Received: 27 April 2023 | Accepted: 16 August 2024

DOI: 10.1111/iej.14140

REVIEW ARTICLE

INTERNATIONAL ENDODONTIC JOURNAL | WILEY

# Efficacy of laser adjuvant therapy in the management of post-operative endodontic pain: A systematic review and meta-analysis

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**Funding information**

Research Funding from West China School/Hospital of Stomatology Sichuan University, Grant/Award Number: RCDWJS2022-5

## Abstract

**Background:** Postoperative endodontic pain (PEP) is crucial in clinical practice. Recently, the effects of various laser adjuvant therapies in endodontic treatments have been widely evaluated. However, as a virtually side-effect-free treatment, its effect on postoperative pain management during endodontic treatment remains controversial.

**Objectives:** This review aimed to compare the efficacy of laser adjuvant therapy for pain management after endodontic treatment.

**Method:** The Cochrane Library, PubMed, Embase, Scopus and Web of Science databases were systematically searched for articles published until 12 February 2023. The risk of bias in the included studies was evaluated based on the Cochrane risk-of-bias assessment tool. Data on continuous outcomes of visual analogue scale pain scores are expressed as standard mean difference (SMD) and dichotomous outcomes of pain prevalence as relative risk (RR).

**Results:** We included 22 studies, of which 15 enrolled 892 patients with visual analogue scale pain scores and 7 enrolled 422 patients with pain prevalence. Of the 22 studies, seven studies had a low risk of bias, 10 had a moderate risk of bias and 5 had a high risk of bias. For pain level, the pooled outcomes indicated reduced pain scores in all laser adjuvant therapy, including low-level laser therapy (SMD = −0.86 [95% CI: −1.16, −0.55] in 24 h and SMD = −0.64 [95% CI: −0.84, −0.43] in 48 h), diode laser therapy (SMD = −0.27 [95% CI: −0.50, −0.04] in 48 h) and photodynamic therapy (SMD = −1.12 [95% CI: −2.18, −0.05] in 24 h). For postoperative pain incidence, a significant correlation was observed with reduced pain incidence rates in the photodynamic therapy group (pooled RR = 0.47 [95% CI: 0.31, 0.72]) but not in the low-level laser therapy group (RR = 0.89 [95% CI: 0.30, 2.70] at 12 h and RR = 0.57 [95% CI: 0.09, 3.72] at 24 h).

**Conclusions:** High-quality evidence suggests that laser adjuvant therapies such as low-level laser therapy, diode laser therapy and photodynamic therapy have a positive impact on reducing postoperative endodontic pain intensity. However, the differences in PEP management effects between laser therapies are unknown, and no significant differences were observed among the subgroups.

**Registration:** CRD 42023402872 (PROSPERO).

**KEYWORDS**

laser therapy, low-level laser therapy, meta-analysis, pain, postoperative, root canal therapy

# INTRODUCTION

Postoperative endodontic pain (PEP) is a common complication of endodontic treatment, with a high prevalence of 40% within 24h and 11% after 1 week (Pak & White, 2011). It manifests as pain or swelling after a few hours or days, requiring an immediate visit to the dental office, substantially affecting the patient's quality of life (Alonaizan & AlFawaz, 2019; Chen et al., 2019). Moreover, this phenomenon can be attributed to the inflammatory process, secondary to localized mechanical, chemical and microbial factors that traumatize the pulp and periapical tissues, and potential extrusion of tooth debris, intracanal medicaments, root canal irrigation solutions and microorganisms through the apical foramen. The release of the inflammatory mediators in this inflammatory response, such as prostaglandins, leukotrienes, bradykinin and serotonin, leads to unexpected pain after treatment (Alonaizan & AlFawaz, 2019; Iqbal et al., 2009). Postoperative pain is influenced by numerous factors, including preoperative pain severity, pulp status, various instrumentation techniques for root canal preparation and the treatment performed; either primary root canal treatment (RCT) or root canal retreatment (RCR) and type of tooth (Di Spirito et al., 2022).

Pain management after endodontic therapy is important in clinical practice. Recently, pharmaceutical treatment has been regarded as a major treatment option in PEP management and is prescribed as prophylactic medications and postoperative analgesics, including nonsteroidal anti-inflammatory drugs (NSAIDs), steroidal anti-inflammatory drugs, acetaminophen, antihistamines, narcotic analgesics, long-lasting anaesthesia and intracanal medication (Di Spirito et al., 2022). However, pharmaceutical treatment is not appropriate for every patient. For example, NSAIDs, the most commonly used analgesics for PEP, are often contraindicated in pregnant or lactating mothers (Leverrier-Penna et al., 2018) and patients with drug allergies (Sipahi Cimen et al., 2023) and are prudent for patients with severe hepatic or renal insufficiency and severe heart failure (Gislason et al., 2009). Laser adjuvant therapy has gradually gained much attention among dentists because it promotes wound healing, pain reduction and disinfection without adverse events (Al-Maweri et al., 2017; Costa et al., 2023; Ren et al., 2015; Wu et al., 2023). Laser therapy can upregulate fibroblast function, dilate blood vessels, accelerate connective tissue repair and have anti-inflammatory effects (Alonaizan & AlFawaz, 2019; Fazlyab et al., 2021).

Over the past decade, the efficacy of various laser adjuvant therapies for PEP management has been evaluated, including diode laser therapy, low-level laser therapy (LLLT), neodymium: yttrium aluminium garnet, erbium, chromium: yttrium scandium gallium garnet, erbium-doped yttrium aluminium garnet laser irradiation and photobiomodulation (PBM). Clinically, LLLT is predominantly utilized in a non-thermal manner using red or near-infrared lasers with a wavelength ranging from 600 to 1000nm and an energy output of 5–500mW for extracanal irradiation through a 200-μm fibre tip positioned approximately 10mm from the root apexes tissue. However, diode laser therapy typically employs a laser with a 940–1000nm wavelength and an energy output of ≥1W for intracanal irradiation through a 200-μm fibre tip (Chen et al., 2019). Nonetheless, the outcomes of laser adjuvant therapy remain controversial (Morsy et al., 2018). reported that pain scores were significantly lower in the laser group on 6 h, 12 h, 24 h, 48 h and 7 day. However, Guimarães et al. (2021) and Naseri et al. (2020) reported no significant correlation between laser irradiation and PEP during any period. Furthermore, Chen et al. (2019) and Alonaizan and AlFawaz (2019) attempted to evaluate the relationship between LLLT and RCT statistically. Nevertheless, the limitations of the data allowed them to conduct a systematic review, which only qualitatively characterized the problem.

