Review Article

pISSN 2383-9309 ▮ eISSN 2383-9317
J Dent Anesth Pain Med 2024;24(3):145-159 ▮ https://doi.org/10.17245/jdapm.2024.24.3.145

The efficacy of photobiomodulation on dental injection pain: a systematic review of randomized clinical trials

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Dental injections are routinely performed and can result in pain and anxiety in patients. This systematic review aimed to evaluate the efficacy of photobiomodulation therapy (PBMT) in dental injections for pain management in patients undergoing dental treatment. Indexed databases, including PubMed, EMBASE, Scopus, ISI Web of Knowledge, and Cochrane Library, were electronically searched without a time limit up to February 2024. A risk of bias evaluation was performed using the Cochrane tool. A preliminary investigation using electronic and manual methods yielded 4,920,881 manuscripts. Based on the eligibility requirements, 13 randomized control trials (RCTs) were included. Self-assessed pain was determined using the visual analog scale, Face, Legs, Activity, Cry, Controllability scale, or Wong–Baker face pain scale. Eight RCTs demonstrated a notable decrease in needle pain in patients undergoing dental needle injections using PBMT. Based on current evidence, PBMT may help reduce needle pain related to dental anesthesia. Further standardized studies are needed to assess the significance of PBMT for postoperative pain in patients undergoing dental injections.

Keywords: Analgesia; Anesthesia; Dentistry; Low-Level Laser Therapy; Pain; Photobiomodulation Therapy.

INTRODUCTION

Dental injection phobia may result in people avoiding dental appointments and care, which can adversely affect an individual's dental health. During dental injections, anxious patients may experience a significant amount of pain requiring alternative methods or preparatory approaches. Adequate knowledge of the components of anesthetic agents, neuroanatomy, and correct injection techniques are the main factors in achieving sufficient local anesthesia. Numerous methods have been used to minimize discomfort during dental anesthetic injections, including using a 27-gauge needle, administering the anesthetic at a slower pace, optimizing the pH of the injection site, and selecting appropriate anesthetic agents. Furthermore, studies have indicated that topical anesthetics administered before needle insertion can reduce pain intensity during subcutaneous and intramuscular injections [1-6].

In a dental setting, local anesthetic injections ensure patient comfort during the procedure. The two common sites are the inferior alveolar (IA) and greater palatine (GP) nerves. Different types of anesthetics, such as lidocaine, articaine, and bupivacaine, are frequently used for these injections. Each type exhibits varying onset times, duration of action, and potency, allowing dentists to tailor anesthesia according to patient needs [7-9]. The mechanism of action of local anesthetics involves

Received: March 21, 2024 • Revised: May 6, 2024 • Accepted: May 7, 2024
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blocking nerve conduction by inhibiting sodium ion influx through voltage-gated sodium channels in the neuronal membranes. Upon administration, anesthetics bind to specific receptor sites within sodium channels, preventing the propagation of action potentials along the nerve fibers. This blockade results in the temporary loss of sensation in the targeted area. The injected anesthetic diffuses to the nerve trunk for IA and GP nerve blocks, blocking impulses from propagating along the respective nerves and effectively numbing the surrounding tissues [10]. A study by Aminabadi et al. in a pediatric population showed that the anatomical location of the injection was an essential determinant of the patient's pain. Administration of local anesthesia to the maxilla has been reported to be more painful than that to the mandible. Furthermore, infiltration into the anterior and posterior segments of the maxilla produces maximum and minimum pain, respectively [11].

Photobiomodulation therapy (PBMT) is a nonthermal light therapy that can reduce pain and inflammation and promote immunomodulation and tissue regeneration. While specific studies have indicated that pain alleviation through PBMT may be attributed to elevated levels of β-endorphins, nitric oxide production, and reduced activity of C-fibers and bradykinin levels, the precise mechanism is poorly understood [12-14]. The pain-relieving benefits of PBMT have been reported in dental hypersensitivity, neuralgias, postoperative endodontic surgery, temporomandibular disorders, tinnitus, myalgia, and ulcers [15-18]. Nevertheless, there has been no comprehensive investigation on the impact of PBMT on pain arising from injections inside the mouth [19,20]. These studies were primarily performed on the maxillary anterior teeth because several studies have shown that the upper incisors are more likely to be sensitive to injections.

The effect of PBMT on locations in the oral cavity other than the anterior maxilla has yet to be reported. Another challenge is the lack of precise knowledge of the specific laser characteristics responsible for inducing pain relief. There is a debate regarding the ideal laser characteristics for pain reduction during local anesthesia, and the existing literature needs to be more comprehensive to determine precisely which laser attributes are most helpful in alleviating discomfort during needle injection in the maxilla [13,21,22]. Therefore, this systematic review aimed to assess the effects of PBMT on needle injection pain in patients undergoing dental procedures.

METHODS

1. Reporting format

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [23]. This systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD42024504876. Due to the high heterogeneity among the included studies, a meta-analysis was not performed.

2. Focused Question

"Is PBMT effective in reducing dental needle injection pain?"

3. Patients, Interventions, Control, Outcome (PICO)

(P) Patients receiving dental injections; (I) PBMT; (C) other modalities; (O) self-perceived pain levels; (S) Randomized Control Trials (RCTs).

4. Eligibility Criteria

The eligibility criteria were as follows: (a) children or adults undergoing dental injections; (b) experimental group, use of PBMT; (c) control group, use of a sham laser or any other intervention; (d) studies that compared experimental and control groups; and (e) RCTs. Case reports and series, letters to the editor, retrospective studies, and non-randomized studies that did not meet the inclusion criteria were excluded. Studies published in English were included to present bias. Studies on children and adult populations were included.

