%)	*P* - Value
Centre	USC		55 (66.3)	
	UB		28 (33.7)	
Sex	Male		40 (48.2)	
	Female		43 (51.8)	
Medicaments	No		61 (73.5)	
	Antihypertensives		10 (12)	
	Antidiabetics		4 (4.8)	
	Anxiolytics		6 (7.2)	
	Others		2 (2.4)	
Tobacco	No		49 (59)	
	Yes		34 (41)	
Alcohol	No		14 (16.9)	
	Yes		69 (83.1)	
Oral hygiene	1		10 (12)	
	2		43 (51.8)	
	3		30 (36.1)	
Reason for extraction	Orthodontia		24 (28.9)	
	Caries		19 (22.9)	
	Pain		15 (18.1)	
	Crowding		13 (15.7)	
	Pericoronitis		12 (14.5)	
Tooth	38	Study	39 (23.5)	.438
		Control	44 (26.5)	
	48	Study	44 (26.5)	
		Control	39 (23.5)	
Pell–Gregory	IA	Study	40 (24.1)	.916
		Control	39 (23.5)	
	IB	Study	5 (3)	
		Control	3 (1.8)	
	IC	Study	7 (4.2)	
		Control	5 (3)	

(*continued on next page*)

Table 2 (*continued*)

Variable		Group	N (%)	*P* - Value
	IIA	Study	11 (6.6)	
		Control	9 (5.4)	
	IIB	Study	16 (9.6)	
		Control	22 (13.3)	
	IIC	Study	1 (0.6)	
		Control	1 (0.6)	
	IIIA	Study	3 (1.8)	
		Control	4 (2.4)	
Winter	Vertical	Study	39 (23.5)	.614
		Control	33 (19.9)	
	Horizontal	Study	22 (13.3)	
		Control	27 (16.3)	
	Mesial	Study	22 (13.3)	
		Control	23 (13.9)	
			Mean ± SD	
Anesthetic use (uni.)		Study	2.14 ± 0.62	.375
		Control	2.22 ± 0.66	
Overall comfort		Study	8.83 ± 1.08	.132
		Control	8.75 ± 1.15	
Surgery time (min.)		Study	33.82 ± 12.05	.889
		Control	33.95 ± 9.17	

1, deficient, 2, regular, 3, good; min., minute; N, Sample size; SD, standard deviation; Oral hygiene, uni., unit.

anti-inflammatory cytokines (IL-10 and TGF-β) ,[29,31] as well as levels of neuropeptides.[32] In other words, PBM stimulates the formation of new blood vessels and enhances microcirculation, which helps modulate inflammation and manage the signals and symptoms of the inflammatory process, primarily through regulation of capillary hydrostatic pressure.[28] This results in a reduction of oedema, pain, and trismus,[33] explaining the statistically significant results observed in the SG compared to the CG.

In a randomized study, Sigaroodi et al.,[22] found that the difference in pain levels between groups was significant at all postoperative evaluation periods, which aligns with the results of the present study. In both studies, pain intensity peaked at 12 hours postoperatively for both groups, and from the next assessment at 24 hours, it began to decline, stabilizing at 3 days postoperatively for the study group (SG) and at 7 days for the control group (CG).

Momeni et al.[21] in 1 of their studies, found significant results for pain using an infrared laser (940 nm) with 20 seconds application per point. In contrast, their earlier study,[34] which used the same device and parameters but with 30 second applications per point, did not yield significant results. Sigaroodi et al.[22] and Eshghpour et al.[20] also reported satisfactory outcomes for pain and oedema using infrared lasers

Table 3. Wilcoxon test for pain assessment using Visual Analog Scale (VAS) measurements and analgesic consumption in both groups.