Given the growing body of clinical research published on this subject, the present systematic review and meta-analysis were conducted to address the following questions: Is there a correlation between the use of laser adjuvant therapy and a reduction in the intensity and incidence rate of PEP? If a correlation exists, what types of laser therapy should be chosen? Are there any key factors affecting the reduction effect?

# METHOD

## Protocol and search strategy

The protocol was pre-registered and accepted by the International Prospective Register of Systematic Reviews (PROSPERO) with the ID number CRD 42023402872. This review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (Page et al., 2021). This was reported based on a systematic review of the Cochrane Handbook for Systematic Reviews.

Two investigators (Z. Luo and Y. Li) searched all relevant literature from the inception of databases up to 12 February 2023, from Cochrane Library, PubMed, Embase, Scopus and Web of Science according to the criteria developed together with the search keywords 'postoperative pain', 'Root Canal Therapy', 'Endodontic treatment', 'Laser Therapy', 'Photobiomodulation Therapy' and 'Low Level Laser Therapies' (Appendix S1) shows the specific search strategy. There were no limitations on the publication, language or region. References of the selected studies and reviews were searched to identify relevant data. Discrepancies were resolved through discussions.

## Inclusion criteria and exclusion criteria

All the selected studies were based on the following inclusion and exclusion criteria.

Inclusion criteria:

1. Randomized clinical trials reporting the efficacy of laser adjuvant therapy on PEP management.
2. Receiving conventional endodontic treatment with no limitations on RCT/RCR or single/multiple visits.
3. Any laser adjuvant therapy, including diode laser, LLLT or PBM.
4. Data on pain assessment, including mean ± SD by visual analogue scale (VAS) or numerical rating scale.
5. Data on pain prevalence and intensity grading (none/mild/moderate/severe).

Exclusion criteria:

1. Studies with <10 sample size.
2. Studies evaluating laser therapy on pain control after endodontic surgery.
3. Studies involving overlapping patients reported in subsequent larger studies were excluded.
4. Studies without data on VAS or numerical rating scale score mean ± SD, pain prevalence and intensity grading.

## Data extraction

From each of the eligible studies, the following data were collected: basic information (author, publication year); information on the population characteristics (number of patients, age and initial diagnosis); information on endodontic treatment (RCT or RCR, single visit or multiple visit and tooth type), laser adjuvant therapy (laser type, wavelength, energy output, exposure time window and position) and outcome data (pain score mean ± SD, pain intensity grading and pain prevalence).

The PEP intensity was measured using a 10-point VAS. Results originally published on a 100-point VAS scale were converted to 10-point VAS scores. When reporting data from the first and second visits, preference was given to the results of the second visit, marking the end of the RCT. When the mean and/or SD were not available, these were estimated from P-values between groups and confidence intervals (CIs), using the Finding Standard Deviations method outlined in the Cochrane Handbook (Higgins et al., 2022) and from the median (range), using the method described by (Luo et al., 2018) and (Wan et al., 2014).

All the data were extracted by two independent authors (Z. Luo and Y. Li). Both authors reviewed all items for correctness after extraction. Discrepancies were resolved by consensus. The data accuracy was confirmed by a third author (Y. He).

## Risk of bias assessment

Quality assessment of the included studies was conducted by two authors (Z. Luo and Y. He) based on the 'risk of bias' assessment tool (Higgins et al., 2022) for seven domains. Each domain was divided into three categories: low risk of bias, unclear risk of bias and high risk of bias. Studies were classified as having a low risk of bias if all domains were evaluated to be low risk, moderate risk of bias if one or more domains were evaluated to be of unknown risk or high risk if any domain was evaluated as high risk.

## Publication bias

Egger's test (Egger et al., 1997) and funnel plots were used to analyse publication bias.

## Data analysis

The primary outcome was the effect of laser adjuvant therapy on PEP control and pain levels were measured at 24 h and 48 h after endodontic treatment. The secondary outcome was pain prevalence after endodontic treatment.

A subgroup analysis was conducted at 24 and 48 h because of the high incidence of PEP in the first 2 days to identify the key factors that may determine the effect of pain control in laser adjuvant therapy. Subgroup analyses were performed according to the endodontic treatment session (single visit, first visit or second visit), RCT or

RCR, symptomatic or asymptomatic disease, diagnosis of irreversible pulpitis, necrotic pulps, apical periodontitis and different tooth types (single-rooted teeth or posterior).

Furthermore, the leave-one-out approach was applied to analyse the impact of each included study and explore its contribution to the overall heterogeneity.

Continuous outcomes (VAS scores) were expressed as standard mean difference (SMD) with a 95% confidence interval (CI). Dichotomous outcomes (pain prevalence) were expressed as relative risk (RR) with 95% CI. To more effectively address the heterogeneity observed across different indicators during pooling, the random effects model was employed when $I^2 \geq 50\%$ or the test of heterogeneity yielded $p \leq .05$. Conversely, the common effect model was utilized if $I^2 < 50\%$ and the test of heterogeneity produced $p > .05$. The Knapp-Hartung method and the Sidik-Jonkman estimator (Sidik & Jonkman, 2005) were used to estimate the inter-study variance, $\tau^2$. The Higgins and Thompson's $I^2$ test was applied to assess inter-study heterogeneity.

Risk of Bias assessment was conducted using Review Manager (RevMan, version 5.4.1) and the remaining analyses were performed using R (version 4.2.1) (R-Core-Team, 2022) and the meta package (Schwarzer, 2007).