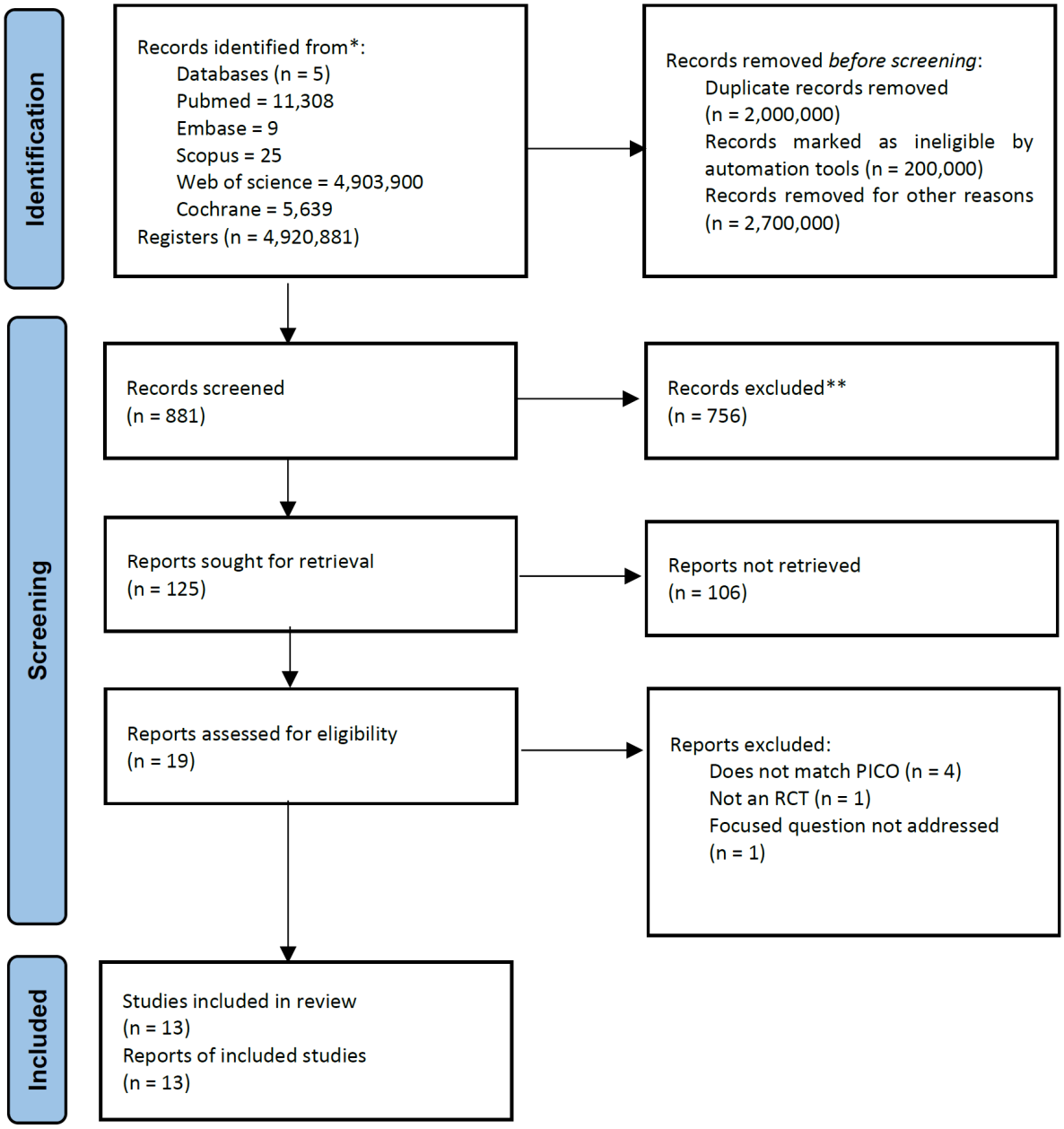

Fig. 1. Study flowchart based on the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. n, number; PICO, patients, interventions, control, outcome; RCT, randomized controlled trials.

5. Search Strategy and Data Extraction

An electronic search was performed of the indexed databases of PubMed, EMBASE, Scopus, ISI Web of Knowledge, and Cochrane Library with no time limitations up to and including February 2024. The following keywords were used: (1) laser biomodulation, (2) low-level laser therapy, (3) injection pain, (4) maxillary anesthesia, (5) local anesthesia injection pain, (6) adults, (7) children, and (8) analgesic effect of photobiomodulation therapy. Specified vital languages were merged using Boolean operators (OR, AND) to broaden the results (Table 1). Subsequently, two authors (MA and VB) assessed the titles and abstracts of the studies identified using the tools mentioned earlier, and the texts of pertinent studies were evaluated independently. Additionally, the reference lists of relevant original studies and review articles were manually searched to identify