Outcome	Period	Group	N	Median	SD	*P* Value	Outcome	Period	Group	N	Median	SD	*P* Value
Pain	Basal	Study	83	0.84	1.23	< .001*	Analgesics			-			
		Control	83	1.74	2.17								
	12 hours	Study	83	3.92	2.49	< .001*				-			
		Control	83	4.92	2.48								
	24 hours	Study	83	3.56	1.91	< .001*		24 hours	Study	55	1.47	0.81	.024*
		Control	83	4.85	2.22				Control	55	1.87	1.38	
	36 hours	Study	83	3.08	1.88	< .001*				-	-		
		Control	83	4.96	2.24								
	48 hours	Study	83	2.31	1.60	< .001*		48 hours	Study	55	2.01	1.08	.005*
		Control	83	4.53	2.01				Control	55	2.52	1.31	
	3 days	Study	83	1.79	1.51	< .001*		3 days	Study	55	1.80	1.29	< .001*
		Control	83	3.83	1.98				Control	55	2.54	1.38	
	4 days	Study	83	1.49	1.34	< .001*		4 days	Study	55	1.27	1.04	< .001*
		Control	83	3.27	1.88				Control	55	2.03	1.24	
	5 days	Study	83	1.20	1.26	< .001*		5 days	Study	55	0.83	0.95	.007*
		Control	83	2.77	1.82				Control	55	1.34	1.19	
	6 days	Study	83	1.02	1.14	< .001*		6 days	Study	55	0.49	0.85	.012*
		Control	83	2.36	1.94				Control	55	0.87	1.00	
	7 days	Study	83	0.85	1.04	< .001*		7 days	Study	55	0.38	0.78	.815
		Control	83	1.33	1.33				Control	55	0.43	0.83	

* When the *p*-value was statistically significant. N, sample size; SD, standard deviation.

(808 nm and 810 nm, respectively), with 30 second applications per point. However, Alan et al.[35] applied 810 nm for 40 seconds and did not achieve good results.

Landucci et al.[17] and Hadad et al.,[19] consistent with our fundings, reported that although facial measurements were higher at 48 hours[17,19] and 7 days[17] postoperatively in both groups compared to the initial measurements, the difference in oedema between the SG and CG was statistically significant. On the other hand, Momeni et al.,[21] did not find significant differences between the groups at any time point, although they reported an increase in facial measurements in the first 2 days in the control group.

Regarding mouth opening, consistent with the results reported by Momeni et al.,[21] the SG showed a reduction at 48 hours postsurgery, returning to preoperative measurements 7 days after the surgery. In contrast, the CG showed a reduction in mouth opening at both time points, resulting in statistically significant differences between the groups at all evaluation periods.

It was anticipated that the SG would have a lower need for rescue medication, as all primary outcomes showed significant differences between the groups, and previous studies have reported a reduction in analgesic use by the SG[21,23,24]. It is important to note that this effect is primarily due to

Table 4. Paired samples T-test for facial oedema and open mouth measures.

Measure	Period	Group	N	Mean	SD	*P*-Value
Facial oedema	Basal	Study	83	103.5	5.80	.670
		Control	83	103.6	6.26	
	48 hours	Study	83	107.0	5.53	< .001*
		Control	83	111.3	7.15	
	7 days	Study	83	105.0	5.97	.011*
		Control	83	106.8	7.69	
Open mouth	Basal	Study	83	44.2	6.31	.124
		Control	83	44.5	6.68	
	48 hours	Study	83	40.2	7.70	< .001*
		Control	83	37.0	9.36	
	7 days	Study	83	44.4	6.44	< .001*
		Control	83	42.1	8.07	

* When the *P*-value was statistically significant. N, sample size; SD, standard deviation.Note: To simplify the analysis and provide a more comprehensive evaluation of facial oedema in millimeters (mm), the M1 and M2 measurements were combined into a single measure by calculating the arithmetic mean. The formula used was as follows: M1 + M2 / 2. This combined oedema value was utilized for all subsequent evaluations and statistical analyses. Raw oedema values are provided in Supplementary File 1.