# RESULTS

## Search result

The systematic search yielded 204 records from the Cochrane Library, PubMed, Embase, Scopus and Web of Science, which were manually added after viewing the references. Fifty records on laser adjuvant therapy, endodontic treatment and PEP were reviewed. After the reviewing, 28 studies were excluded for the reasons showed in Figure 1 (Alonaizan & AlFawaz, 2019; Anagnostaki et al., 2020; Arshad et al., 2019; Arslan et al., 2018; Barciela et al., 2019; Brignardello-Petersen, 1939; Chen et al., 2019; Dedania et al., 2021; Erkan et al., 2022; Guerreiro et al., 2021; Hadad et al., 2022; Koba et al., 1999; Kreisler et al., 2004; Liapis et al., 2021; Mandras et al., 2020; Meire et al., 2022; Metin et al., 2018; Moghadam et al., 2021; Myers & McDaniel, 1991; Nivedhitha & Swarna, 2021; Nunes et al., 2020; Payer et al., 2005; Ribeiro et al., 2012; Simon et al., 2018; Souza et al., 2021; Suter et al., 2020; Vahdatinia et al., 2019; Yoo et al., 2014), 22 studies (Alves-Silva et al., 2022; Arslan et al., 2017, 2018; Asnaashari et al., 2011, 2017; Coelho et al., 2019; Dagher et al., 2019; Doğanay Yıldız et al., 2019; Fazlyab et al., 2021; Genc Sen & Kaya, 2019; Guimarães et al., 2021; Ismail et al., 2023; Kaplan et al., 2021, 2022; Lopes et al., 2019; Morsy et al., 2018; Nabi et al., 2018; Naseri et al., 2020; Shah et al., 2021; Tunc et al., 2021; Vilas-Boas et al., 2021; Yoshinari et al., 2019) were included in the systematic review and meta-analysis, 15 studies (Arslan et al., 2017, 2018; Asnaashari et al., 2011; Coelho et al., 2019; Dagher et al., 2019; Doğanay Yıldız et al., 2019; Fazlyab et al., 2021; Genc Sen & Kaya, 2019; Guimarães et al., 2021; Ismail et al., 2023; Kaplan et al., 2021, 2022; Lopes et al., 2019; Morsy et al., 2018; Nabi et al., 2018; Naseri et al., 2020; Tunc et al., 2021; Yoshinari et al., 2019) enrolled 892 patients with continuous data mean ± SD VAS pain score and seven studies (Alves-Silva et al., 2022; Asnaashari et al., 2017; Coelho

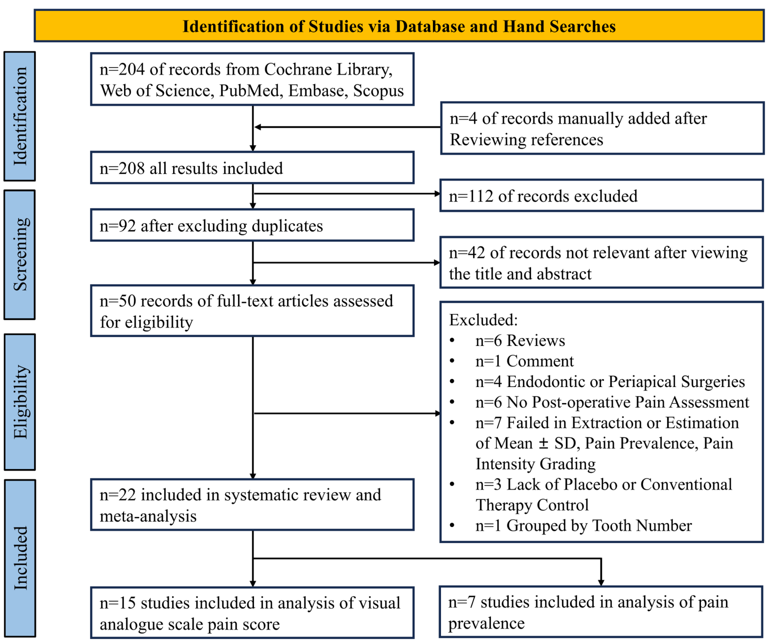


**FIGURE 1** PRISMA flow diagram.

**TABLE 1** Basic characteristics of included studies.

| | Population character | | Character of RCT | |
|---|---|---|---|---|
| **Author, year** | **Number and age (E vs C)** | **Diagnosis** | **Type of RCT** | **Tooth type** |
| Genc Sen (2019) | 37 vs 36 age(range): 18–52 | a. Chronic periapical infection<br>b. asymptomatic | Single-visit RCR | Single-rooted teeth |
| Kaplan et al. (2021) | 30 vs 30 age(range): 18–65 | a. Apical periodontitis<br>b. Asymptomatic | Two visits RCT | Single-rooted teeth |
| Morsy et al. (2018) | 28 vs 28 age (range): 18–35 | a. Chronic periapical lesions and necrotic pulp<br>b. Asymptomatic | Two visits RCT | Central upper teeth |
| Dagher et al. (2019) | 25 vs 31 age(range): 19–73 | a. Asymptomatic or symptomatic irreversible pulpitis, symptomatic pulpal necrosis with or without apical periodontitis<br>b. Symptomatic or asymptomatic | Single-visit RCT | Premolar or molar teeth |
| Ismail et al. (2023) | (male)<br>60 vs 60 (LAI vs C) age(range): 18–50 | a. Symptomatic apical periodontitis<br>b. Symptomatic | Single-visit RCT | Mandibular permanent molars |
| | (male)<br>60 vs 60 (LLLT vs C) age: 18–50 (range) | a. Symptomatic apical periodontitis<br>b. Symptomatic | Single-visit RCT | Mandibular permanent molars |
| Arslan et al. (2017) | 16 vs 17 age (mean): 32.6 vs 25.8 | a. Periapical lesions with scores 2 or 3 by PAI<br>b. Had a pain 100 mmVAS <50 and a percussion pain 100mmVAS <50 | Two visits RCR | Mandibular molars |
| Asnaashari et al. (2011) | 40 vs 40 age (mean): 31.9 vs 27.9 | NA | Single-visit RCT | First permanent molars |
| Asnaashari et al. (2017) | 41 vs 20 | NA | Single-visit RCR | Posterior teeth |
| Fazlyab et al. (2021) | 18 vs 18 age (range): 28–59 | a. Symptomatic apical periodontitis<br>b. Symptomatic | Single-visit RCR | First or second mandibular molars |
| Lopes et al. (2019) | 30 vs 30 age (range): 18–60 | a. Irreversible pulpitis<br>b. Little or none pain<br>c. Cold pulp test positively | Single-visit RCT | Lower molar teeth |
| Naseri et al. (2020) | 25 vs 25 age (range): 18–60 | a. Irreversible pulpitis<br>b. Symptomatic | Single-visit RCT | Molar tooth |
| | 25 vs 25 age (range): 18–60 | a. Irreversible pulpitis<br>b. Symptomatic | Single-visit RCT | Molar tooth |
| Shah et al. (2021) | 20 vs 20 | a. Nonvital pulps and apical periodontitis<br>b. Periapical lesion >2 mm and <8 mm | Two-visits RCT | Permanent single-rooted teeth |