Table 1. Search strategy for electronic databases

Database Search	Keywords	Results
PubMed	(Low laser therapy MeSH Terms]) OR Low laser therapy [Title/Abstract]) AND local anesthesia [Title/Abstract]) OR maxillary anesthesia [Title/Abstract]) OR infiltration [Title/Abstract]) OR anesthesia [Title/Abstract]) AND post-operative pain Title/Abstract]) OR local anesthesia AND pain [Title/Abstract]) OR discomfort [Title/Abstract]).	11308
Embase	(Effects AND of AND 'low level' AND laser AND therapy AND on AND injection AND pain AND during AND local AND anesthesia OR (effects AND of AND low AND level)) AND ('laser'/exp OR laser) AND ('therapy'/exp OR therapy) AND on AND ('injection'/exp OR injection) AND ('pain'/exp OR pain) AND during AND local AND ('anesthesia'/exp OR anesthesia)	9
Scopus	effects AND of AND low AND level AND laser AND therapy AND on AND injection AND pain AND during AND local AND anesthesia	25
Web of Science	(“infiltration injection”) OR (“maxillary anesthesia injection”) OR (“low-level laser therapy”) OR (“laser therapy”’) OR (“photobiomodulation therapy”) OR (“photobiomodulation”) OR (“adults”) OR (“Children”) OR (“pain”) OR (“discomfort”)	4,903,900
Cochrane	(“infiltration injection”) OR (“maxillary anesthesia injection”) OR (“low-level laser therapy”) OR (“laser therapy”’) OR (“photobiomodulation therapy”) OR (“photobiomodulation”) OR (“adults”) OR (“Children”) OR (“pain”) OR (“discomfort”)	5639

MeSH, medical subject headings.

Table 2. List of excluded studies at full-text review with reasons for exclusion

References	Reasons for the Exclusion
Hajar Mahmoud Diab PMID 37861636	A focused question needs to be addressed.
Farhad Sobouti PMID 33796965	Did not qualify for PICO
B Sandhyarani PMID:	Did not qualify for PICO
Bhagyashree Jagtap PMID: 31338422	Not an RCT
Salma Musa Adam Abduljalil PMID:	Did not qualify for PICO
Elham Khoshbin PMID 37738369	Did not qualify for PICO

PICO, patients, interventions, control, outcome; PMID, PubMed identifier; RCT, randomized controlled trials.

potentially overlooked studies in the initial phase. Any discrepancies were addressed through discussion with a third researcher (JK). Two independent reviewers (MA and VB) performed adjusted and unadjusted data extraction from the full manuscripts that matched the eligibility criteria on an Excel sheet. This allowed for an initial understanding of the patient's characteristics and possible confounding factors. Evaluation of heterogeneity deemed the meta-analysis unsuitable. Data were entered into separate tables focusing on the general characteristics of the included studies, injections, lasers, anesthetics, and outcome variables. Descriptive syntheses of the effect size and magnitude direction were emphasized to present the outcomes.

RESULTS

1. Study selection and general characteristics of included studies

An initial search revealed 4,920,881 studies (PubMed, 11,308; Embase, 9; Scopus, 25; Web of Science, 4,903,900; and Cochrane Library 5,639). After eliminating duplicates, 881 studies were included in the analysis. Five additional studies were included from the manual search. After reviewing the titles and abstracts, 19 studies were thoroughly evaluated, and six were excluded (Table 2). Consequently, 13 RCTs were included, and data were extracted (Fig. 1). All included studies had a parallel-group design consisting of an intervention group utilizing PBMT and a control group receiving other types of treatment or no treatment. The number of participants ranged from 30 to 163, with a mean age of 7 to 38.3 years. Notably, two studies did not include the mean age of the participants [24,25]. Both male and female patients were included in the studies, and none reported patient dropouts. Additionally, the duration of the studies was documented in three studies and ranged from 4 days to 18 months (Table 3).

2. General characteristics of injections and anesthetic

Eight RCTs reported using lidocaine with epinephrine,

Table 3. General characteristics of the study

Author	Year	Study Design	Country	Number of participants		Gender		Mean age	Study group	Control group	Duration of Study
				Study	Control	M	F				
Bisma Khan, et al. [24]	2023	Split mouth and parallel	India	120	0	NR	NR	NR	PBMT	1. Group 1: topical anesthesia, contralateral side 40 2. Group II: pre-cooling of the injection site, contralateral side = 40 3. Group III: vibration, contralateral side = 40	18 months
Bahman Seraj, et al. [34]	2023	Double-blinded RCT	Iran	32	32	20	40	7 yrs.	Benzocaine gel + PBMT	Benzocaine gel + Sham laser	NR
Dalya Dehgan, et al. [27]	2022	Triple-blind RCT	Turkey	120	40	81	79	NR	PBMT with different settings and then Lidocaine gel with (3 groups)	Lidocaine gel without laser	NR
Farzaneh Afkhami, et al. [31]	2020	Split mouth triple blinded RCT	Iran	30	30	20	10	26.5 yrs.	PBMT	Sham laser	NR
Fatema Shekarchi, et al. [32]	2022	Split-mouth triple-blind RCT	Iran	30	30	NR	NR	7.07	PBMT + placebo gel + injection	sham laser + 20% Benzocaine topical anesthesia gel (other side)	Seven days
Gul Uçar, et al. [29]	2021	Crossover RCT	Turkey	60	60	30	30	7.11 yrs.	Topical anesthesia + PBMT	Topical anesthesia (contralateral side second session) + laser turned off	4-7 days
Hamid Kermanshah, et al. [30]	2022	Triple blind RCT	Iran	32	32	9	23	36.4 yrs.	PBMT	A sham laser (contralateral side)	Seven days
Ippli Amruthavarshini, et al. [25]	2021	Crossover RCT	India	10	20	NR	NR	NR	PBMT	2NDgroup:ice Third group: LA gel	NR
Jacco. G. C. Tuk, et al. [26]	2015	Double-blind RCT	Netherlands	83	80	81	82	31 yrs.	PBMT	No irradiation	Four months
Mesut Elbay, et al. [28]	2023	RCT	Turkey	120	40	85	75	8.65 yrs.	1) PBMT applied for 20 sec 2) PBMT applied for 30 sec 3) PBMT applied for 40 secs	Placebo laser	NR
Roohollah Sharifi, et al. [33]	2021	Triple-blind RCT	Iran	84	84	43	41	24.76 ± 2.63	PBMT	PBMT without power on(contralateral)	14 days
Sholeh Ghabraeia, et al. [22]	2020	RCT	Iran	22	34	27	29	38.3 yrs.	PBMT	1) PBMT without radiation (placebo) 2) No pre-treatment before in	NR
Sajee Sattayut, et al. [35]	2014	Double-blind RCT	Thailand	10	30	40	40	21 yrs.	PBMT	1) Benzocaine gel 2) Heavy pressure 3) Light pressure	NR