PBM therapy, which influences nerve fibers in 2 ways: directly, by controlling neuropeptide levels,[32] and by reducing compression on them, as it decreases oedema of the soft tissues around the surgical site.[28]

General comfort had not been evaluated in previous studies, or at least we did not find any that did. Therefore, this is the first study to analyze patient perception of PBM therapy. No significant differences were observed between the average scores of the 2 groups. Scores above 8 suggest that, overall, patients had a positive experience. An important point to note is that the duration of surgery was similar in both groups, which helps reduce potential bias related to the surgical procedure.[4]

Considering the results from previously conducted randomized studies, which demonstrated statistically significant improvements in outcomes with PBM application, we would expect a relatively broad therapeutic window. Overall, studies have used various devices with different powers, wavelengths, and protocols, reporting a range of total energy and energy density from 12-48 J and 7.5-142.51 J/cm², respectively.[17,20-22,24] It was observed that for optimal results, a higher wavelength (nm) requires less application time (s), and more sessions reduce the energy dose needed per point, confirming that PBM has a cumulative effect.[27] Momeni et al.[21] provided a single PBM session with 10 J/cm² per point, while Eshghpour et al.[20] and Kazancioglu et al.[24] applied 2 and 4 PBM sessions, respectively, delivering a total energy density of 42.8 J/cm² and 16 J/cm². Conversely, Koparal et al.[36] and Eroglu et al.[37] used a single session of 4 J/cm² per point and did not report statistically significant results, similar to Alan et al.,[35] who also applied 4 J/cm² per point but in 2 sessions.

In our study, an energy of 3 J and a dose of 99.9 J/cm² per point were applied, which seems compatible with the therapeutic window proposed for conditions such as pain and oedema.[38-40] However, this was not the actual dose received by the target tissues. Considering that the target tissues for modulating the inflammatory process are deeper tissues, the estimated dose received was approximately 9 J/cm². This estimation is based on studies reporting a high degree of optical scattering affecting red and infrared laser sources,[41,42] leading to energy losses. For a penetration depth of 1 cm, tissues receives only about 10% of the energy applied at the surface.[43]

About the minimum interval of 21 days between extractions, it is important to highlight, was established to allow for the necessary biological recovery time[44] and to mitigate the potential abscopal effect of PBM.[45] This effect, initially observed in radiotherapy,[46,47] refers to a phenomenon where localized treatment can produce benefits in distant areas, mediated by systemic responses such as the modulation of inflammatory cytokines.[45] In PBM, studies indicate that applying light to regions such as muscles or bones can benefit nonirradiated areas due to the reduction of pro-inflammatory cytokines, the increase in anti-inflammatory cytokines, and the proliferation of stem cells.[47,48] By adhering to this interval, we aim to prevent any systemic effects of PBM from the first surgery from influencing the inflammatory response of the second. This approach allows for a more reliable assessment of PBM's local effects on the control of postoperative pain, oedema, and trismus.

Among the strengths of this study is its design, which minimizes interindividual variability by having each subject serve as their own control. This approach minimizes variability between participants and increases the study's power, while also decreasing the required sample size.[18,49] On the other hand, a potential weakness is that patients may use their experience of pain from the first surgery as a reference when rating pain from the second surgery. However, we hope this does not pose a significant issue, as the order in which patients were assigned to the study group (SG) and control group (CG) was randomized.

We believe that this study reinforces the positive impact of PBM in improving recovery and postoperative comfort following the extraction of lower third molars, both from the patient's perspective and in terms of treatment reliability. Our findings contribute to evidence-based in practice and underscore the importance of using optimized protocols, as provided in Table 1.

CONCLUSION

Based on the collected data and statistical analysis, the use of infrared diode laser, applied both intraorally and extraorally in a single postoperative session, demonstrates significant benefits for managing pain, oedema, and trismus following mandibular third molar extraction. It is recommended that PBM be more widely adopted as an effective complementary therapy for postoperative management in these patients.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

GISELA CRISTINA VIANNA CAMOLESI: Writing – original draft, Validation, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **AHMED SAMIR EL KATTAN:** Writing – review & editing, Validation, Investigation. **JOSÉ LOPEZ-LOPEZ:** Writing – review & editing, Project administration, Methodology, Investigation. **ANDRÉS BLANCO-CARRIÓN:** Writing – review & editing, Visualization, Conceptualization. **ABEL GARCÍA-GARCÍA:** Writing – review & editing, Visualization, Conceptualization. **MARIO PÉREZ-SAYÁNS:** Writing – review & editing, Supervision, Software, Project administration, Methodology, Formal analysis, Data curation, Conceptualization.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jebdp.2024.102080.