| Character of laser adjuvant therapy | | | Outcomes | |
|---|---|---|---|---|
| **Laser exposure position and intracanal media** | **Laser exposure time window** | **Output and type of laser** | **Pain assessment by 10-point VAS (E vs C)** | **Additional pain assessment** |
| Through a 200-μm fibre tip in canal | Root canal disinfection after root canal irrigation | 1W<br>940-nm diode laser | Mean ± SD VAS score at 24 h/48 h/72 h by after the single visit | Percussion pain on 4th day: 0.22 ± 0.48 vs 0.72 ± 0.88 |
| Through a 200-μm fibre tip in canal | Root canal disinfection after root canal irrigation | 1.2W<br>980-nm diode laser | Mean ± SD VAS score at 8 h/24 h/48 h/72 h after the first and second visit | 8 h/24 h/48 h/7 days VAS pain intensity grading (None, Mild, Moderate, Severe) |
| Through a 200-μm fibre tip in canal | Root canal disinfection after root canal irrigation | 1.2 W pulsed mode<br>980-nm diode laser | Mean ± SD at 6 h/12 h/48 h/7 days VAS score after the second visit | 6 h/12 h/24 h/48 h/7 days VAS pain intensity grading (None, Mild, Moderate, Severe) |
| a. Through a tip of 600 μm diameter and 9 mm length in canal<br>b. EDTA, 5.25% NaOCl and distilled water in canal | LAI while final root canal irrigation | 0.3 W pulsed mode<br>Er:YAG 2940 nm laser | Mean ± SD VAS score at 1–7 days after the single visit | Percussion pain at Day 7 |
| a. EDTA, normal saline<br>b. A 200-μm fibre tip in canal | LAI while final root canal irrigation | 2.5 W<br>(LAI)980-nm diode laser | Mean ± SD VAS score at 24 h/48 h/72 h after the single visit | |
| Through a 200-μm fibre tip on the oral mucosa | Root canal disinfection after root canal irrigation | NA (LLLT)980-nm diode laser | Mean ± SD VAS score at 24 h/48 h/72 h after the single visit | |
| Through a 200-μm fibre tip approximately 10 mm to the mesial and distal root apexes tissue | After root canal medication and temporary restoration | 0.5 W<br>970 ± 15 nm diode laser | Mean ± SD VAS score at 1–7 days after the second visit | Preoperative percussion pain: 1.456 ± 1.419 vs 1.888 ± 1.863<br>Preoperative percussion pain: 0.338 ± 0.837 vs 0.918 ± 1.357<br>Preoperative palpation pain: 0 vs 0<br>Preoperative palpation pain |
| On both the buccal and lingual mucosae at the level of the apices | After root canal filling | 100 mW<br>980-nm diode laser | Mean VAS score and *p* value at 4 h/8 h/12 h/24 h/48 h after the single visit | |
| Fibre diameter 600 μm on the buccal and lingual mucosa overlying the apices of the target tooth | After root canal preparation | 100 mW<br>808 nm | NA | 4 h/8 h/12 h/24 h/48 h VAS pain intensity grading (None, Mild, Moderate, Severe, Very severe) |
| The soft tissues covering the mesial and distal apices of the tooth from the buccal side | After root canal filling | 0.5 W<br>980-nm diode laser | Mean ± SD VAS score at 4 h/8 h/12 h/24 h/48 h/72 h/7 days after the single visit | |
| The gingiva on the buccal and lingual aspects, corresponded to the root apex | After root canal filling | 0.1 W<br>808 nm | Mean ± SD VAS score at 6 h/12 h/24 h after the single visit | 6 h/12 h/24 h VRS pain intensity grading (None, Mild, Moderate, Severe) |
| On buccal of mesial and distal mucosa overlying apices of the target tooth | After root canal filling | 100 mW<br>808 nm | Mean ± SD VAS score at 4 h/8 h/24 h/48 h after the single visit | |
| On buccal and lingual of mesial and distal mucosa overlying apices of the target tooth | After root canal filling | 100 mW<br>808 nm | Mean ± SD VAS score at 4 h/8 h/24 h/48 h after the single visit | |
| The peri-apex out of the canal | After root canal medication | 100 mW<br>660 nm | Mean ± SD VAS score at 7 days/14 days after the first visit | |

(Continues)