F, female; M, male; NR, not reported; PBMT, photobiomodulation therapy; RCT, randomized controlled trial; yrs, years.

and four reported using articaine with epinephrine [26-29]. Khan et al. did not report the type of anesthesia used [24]. The injection was performed by different providers, clinicians injected the local anesthetic in two studies [30,31], pediatric dentists in three study [27-29], a blinded investigator in two studies [32,33], a principal investigator in one study [25], an oral and maxillofacial surgeon (OMFS) in one study [26], a senior post-graduate student of pediatric dentistry in one study [34], a general dentist in one study [35] and two RCTs did not indicate who performed the injections [22,24]. Eleven RCTs indicated the use of a 27-gauge needle, while two studies

Table 4. Characteristics of injection

Author	Teeth	Procedure	Location of injection	Type of anesthesia	Needle gauge	Number of injections	The volume of inj/time	Number of cartridges	Site of injection	Injection technique	Provider
Bisma Khan, et al. [24]	Primary and mand molars	Bilateral extraction	Post mand	NR	NR	NR	NR	NR	NR	IANB	NR
Bahman Seraj, et al. [34]	Primary max molars	Require extraction or SS crown	Post max	2% Lidocaine plus 1:100000 Epinephrine	27	1	1 ml /min	1	Buccal and palatal	Infiltration	Senior post-graduate student of pediatric dentistry
Dalya Dehgan, et al. [27]	Primary first molar	Operative procedure	Post max or mand	4% articaine hydrochloride with 1/100 000 epinephrine	27	1	1 ml	1 (1 ml)	Buccal	Infiltration	An experienced pediatric dentist who was blinded
Farzaneh Afkhami, et al. [31]	Upper max canine	No pathology	Ant max	2% Lidocaine plus epinephrine 1:100,000	27	1	1 ml/min	1 (half)	Buccal	Infiltration	Clinician
Fatema Shekarchi, et al. [32]	Max second primary molar	Pulpotomy and SS crown	Post max	2% lidocaine/1:100 000 epinephrine	NR	NR	NR	NR	Buccal	Infiltration	Blinded operator
Gul Uçar, et al. [29]	Primary and molars	Reversible pulpits requiring pulpotomy	Post mand	4% Articaine hydrochloride with 1/100 000 epinephrine	27	1	1 ml	1	Buccal	Infiltration	Pediatric Dentist
Hamid Kermanshah, et al. [30]	Max incisors	Carious	Ant max	2% Lidocaine 2% plus 1:80 000 epinephrine	27	1	0.6 ml	1	Buccal	Infiltration	Clinician
Ippli Amruthavarshini, et al. [25]	Primary max post	Extraction	Post max	Lignox 2%	NR	NR	1 ml/min	NR	Buccal	Infiltration	Principle Investigator
Jacco G. C. Tuk, et al. [26]	Third molar	Extraction	Post mand or post max	Articaine/hydrochloride 40 mg with epinephrine 0.01 mg	27	1	NR	1	Buccal and palatal	1. Infiltration 2. IANB	Oral maxillofacial Surgeon
Mesut Elbay, et al. [28]	Max or mand 1stmolar	No pathology	Post mand or max	Articaine with epi using a 2 ml disposable syringe	27	1	1 ml	1	Buccal	Infiltration	Pediatric Dentist
Roohollah Sharifi, [33]	Max central incisors	Carious	Ant max	2% lidocaine plus 1:100,000 epinephrine	27	NR	NR	NR	Buccal	Infiltration	Blinded operator
Sholeh Ghabraeia et al. [22]	Max canine or incisor	Reversible pulpitis	Ant max	Lidocaine 2% with epi	27	1	1ml/min	1	Buccal	Infiltration	NR
Sajee Sattayut, et al. [35]	Max first molar	NA	Post max	2% Lidocaine with 1:100,000 epinephrine	27	1	0.5	1	Palatal	Infiltration	Dentist

ant, anterior; IANB, inferior alveolar nerve block; Max, maxilla; mand, mandibular; min, minute; NA, not applicable; NR, not reported; post, posterior; SS, stainless steel.

did not disclose the needle size [24,25]. The injection technique used was mostly buccal infiltration [22,25,30, 31,34]; two studies reported using both buccal and palatal injection [26,34], one reported using palatal injection only [35] and one did indicate the injection technique [24]. All studies used only one injection; however, three did not report the number of injection used [24,25,32]. All studies used only one cartridge, and four did not report the number used [24,25,32,33]. There was a marked variety among the included studies concerning injection location (Table 4).