REFERENCES

1. Bailey E, Kashbour W, Shah N, Worthington H V, Renton TF, Coulthard P. Surgical techniques for the removal of mandibular wisdom teeth. *Cochrane Database Syst Rev*. 2020;7(7):CD004345.
2. Sánchez-Garcés M-Á, Toledano-Serrabona J, Camps-Font O, et al. Diagnosis and indications for the extraction of third molars - the SECIB clinical practice guideline. *Med Oral Patol Oral Cir Bucal*. 2024;29(4):e545–e551.
3. Steed MB. The indications for third-molar extractions. *J Am Dent Assoc*. 2014;145(6):570–573.
4. Duarte-Rodrigues L, Miranda EFP, Souza TO, de Paiva HN, Falci SGM, Galvão EL. Third molar removal and its impact on quality of life: systematic review and meta-analysis. *Qual life Res*. 2018;27(10):2477–2489.
5. Costa MDM de A, Paranhos LR, de Almeida VL, Oliveira LM, Vieira W de A, Dechichi P. Do blood concentrates influence inflammatory signs and symptoms after mandibular third molar surgery? A systematic review and network meta-analysis of randomized clinical trials. *Clin Oral Investig*. 2023;27(12):7045–7078.
6. Gojayeva G, Tekin G, Saruhan Kose N, Dereci O, Kosar YC, Caliskan G. Evaluation of complications and quality of life of patient after surgical extraction of mandibular impacted third molar teeth. *BMC Oral Health*. 2024;24(1):131.
7. Firoozi P, Souza MRF, de Souza GM, Fernandes IA, Galvão EL, Falci SGM. Does kinesio taping reduce pain, swelling, and trismus after mandibular third molar surgery? A systematic review and meta-analysis. *Oral Maxillofac Surg*. 2022;26(4):535–553.
8. Zheng X, Luo S, Huang C, Wang Z, Lin X. Comparison of kinesiology tape and cryotherapy on postoperative reaction following third molar extraction: a randomized clinical trial. *Quintessence Int*. 2022;53(9):772–777.
9. Liu S, You Z, Ma C, Wang Y, Zhao H. Effectiveness of drainage in mandibular third molar surgery: a systematic review and meta–analysis. *J oral Maxillofac Surg*. 2018;76(8):1640–1650.
10. do Nascimento-Júnior EM, Dos Santos GMS, Tavares Mendes ML, et al. Cryotherapy in reducing pain, trismus, and facial swelling after third-molar surgery: systematic review and meta-analysis of randomized clinical trials. *J Am Dent Assoc*. 2019;150(4):269–277.
11. Dompe C, Moncrieff L, Matys J, et al. Photobiomodulation-underlying mechanism and clinical applications. *J Clin Med*. 2020;9(6):17–24.
12. Camolesi GCV, Silva FFVE, Aulestia-Viera PV, Marichalar–Mendía X, Gándara-Vila P, Pérez-Sayáns M. Is the photobiomodulation therapy effective in controlling post-surgical side effects after the extraction of mandibular third molars? A systematic review and meta-analysis. *J Evid Based Dent Pract*. 2024;24(2):101983.
13. World Medical AssociationDeclaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191–2194.
14. Schulz KF, Altman DG, Moher DGroup the C. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMC Med*. 2010;8(1):18. doi:10.1186/1741-7015-8-18.
15. Winter GB. Impacted mandibular third molars. *St Louis Am Med B*. 1926:241–279.
16. Pell GJ. Impacted mandibular third molars, classification and modified technique for removal. *Dent Dig*. 1933;39:330–338.
17. Landucci A, Wosny AC, Uetanabaro LC, Moro A, Araujo MR. Efficacy of a single dose of low-level laser therapy in reduc-

ing pain, swelling, and trismus following third molar extraction surgery. *Int J Oral Maxillofac Surg*. 2016;45(3):392–398.