**TABLE 1** (Continued)

| | Population character | | Character of RCT | |
|---|---|---|---|---|
| **Author, year** | **Number and age (E vs C)** | **Diagnosis** | **Type of RCT** | **Tooth type** |
| Nabi (2018) | 30 vs 30 age (range): 18–65 | a. Irreversible pulpitis and vital pulp<br>b. Symptomatic | Single-visit RCT | Single-rooted and single-canal teeth |
| Guimarães et al. (2021) | 35 vs 35 age (mean): 41.9 vs 41.0 | a. Necrotic pulps and asymptomatic apical periodontitis<br>b. Asymptomatic | Single-visit RCT | Permanent single-rooted teeth |
| Tunc et al. (2021) | 17 vs 17 (vital teeth) 17 vs 17 (none-vital teeth) age(range): 18–50 | a. Symptomatic irreversible pulpitis and asymptomatic necrotic pulps<br>b. With no periapical inflammation | Single-visit RCT | Permanent single-rooted teeth |
| | 17 vs 17 (vital teeth) 17 vs 17 (none-vital teeth) age(range): 18–50 | a. Symptomatic irreversible pulpitis and asymptomatic necrotic pulps<br>b. with no periapical inflammation | Single-visit RCT | Permanent single-rooted teeth |
| Kaplan (2022) | 20 vs 20 age (range): 18–65 | a. Apical periodontitis<br>b. Symptomatic | Two-visits RCR | Mandibular molar teeth |
| Vilas-Boas et al. (2021) | 33 vs 32 age (mean):44.9 vs 47.5 | a. Apical periodontitis<br>b. Symptomatic | Two visits RCT | Posterior Teeth |
| Yoshinari et al. (2019) | 10 vs 10 (self-control) age (range): 21–77 | a. Apical periodontitis<br>b. Asymptomatic | Single-visit RCT | Uniradicular teeth |
| Alves-Silva et al. (2022) | 30 vs 30 age(range): 18–62 | a. Pulp necrosis and periapical lesions<br>b. Asymptomatic | Single-visit RCT | Permanent single-rooted teeth |
| Coelho et al. (2019) | 30 vs 30 age (mean): 46.7 vs 47.0 | a. Necrotic pulps<br>b. Asymptomatic | Single-visit RCT | Permanent single-rooted teeth |
| Arslan et al. (2018) | 13 vs 13 age (mean): 24 vs 28.1 | a. Apical periodontitis<br>b. Symptomatic | Single-visit RCT | Mandibular molar teeth |
| | 13 vs 13 age (mean): 27 vs 28.1 | a. Apical periodontitis<br>b. Symptomatic | Single-visit RCT | Mandibular molar teeth |
| Doğanay Yıldız & Arslan (2018) | 13 vs 13 age (range): 18–65 | a. Apical periodontitis<br>b. Symptomatic | Single-visit RCT | Mandibular molar teeth |

Abbreviations: C, control group; d, day; E, experimental group; EDTA, ethylene diamine tetraacetie acid; Er:YAG, erbium: yttrium-aluminium-garnet; h, hour; LAI, laser-activated irrigation; LLLT, low-level laser therapy; NA, not available; PDT, photodynamic therapy; RCR, root canal retreatment; RCT, root canal treatment; SD, standard deviation; VAS, visual analogue scale; W, watt.

| Character of laser adjuvant therapy | | | Outcomes | |
|---|---|---|---|---|
| Laser exposure position and intracanal media | Laser exposure time window | Output and type of laser | Pain assessment by 10-point VAS (E vs C) | Additional pain assessment |
| The periapical region of the teeth both bucally as well as lingually | After root canal filling | 12–16 mW<br>905 nm | Mean VAS score and *p* value at 4 h/8 h/12 h/24 h/48 h after the single visit | |
| PDT: methylene blue solution and irradiated inside the root canal with a 55-mm optical fibre<br>LLLT: in the buccal and palatal/lingual gingiva located in the periapical region | After the root canal filling | PDT: 100 mW<br>LLLT:100 mW<br>PDT: 660 ± 10 nm<br>LLLT: 808 ± 10 nm<br>(PDT + LLLT) | Mean ± SD VAS score at 1–7 days/14 days/30 days after the single visit | day 1–day 7/day 14/day 30 VAS pain intensity grading (None, Mild, Moderate, Severe) |
| A 200-μm fibre tip into canal | Disinfection after root canal irrigation | 1 W<br>1064-nm Nd:YAG | (symptomatic vital teeth) Mean ± SD VAS score at 12 h/24 h/48 h/72 h after the single visit (asymptomatic none vital teeth) Mean ± SD VAS score at 12 h/24 h/48 h/72 h after the single visit | |
| 200-μm fibre tip into canal | Disinfection after root canal irrigation | 1 W<br>940-nm diode laser | (symptomatic vital teeth) Mean ± SD VAS score at 12 h/24 h/48 h/72 h after the single visit (asymptomatic none vital teeth) Mean ± SD VAS score at 12 h/24 h/48 h/72 h after the single visit | |
| A 200-μm fibre tip into canal | Disinfection after root canal irrigation | 1.2 W pulsed mode<br>980-nm diode laser | Mean ± SD VAS score at 8 h/24 h/48 h/72 h after the first visit | |
| PDT: methylene blue into the canal | Disinfection after root canal irrigation and medication | 100 mW<br>660 nm laser | Median (range) VAS score at 24 h/72 h/7 days after the single first visit | 24 h/72 h/7 day VAS pain intensity grading (None, Mild, Moderate, Severe) |
| PDT: Chimiolux 5 into the canal | Disinfection after root canal irrigation | 100 mW/cm$^2$<br>660 nm laser | Mean ± SD VAS score at 6 h/12 h/24 h/36 h/48 h/72 h after the single visit | |
| PDT: methylene blue into the canal | Disinfection after root canal irrigation | 100 mW | Median (range) VAS score at 8 h/12 h/24 h/48 h/72 h/7 d after the single visit single | 8 h/12 h/24 h/48 h/72 h/7 days VAS pain intensity grading (None, Mild, Moderate, Severe) |
| PDT: methylene blue into the canal | Disinfection after root canal irrigation | 100 mW | Mean ± SD VAS score at 24 h/72 h/7 days after the single visit | 24 h/72 h/7 days VAS pain intensity grading (None, Mild, Moderate, Severe) |
| A 200 μm optical tip intracanal | Disinfection after root canal irrigation | 2 W<br>970 ± 15 nm diode laser | Mean ± SD VAS score at 7 days after the single visit | |
| 200-μm optical fibre on the tissue around the apex of the root | After root canal filling | 0.5 W<br>970 ± 15 nm diode laser | Mean ± SD VAS score at 7 days after the single visit | |
| 200-μm optical fibre on the tissue around the apex of the root | After root canal filling | 0.5 W<br>970 ± 15-nm diode laser | Mean ± SD VAS score at 1 days/3 days/5 days/7 days after the single visit | |

et al., 2019; Guimarães et al., 2021; Kaplan et al., 2021; Lopes et al., 2019; Morsy et al., 2018; Vilas-Boas et al., 2021) enrolled 422 patients with dichotomous outcomes of pain prevalence. Figure 1 presents a flowchart of the literature search.