3. General characteristics of lasers

Nine RCTs reported using continuous pulses [22,26-29,

Table 5. Characteristics of lasers

Author	Type of laser	Site of application	laser's focal spot size	Emission frequency	Power	Irradiance/ power density	Energy density/ Fluence	Wavelength	Mode	Duration	Other treatment
Bisma Khan, et al. [24]	NR	NR	NR	NR	NR	NR	15 J/cm^2	980 nm	NR	20 sec	Lidocaine hydrochloride gel 2% Precooling with ice tube Vibration device
Bahman Seraj, et al. [34]	Diode laser irradiation (Fox; A.R.C Laser, GmbH, Nuremberg, Germany	Buccal and palatal mucosa	0.5 cm^2	Continuous	0.2 W	200 mW/ cm^2	5.2 J/cm^2	810 nm	Not contact	13 sec	20% benzocaine LA gel
Dalya Dehgan, et al. [27]	Diode laser (EpiX; Biolase Technology, Inc. USA)	Buccal mucosa	0.087 cm^2	Continuous	G1 = 0.3 W G2 = 0.4 W G3 = 0.5 W	NR	G1 = 69 J/cm^2, G2 = 92 J/cm^2, G3 = 115 J/cm^2	940 nm	Non-contact	20 sec	10% Lidocaine gel and sham laser
Farzaneh Afkhami, et al. [31]	Epic 10; BIOLASE Inc., Foothill Ranch, USA)	Buccal mucosa	0.785 cm^2	Continuous	0.2 W	NR	15.28 J/cm^2	940 nm	Contact	60 sec	Sham laser
Fatema Shekarchi, et al [32]	Diode laser (Konftec, Corporation, New Taipei City, Taiwan	Buccal mucosa	0.5 cm^2	NR	0.25	NR	32.5 J cm^2	NR	Contact	65 sec	Topical gel
Gul Uçar, et al. [29]	LLT was applied by using a diode laser (Cheese Dental Diode Laser; GIGAA LASER, Wuhan Gigaa Optronics Technology Co., China)	Bucca mucosa	0.087 cm^2	Continuous	0.3 W	NR	69 J/cm^2	810 nm	Non-contact	20 sec	Topical LA gel
Hamid Kermanshah, et al. [30]	AlGaAs diode laser (pocket laser 88 dents Italy)	Buccal mucosa	0.5 cm^2	NR	1.5 W	1.8 W/ cm2	72.5 J/cm^2	915 nm	Contact	40 sec	Sham laser
Ippli Amruthavarshin, et al. [25]	Laser biostimulation (Diode Laser, DenLase, China Daheng Group, Inc.)	Buccal mucosa	NR	Pulsated	0.3 W	NR	NR	810 nm	Non-contact	60 sec	ICE and topical gel
Jacco G. C. Tuk, et al. [26]	e LX2 Control Unit with a single-laser dental probe	Buccal and palatal mucosa	0.088 cm^2	Continuous	0.198 W	NR	67.5 J/cm^2	810 nm	NR	30 sec twice	NR
Mesut Elbay, et al. [28]	A diode laser was used (EpiX; Biolase)	Buccal mucosa	0.087 cm^2	Continuous	0.3 W	NR	G1=69 J/cm^2 G2=103 J/cm^2 G3= 138 J/cm^2	940 nm	Non-contact	20,30 and 40 sec	Placebo laser
Roohollah Sharifi, et al. [33]	A laser diode (L; Quicklase Ltd., Canterbury, UK)	Buccal mucosa	225 mm^2	Continuous	0.5	NR	4 J/cm^2	810+980 nm	Contact	20 sec	Sham laser
Sholeh Ghabraeia, et al. [22]	A laser diode (Simpler, Doctorsmile, Italy)	Buccal mucosa	0.384 cm^2	Continuous	0.3 W	NR	15.62 J/cm^2	980 nm	Contact	20 sec	LLT without radiation (placebo) and no pre-treatment with LLT before injection
Sajee Sattayut, et al. [35]	Low-intensity laser	palatal mucosa	0.13 cm^2	Continuous	0.3 W	NR	27.69 J/cm^2	790 nm	Non-contact	120 sec	20% benzocaine gel and light touch using probe and pressure

G, group; LA, local anesthetic; LLT, low-level laser therapy; NR, not reported; sec, seconds.

31,33-35], one study reported using pulsated [25], and three did not report the emission frequency [24,30,32]. Five RCTs reported that the laser treatment had contact with the injection site [22,30-33], six reported no contact [25,27-29,34,35], and this was not indicated in two studies [26,36]. The reported laser length varied from 20–