18. Smaïl-Faugeron V, Fron-Chabouis H, Courson F, Durieux P. Comparison of intervention effects in split-mouth and parallel-arm randomized controlled trials: a meta-epidemiological study. *BMC Med Res Methodol*. 2014;14:64.
19. Hadad H, Santos AFP, de Jesus LK, et al. Photobiomodulation therapy improves postoperative pain and edema in third molar surgeries: a randomized, comparative, double-blind, and prospective clinical trial. *J Oral Maxillofac Surg*. 2022;80(1):37.e1–37.e12.
20. Eshghpour M, Ahrari F, Takallu M. Is low-level laser therapy effective in the management of pain and swelling after mandibular third molar surgery? *J Oral Maxillofac Surg*. 2016;74(7):1322.e1-8.
21. Momeni E, Kazemi F, Sanaei-Rad P. Extraoral low-level laser therapy can decrease pain but not edema and trismus after surgical extraction of impacted mandibular third molars: a randomized, placebo-controlled clinical trial. *BMC Oral Health*. 2022;22(1):417.
22. Sigaroodi AK, Motevasseli S, Maleki D, Maleki D, Fard RS. Low-level laser and management of common complications after the mandibular third molar surgery: a double-blind randomized clinical trial. *Dent Res J (Isfahan)*. 2023;20(14):1–10.
23. Singh V, Garg A, Bhagol A, Savarna S, Agarwal SK. Photobiomodulation alleviates postoperative discomfort after mandibular third molar surgery. *J Oral Maxillofac Surg*. 2019;77(12):2412–2421.
24. Kazancioglu HO, Ezirganli S, Demirtas N. Comparison of the influence of ozone and laser therapies on pain, swelling, and trismus following impacted third-molar surgery. *Lasers Med Sci*. 2014;29(4):1313–1319.
25. Jenkins PA, Carroll JD. How to report low-level laser therapy (LLLT)/photomedicine dose and beam parameters in clinical and laboratory studies. *Photomed Laser Surg*. 2011;29(12):785–787.
26. Parker S, Grzech-Leśniak K, Cronshaw M, Matys J, Jr AB. Nammour S. Full operating parameter recording as an essential component of the reproducibility of laser-tissue interaction and treatments. In: *Advances in Clinical and Experimental Medicine : Official Organ*. Poland: Wroclaw Medical University; 2024:653–656.
27. Nie F, Hao S, Ji Y, et al. Biphasic dose response in the anti-inflammation experiment of PBM. *Lasers Med Sci*. 2023;38(1):66.
28. de Freitas LF, Hamblin MR. Proposed mechanisms of photobiomodulation or low-level light therapy. *IEEE J Sel Top quantum Electron*. 2016;22(3):7000417.
29. Wu J-Y, Chen C-H, Wang C-Z, Ho M-L, Yeh M-L, Wang Y-H. Low-power laser irradiation suppresses inflammatory response of human adipose-derived stem cells by modulating intracellular cyclic AMP level and NF-κb activity. *PLoS One*. 2013;8(1):e54067.
30. Cheng K, Martin LF, Slepian MJ, Patwardhan AM, Ibrahim MM. Mechanisms and pathways of pain photobiomodulation: a narrative review. *J Pain*. 2021;22(7):763–777.
31. Abidi AH, Mayall RE, Ruan CX, Ou KL, Walinski CJ. Immunomodulatory activity seen as a result of photobiomodulation therapy in stimulated primary human fibroblasts. *Arch Oral Biol*. 2021;121:104968.
32. Aisaiti A, Zhou Y, Wen Y, et al. Effect of photobiomodulation therapy on painful temporomandibular disorders. *Sci Rep*. 2021;11(1):9049. doi:10.1038/s41598-021-87265-0.
33. Hamblin MR. Mechanisms and applications of the anti-inflammatory effects of photobiomodulation. *AIMS Biophys*. 2017;4(3):337–361.
34. Momeni E, Barati H, Arbabi MR, Jalali B, Moosavi M-S. Low-level laser therapy using laser diode 940 nm in the mandibular impacted third molar surgery: double-blind randomized clinical trial. *BMC Oral Health*. 2021;21(1):77.
35. Alan H, Yolcu Ü, Koparal M, Özgür C, Öztürk SA, Malkoç S. Evaluation of the effects of the low-level laser therapy on swelling, pain, and trismus after removal of impacted lower third molar. *Head Face Med*. 2016;12(1):25.
36. Koparal M, Kucuk AO, Alan H, Asutay F, Avci M. Effects of low-level laser therapy following surgical extraction of the lower third molar with objective measurement of swelling using a three-dimensional system. *Exp Ther Med*. 2018;15(4):3820–3826.
37. Eroglu CN, Keskin Tunc S. Effectiveness of single session of low-level laser therapy with a 940 nm wavelength diode laser on pain, swelling, and trismus after impacted third molar surgery. *Photomed Laser Surg*. 2016;34(9):406–410.
38. Carroll JD, Milward MR, Cooper PR, Hadis M, Palin WM. Developments in low level light therapy (LLLT) for dentistry. *Dent Mater*. 2014;30(5):465–475.
39. Na S, TruongVo T, Jiang F, et al. Dose analysis of photobiomodulation therapy on osteoblast, osteoclast, and osteocyte. *J Biomed Opt*. 2018 Jul;23(7):1–8.
40. Cronshaw M, Parker S, Arany P. Feeling the heat: evolutionary and microbial basis for the analgesic mechanisms of photobiomodulation therapy. *Photobiomodul, Photomed Laser Surg*. 2019;37(9):517–526.
41. Barbora A, Bohar O, Sivan AA, Magory E, Nause A, Minnes R. Higher pulse frequency of near-infrared laser irradiation increases penetration depth for novel biomedical applications. *PLoS One*. 2021;16(1):e0245350.
42. Hamdy O, Mohammed HS. Variations in tissue optical parameters with the incident power of an infrared laser. *PLoS One*. 2022;17(1):e0263164.
43. Parker S, Cronshaw M, Grootveld M. Photobiomodulation delivery parameters in dentistry: an evidence-based approach. *Photobiomodul Photomed Laser Surg*. 2022;40(1):42–50.