## Baseline characters

All studies were parallel randomized clinical trials conducted between 2011 and 2023. Twelve studies analysed the PEP management of LLLT, seven studies analysed the diode laser PEP reduction effect and five studies analysed the relationship between photodynamic therapy (PDT) and PEP management. Detailed information on the population characteristics (number, age and initial diagnosis), treatment characteristics (RCT and laser adjuvant therapy characteristics) and outcomes are presented in Table 1. Funding for each study is reported in Table S1.

## Effect of LLLT on PEP reduction

In the analysis of PEP intensity mitigation, data regarding the mean ± SD at 24 and 48 h were extracted from a total of eight studies (Arslan et al., 2017; Asnaashari et al., 2011; Doğanay Yıldız & Arslan, 2018; Fazlyab et al., 2021; Ismail et al., 2023; Lopes et al., 2019; Nabi et al., 2018; Naseri et al., 2020) and SD in one studies (Asnaashari et al., 2011) was assessed from *p*-values between groups and mean using the Finding Standard Deviations approach described by Cochrane Handbook. LLLT was significantly correlated with PEP reduction in patients receiving endodontic treatment in the 24 h group (Figure 2a) (pooled SMD = −0.86 (95%CI: −1.16 to 0.55)) by random effect model ($I^2 = 60\%$) and 48 h group (pooled SMD = −0.64 (95%CI: −0.84 to 0.43)) by common effect model ($I^2 = 32\%$) (Figure 2b).

We performed a leave-one-out influence analysis for the 24 h group to explain the significant heterogeneity ($I^2 = 60\%$, $p < .01$) observed in the 24-h group, a leave-one-out sensitivity analysis was conducted. It was found that the study by (Ismail et al., 2023) was the primary source of heterogeneity. After its exclusion, the pooled SMD for the VAS was −0.72 (95% CI: −0.94, −0.50), with no heterogeneity ($I^2 = 0\%$), suggesting a more pronounced effect of LLLT when accounting for study-specific variability (Figure S1).

The prevalence of PEP was also reported in two studies (Asnaashari et al., 2017; Lopes et al., 2019). However, no significant correlation was found between PEP reduction and LLLT in either the 12-h group (pooled RR = 0.89, 95% CI: 0.30, 2.70, $I^2 = 74\%$) (Figure S2a) or the 24-h group (pooled RR = 0.57, 95% CI: 0.09, 3.72) (Figure S2b).

A subgroup analysis of the PEP reduction effect of LLLT in the 24 h and 48 h groups was also conducted and no significant differences were observed between the subgroups. Detailed information can be found in the Supplementary Materials (Appendix S1. Subgroup analysis and Figures S3–S11).

## Effect of PEP reduction of diode laser therapy

For the analysis of PEP intensity mitigation, the mean ± SD at 24 h and 48 h was extracted from six studies (Genc Sen & Kaya, 2019; Ismail et al., 2023; Kaplan et al., 2021, 2022; Morsy et al., 2018; Tunc et al., 2021). Diode laser therapy was significantly associated with PEP reduction in patients undergoing endodontic treatment in the 48-h group (pooled SMD = −0.27, 95% CI: −0.50, −0.04) using a fixed effects model with $I^2 = 44\%$ (Figure 3a). However, no significant correlation was observed in the 24-h group using a random effects model (pooled SMD = −0.46, 95% CI: −0.95, 0.02) with an $I^2$ of 75% (Figure 3b).

A leave-one-out sensitivity analysis was conducted to address the significant heterogeneity ($I^2 = 75\%$, $p < 0.01$) observed in the 24-h group. The study by (Morsy et al., 2018) was identified as the main source of heterogeneity. Notably, after excluding this study, the pooled results (SMD = −0.34, 95% CI: −0.57, −0.12, $I^2 = 38\%$) indicated a significant association between diode laser therapy and PEP reduction in the 24-h group, which may provide a more accurate reflection of the treatment effect (Figure S12).

The prevalence of PEP was extracted in two studies (Kaplan et al., 2021; Morsy et al., 2018). The pooled results indicated a significant correlation between diode laser therapy and a reduction in PEP prevalence in the 24-h group (pooled RR = 0.17, 95% CI: 0.08, 0.38, $I^2 = 24\%$) (Figure S13a) but not in the 48-h group (RR = 0.19, 95% CI: 0.02, 1.64) (Figure S13b).

Subgroup analyses of the PEP reduction effect of diode laser therapy on 24- and 48-h groups were also conducted and no significant differences were observed between the subgroups. Detailed information is presented in the Supplementary Material (Appendix S1. Subgroup analysis and Figures S14–S22).

## Effect of PEP reduction of PDT

To explore the impact of PDT on PEP intensity reduction, data on the mean ± SD at 24 h was collected from two studies (Coelho et al., 2019; Yoshinari et al., 2019).