Table 6. Study outcomes characteristics

Author	Who evaluates the pain	Parameters assessed	The interval of pain evaluation	Statistical significance	Outcome	Follow up	Post-operative medi-cation	Adverse effect
Bisma Khan, et al. [24]	The researcher.	VAS Wong-Baker FLACC	NR	$P < 0.05$	PBMT was found to be an effective means of reducing injection pain, demonstrating much better efficacy than other tested methods.	NR	NR	NR
Bahman Seraj, et al. [34]	The researcher.	VAS MBPS	Immediately after inj in the buccal and palatal mucosa.	$P > 0.05$	PBMT had no additional significant effect compared to topical anesthesia on pain intensity reduction.	NR	NR	NR
Dalya Dehgan, et al. [27]	The investigator.	Wong-Baker FLACC	Immediately after the administration of the inj.	$P < 0.05$	PBMT with different output power levels before topical anesthesia was effective in reducing LA injection pain.	NR	NR	None
Farzaneh Afkhami, et al. [31]	The researcher.	VAS	Immediately after the completion of the inj in the test quadrant.	$P < 0.05$	The PBMT therapy before dental anesthetic injections has no clinical advantage for reducing injection pain.	NR	NR	NR
Fatema Shekarchi, et al. [32]	The parents.	Wong–Baker Heart Rate.	Immediately after the injection and One hr. and 24 hrs. after inj.	$P < 0.05$	PBMT can be used as an effective non-pharmacological technique for controlling injection pain.	NR	Analgesics	None
Gul Uçar, et al. [29]	The investigator.	Wong-Baker PRS FLACC	At needle insertion and anesthetic solution deposition.	$P < 0.05$ for PRS $P > 0.05$ for FLACC	Applying topical anesthesia + LLLT before local infiltration anesthesia reduced injection pain and did not affect anesthesia efficacy and duration in children.	No	NR	None
Hamid Kermanshah, et al. [30]	The investigator.	NPRS	Immediately after inj.	$P < 0.05$	The PBMT, compared to the sham laser, was effective in decreasing pain perception due to needle insertion and LA injection.	NR	NR	NR
Ippli Amruthavarshini, et al. [25]	The investigator.	Wong-Baker SEM	During the administration of local anesthesia.	$P < 0.05$	Laser biostimulation was less effective than LA gel and pre-cooling with ice in reducing injection pain.	No	NR	NR
Jacco G. C. Tuk, et al. [26]	The patient.	Questionnaire BVP sensor SC/GSR sensor	Before and after local anesthetic inj.	$P > 0.05$	LLLT did not effectively decrease the pain felt during local anesthetic injections.	NR	NR	NR
Mesut Elbay, et al. [28]	The investigator.	Wong-Baker FLACC	Immediately after the inj.	$P > 0.05$	Application of PBMT + topical anesthesia did not differ in reducing injection pain compared to placebo PBMT + topical anesthesia.	Follow up after one month to assess the behavior	NR	Lip biting
Roohollah Sharifi, et al. [33]	The researcher.	VAS	Before the injection and immediately after the inj.	$P < 0.05$ for females and $P > 0.05$ for males.	Low-level laser therapy can be successfully used to decrease the level of pain experienced during infiltration anesthesia of the anterior maxilla.	NR	NR	NR
Sholeh Ghabraeia, et al. [22]	The patients.	VAS	During the inj.	$P < 0.05$	Diode laser significantly reduced the local anesthesia injection pain in the anterior maxillary region without superiority over placebo irradiation.	No	NR	NR
Sajee Sattayut, et al. [35]	The researcher.	VAS	After local anesthetic inj.	$P > 0.05$	No statistically significant differences in pain scores were noted among low-intensity laser, 20% benzocaine, pressure, and light touch.	NR	NR	NR

BVP, blood volume pulse; FLACC, Face, Legs, Activity, Cry, and Consolability; hr, hour; inj, injection; LA, local anesthetic; LLLT, low-level laser therapy; MBPS, modified behavioral pain scale; NPRS, numerical pain rating scale; NR, not reported; PBMT, photobiomodulation therapy; PRS, pain rating scale; SC/GSR, sweat conductance or galvanic skin response; SEM, Sound Eyes Motor scale; VAS, Visual analog scale.

40 seconds to 1–2 minutes. The reported wavelengths ranged from 790 to 980 nm. Five studies reported a wavelength of 810 nm [25,26,29,33,34], one reported 915 mm [30], one reported 790 nm [35], three reported 940 nm [27,28,31], and three reported 980 nm [22,24,33]. All studies only used the laser on the buccal area, two on the buccal and palatal mucosa [26,34], and only one on the palatal region [35]. Significant differences were found among the included studies regarding diagnosis, number of teeth, laser type, laser power, energy density, and focal

Table 7. Risk of bias of the included randomized controlled clinical trials

Author	Random sequence generation	Allocation concealment	Blinding of participants and researchers	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting	Other bias	Overall
Bisma Khan, et al. [24]	Low	Low	High	High	Low	Low	Low	unclear
Bahman Seraj, et al. [34]	Low	Low	Low	Low	Low	Low	Low	Low
Dalya Dehgan, et al. [27]	Low	Low	Low	Low	Low	Low	Low	Low
Farzaneh Afkhami, et al. [31]	Low	Low	Low	Low	Low	Low	Low	Low
Fatema Shekarchi, et al. [32]	Low	Low	Low	Low	Low	Low	Low	Low
Gul Uçar, et al. [29]	Low	Low	Low	Low	Low	Low	Low	Low
Hamid Kermanshah, et al. [30]	Low	Low	Low	Low	Low	Low	Low	Low
Ippli Amruthavarshini, et al. [25]	Low	Low	Some concerns	High	Low	Low	Low	unclear
Jacco G. C. Tuk, et al. [26]	Low	Low	Low	Low	Low	Low	Low	Low
Mesut Elbay, et al. [28]	Low	Low	Low	Low	High	Low	Low	unclear
Roohollah Sharifi, et al. [33]	Low	Low	Low	Low	Low	Low	Low	Low
Sholeh Ghabraeia, et al. [22]	Low	Low	Some concerns	High	Low	Low	Low	unclear
Sajee Sattayut, et al. [35]	Low	Low	Low	Low	Low	Low	Low	Low

spot area (Table 5).