44. Scarano A, Lorusso F, Postiglione F, Mastrangelo F, Petrini M. Photobiomodulation enhances the healing of postextraction alveolar sockets: A randomized clinical trial with histomorphometric analysis and immunohistochemistry. *J Oral Maxillofac Surg*. 2021;79(1):57.e1–57.e12. doi:10.1016/j.joms.2020.09.008.

45. Baskerville R, Krijgsveld N, Esser P, Jeffery G, Poulton J. The effect of photobiomodulation on the treatment of hereditary mitochondrial diseases. *J Lasers Med Sci*. 2023;14:e41.

46. Reynders K, Illidge T, Siva S, Chang JY, De Ruysscher D. The abscopal effect of local radiotherapy: using immunotherapy to make a rare event clinically relevant. *Cancer Treat Rev*. 2015;41(6):503–510.

47. Ailioaie LM, Litscher G. Probiotics, photobiomodulation, and disease management: controversies and challenges. *Int J Mol Sci*. 2021;22(9):4942. doi:10.3390/ijms22094942.

48. Liebert A, Krause A, Goonetilleke N, Bicknell B, Kiat H. A role for photobiomodulation in the prevention of myocardial ischemic reperfusion injury: a systematic review and potential molecular mechanisms. *Sci Rep*. 2017;7(1):42386 Available from:. doi:10.1038/srep42386.

49. Lesaffre E, Garcia Zattera M-J, Redmond C, Huber H, Needleman I. Reported methodological quality of split-mouth studies. *J Clin Periodontol*. 2007;34(9):756–761.