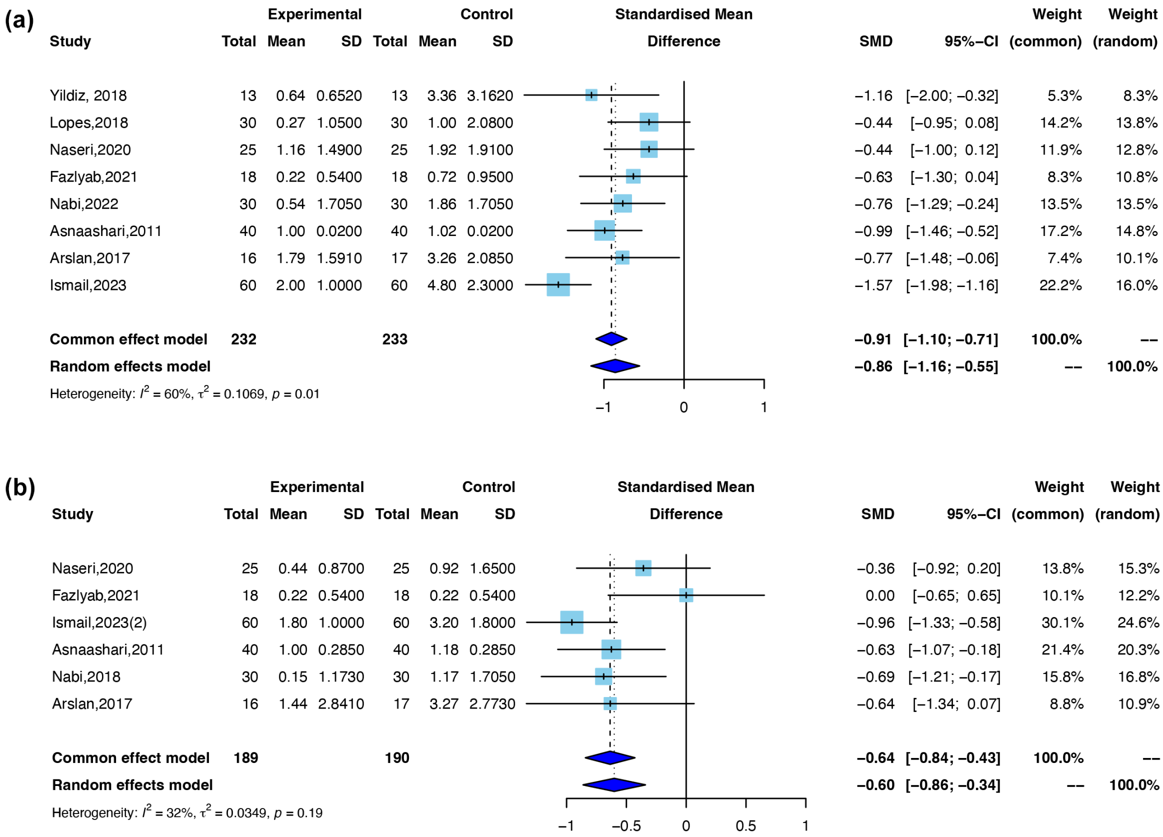


**FIGURE 2** Forest plot of the effect of postoperative endodontic pain (PEP) reduction of low-level laser therapy (LLLT) on different time periods. (a) 24 h group; (b) 48 h group.

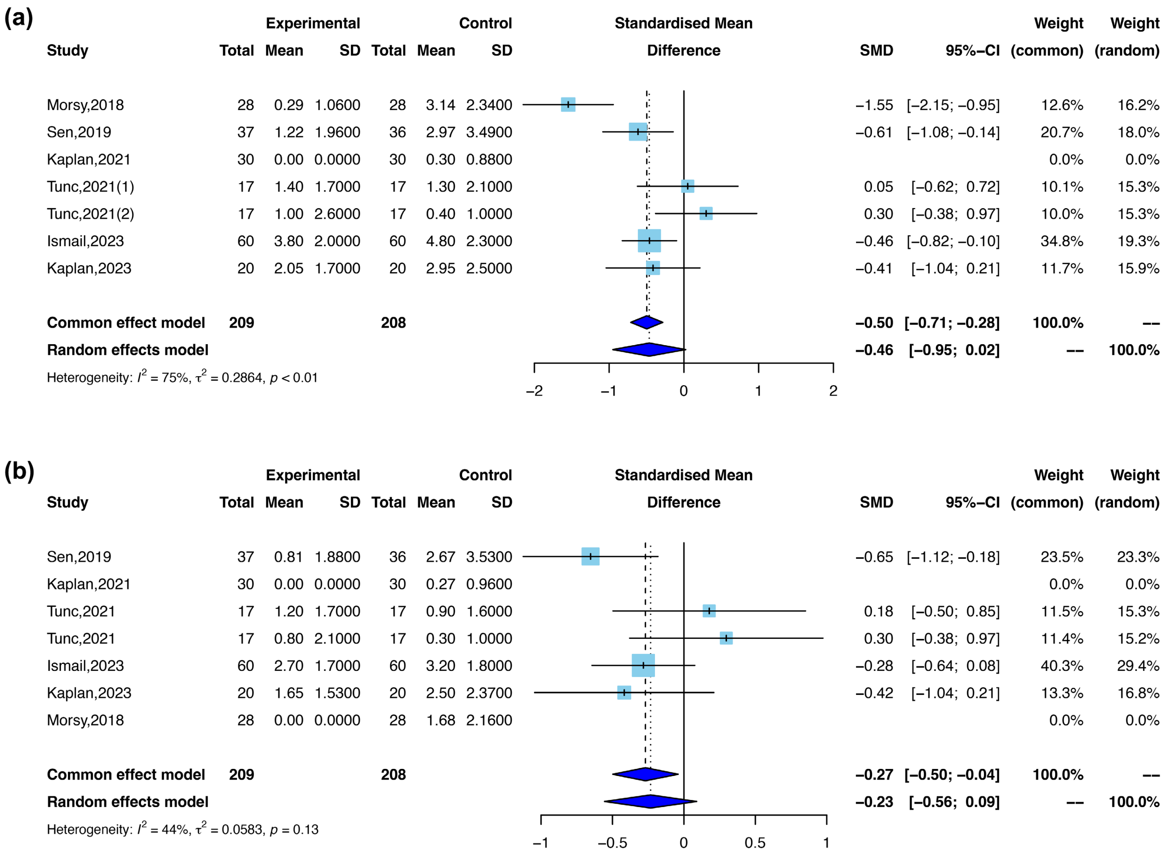


**FIGURE 3** Forest plot of the effect of PEP reduction of Diode laser therapy on different time periods. (a) 24 h group; (b) 48 h group.