4. Characteristics of outcome variables

Ten RCTs reported that the researcher or investigator evaluated the pain [24,25,27-31,33-35]. Two RCTs reported that the patient evaluated the pain [22,26], and one RCT reported that the parent evaluated the pain [32]. Six RCTs used the visual analog scale (VAS) [22,24,31, 33-35], four used the Face, Legs, Activity, Cry, Controllability scale (FLACC)[24,27-29], and five used the Wong–Baker face pain scale (WBFPS) [24,25,27,28, 32] to assess self-perceived pain. Tuk et al. used physiologic parameters (heart rate and sweat response), and a questionnaire was used [26]. Seven RCTs [27,28, 30-32,34,35] recorded the pain evaluation immediately following the injection, 2 [22,25] during, and 2 [26,33] recorded the pain evaluation before and after the injection. One study evaluated the pain twice: once during PBMT application and once after the injection [22]. One study did not report the interval of pain evaluation [24]. Among the reviewed studies, 7 RCTs revealed statistically significant differences in pain levels between the laser treatment and additional treatments [22,24,25, 27,30-32]and four [26,28,34,35] reported no statistically significant differences in pain levels between the laser and other treatments. One study reported statistically significant differences in pain levels on the Wong–Baker face pain scale and no statistically significant differences on the FLACC scale [29]. Sharifi et al. reported statistically significant differences in pain levels in females but not in males [33] (Table 6).

5. Risk of bias

The risk of bias (RoB) was performed using the Cochrane RoB tool for interventions, RevMan 5.4 software. The Cochrane collaboration guidelines evaluated the likelihood of bias in the included RCTs in six dimensions: i) sequence generation, ii) allocation

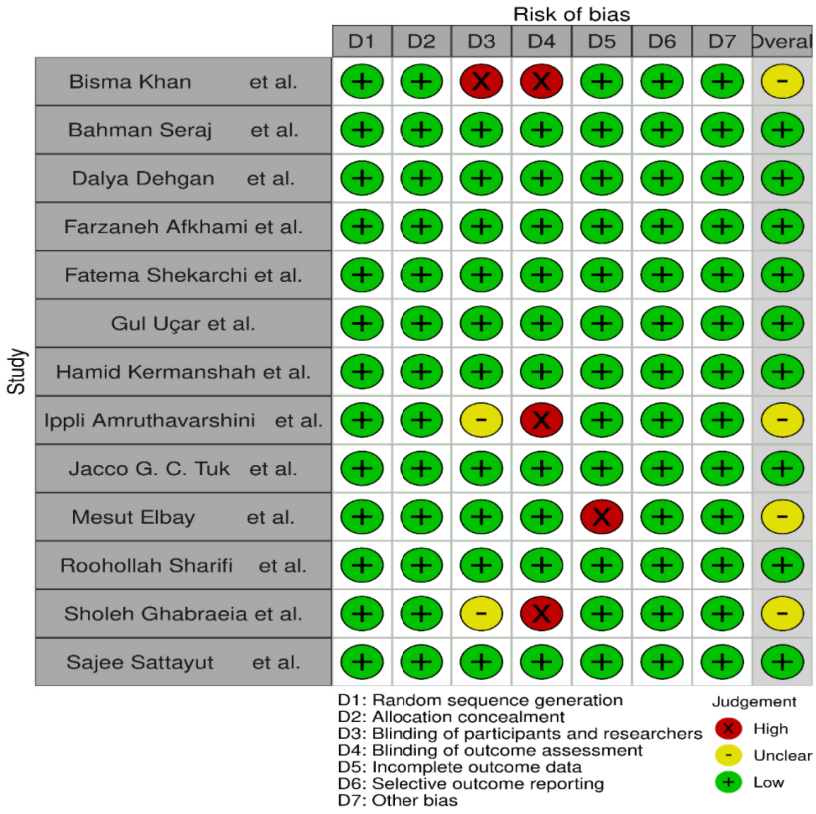

Fig. 2. Traffic light plot

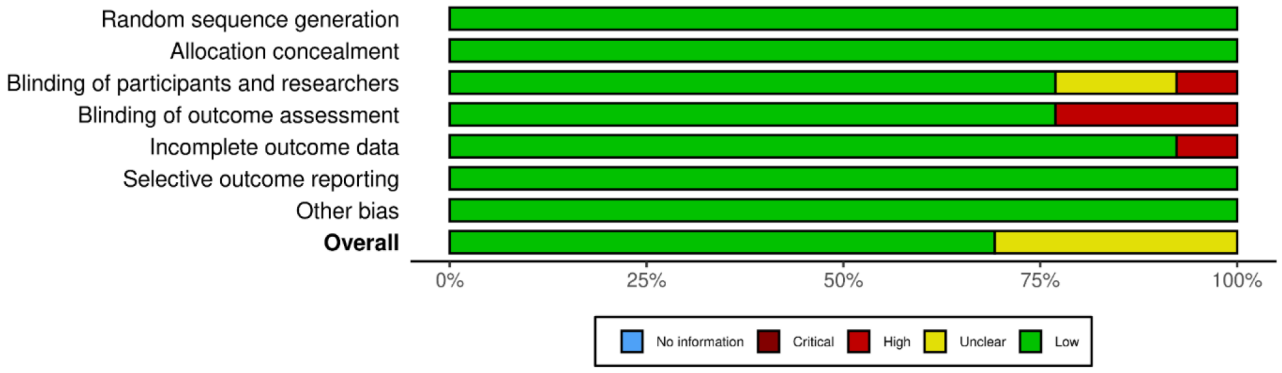

Fig. 3. Overall risk of bias

concealment, iii) blinding of participants and outcome assessors, iv) incomplete outcome data, v) selective outcome reporting, and vi) other sources of bias [37]. The RoB across individual studies was assessed by two authors (MA and LJ). The overall RoB was classified as high, low, or unclear. Overall, nine RCTs had a low RoB, whereas four had an unclear RoB. The main reasons for bias were the lack of blinding of participants and researchers, lack of blinding of the outcome assessment, and incomplete data in one article. None of the RCTs reported a power analysis for sample size estimation (Table 7, Fig. 2 and Fig. 3).

DISCUSSION

Anesthesia administration via injection is a critical in dental procedures. Individuals undergoing dental

treatment frequently express apprehension regarding the discomfort associated with anesthetic injections. Administering painless anesthetic injections can enhance patient comfort, foster better cooperation, positively affect treatment quality, and build trust with patients. Various factors determine the needle pain experienced during injection, including needle sharpness, injection velocity, solution temperature, and patient anxiety (14). Other pre-injection techniques that relieve pain include topical gels, pre-cooling at the injection site, and application of pressure [38]. Topical cold application stimulates myelinated A-fibers and engages pain pathways related to inhibition, thereby mitigating pain perception [39]. The exact mechanism of PBMT is unknown; however, it may induce immediate pain relief by modulating neurophysiological processes in the peripheral nerves [13,40].

This study was conducted to assess self-reported pain levels following PBMT in patients undergoing anesthesia injections in the oral cavity. After applying strict eligibility criteria, 13 RCTs were analyzed for data extraction. The RCT by Afkhami et al. summarized that pre-application of PBMT significantly reduced pain levels during injection [31]. Kermanshah et al. reported that lasers had a notable impact on reducing discomfort during either needle insertion or injection, and no correlation between anxiety levels from prior dental injections and pain perception was observed [30]. Bisma et al. reported that among the tested methods, PBMT was the best at alleviating injection pain compared to topical anesthesia, precooling, and the vibration method [24].

Sharifi et al. showed that PBMT alleviated pain experienced during anterior maxillary infiltration and also decreased pain to a greater extent in females than in males [33]. Dehgan et al. also compared different powers of PBMT using a sham laser. They concluded that PBMT utilizing a 940-nm diode laser at various output power levels (0.3 W, 0.4 W, or 0.5 W) before topical gel use effectively decreased pain associated with local anesthetic injection, irrespective of characteristics such as sex, age, and jaw differences in children [27].

Seraj et al. reported no significant difference in pain scores during local anesthesia injection between the PBMT and control groups in either the buccal or palatal mucosa [34]. Ucar et al. evaluated the effect of combined PBMT and topical anesthesia on injection pain in children undergoing pulpotomy. They found that PBMT (using a diode laser-810 nm; continuous mode; 0.3 W; 20-sec exposure; 69-J/cm^2) decreased injection discomfort [29]. Conversely, Amrutavarshini et al. reported that PBMT was less effective than topical gel or precooling with ice [25]. However, Shekarchi et al. found that the injection pain values were significantly lower with PBMT than with topical anesthesia [32].

Elbay et al. reported that patients pretreated with PBMT experienced less pain during injection than patients who received injection without pretreatment. However, the difference between the experimental and placebo groups where the laser probe was placed in the vestibule without irradiation was not significant [28]. Sattayut et al. found that the injection pain in the palatal region remained unaffected [35]. Additionally, Ghabraei et al., using parameters of 980 nm wavelength, contact mode, 0.3 W power, 15.62 J/cm^2 energy density, 0.384 cm2 focal spot area, and 6 J energy for 20 seconds, reported that PBMT application before local anesthesia injection decreased pain levels during the infusion but did not demonstrate superiority over the placebo [22].

The use of PBMT for pain management has been thoroughly documented in the literature. Evidence suggests that lasers can serve as a successful approach for pain relief following nonsurgical root canal therapy and intramuscular injection [41,42]. Tanboga et al. reported that pediatric patients who underwent PBMT before cavity preparation experienced reduced pain levels during the procedure [43]. Similarly, Shapiro et al. reported that PBMT application with lidocaine led to a significant reduction in needle insertion pain during intramuscular injections [42]. Furthermore, Jagtap et al. reported that a laser before local anesthetic injections for tooth extraction substantially alleviated injection discomfort [44].

The strength of this systematic review was the inclusion of only RCTs. However, the variability observed among these RCTs posed challenges when conducting a quantitative assessment (meta-analysis) of the extracted data. However, a drawback of this review is the methodological irregularities observed, such as variations in cartridge temperature, injection speed, pressure, interval of pain assessment, pain assessment scales, duration of pain evaluation, total study duration, and small sample size. These inconsistencies may diminish our understanding of group differences owing to inadequate statistical power. PBMT involves many parameters, including power, wavelength, irradiation time, energy density, power density, focal spot area, and variations that can induce different biological responses within tissues. However, a consensus regarding the ideal parameter settings has not yet been established [45,46]. Hence, differences in these parameters may explain the differences in the results.

Measuring pain presents a significant challenge, mainly when dealing with children, owing to their limited experience, vocabulary, inferior cognitive abilities, and not fully developed range for expression [36]. Self-reporting discomfort in children is unreliable because it is based on developmental, environmental, and anxiety issues [47]. Therefore, it is essential to complement self-report measures with observational and physiological assessments.

Conclusion

Eight RCTs demonstrated a notable decrease in needle pain in patients who underwent dental needle injections using PBMT. Based on current evidence, PBMT may help reduce needle pain related to dental anesthesia. Future research should focus on conducting randomized controlled trials that adhere to strict methodological standards and ensure homogeneity to assess the relationship between PBMT and other treatments. Healthcare providers should communicate the potential pain associated with dental injections to prospective patients. Moreover, conducting power-adjusted, controlled clinical trials with larger sample sizes would provide more advanced insights into the effectiveness of different pain management approaches.

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ACKNOWLEDGEMENTS: We thank the Division of Orofacial Pain for allowing us the opportunity to conduct this systematic review.

REGISTRATION NUMBER: PROSPERO CRD42024504876

CONFLICT OF INTEREST: The authors have no personal or financial conflicts to declare.

FUNDING: No funding received.

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