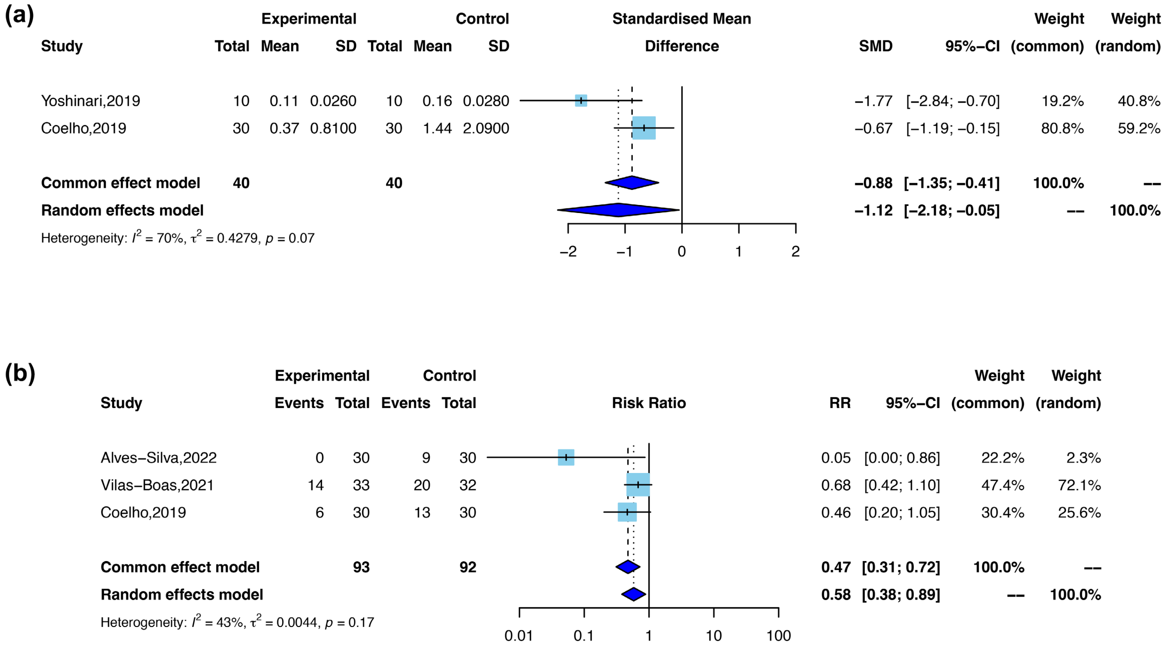


**FIGURE 4** Forest plot of the effect of PEP reduction of PDT. (a) intensity reduction in 24 h; (b) pain prevalence reduction in 24 h.

PDT was found to be significantly correlated with PEP reduction in the 24-h group (pooled SMD = −1.12, 95% CI: −2.18, −0.05) using a random-effect model ($I^2$ = 70%) (Figure 4a).

Postoperative endodontic pain prevalence was obtained from three studies (Alves-Silva et al., 2022; Coelho et al., 2019; Vilas-Boas et al., 2021) and indicated a significant correlation between PDT and reduced PEP prevalence in the 24-h group (pooled RR = 0.47, 95% CI: 0.31, 0.72, $I^2$ = 43%; Figure 4b).

## Risk of bias assessment

The 'risk of bias' assessment tool was used for quality evaluation (Figure 5). Of the 22 included studies, 7 studies had a low risk of bias (Genc Sen & Kaya, 2019; Guimarães et al., 2021; Ismail et al., 2023; Lopes et al., 2019; Morsy et al., 2018; Naseri et al., 2020; Shah et al., 2021), 10 studies were assessed to have a moderate risk of bias (Alves-Silva et al., 2022; Arslan et al., 2018; Asnaashari et al., 2011, 2017; Coelho et al., 2019; Doğanay Yıldız et al., 2019; Fazlyab et al., 2021; Nabi et al., 2018; Vilas-Boas et al., 2021; Yoshinari et al., 2019) and 5 studies had a high risk of bias (Arslan et al., 2017; Dagher et al., 2019; Kaplan et al., 2021, 2022; Yoshinari et al., 2019). All 22 included studies were randomized, and 16 studies used the Randomizer web program (www.randomizer.org), Sealed Envelope method or additional feasible methods. The remaining six studies did not provide a detailed description of the randomization methods (Arslan et al., 2018; Asnaashari et al., 2011, 2017; Nabi et al., 2018; Vilas-Boas et al., 2021; Yoshinari et al., 2019). Of the included studies, 11 studies stated the allocation concealment method (Alves-Silva et al., 2022; Arslan et al., 2018; Asnaashari et al., 2011, 2017; Doğanay Yıldız et al., 2019; Fazlyab et al., 2021; Nabi et al., 2018; Tunc et al., 2021; Vilas-Boas et al., 2021; Yoshinari et al., 2019), 14 studies mentioned blinding of patients and 4 studies with moderate risk of bias did not provide specific details about their blinding procedures (Asnaashari et al., 2011; Doğanay Yıldız et al., 2019; Nabi et al., 2018; Vilas-Boas et al., 2021). Furthermore, four studies without fake laser control were considered to have a high risk of bias as a result of the potential destruction of patient blinding (Dagher et al., 2019; Kaplan et al., 2021, 2022; Tunc et al., 2021). Only one study, which did not provide details of predetermined outcome metrics, was considered at moderate risk of bias (Arslan et al., 2018). Additionally, seven studies exhibited moderate bias from other sources due to missing information about the operators or endodontists performing the endodontic therapy, potentially leading to interpersonal variability (Asnaashari et al., 2011, 2017; Coelho et al., 2019; Doğanay Yıldız et al., 2019; Nabi et al., 2018; Vilas-Boas et al., 2021; Yoshinari et al., 2019). Notably, none of these included studies displayed bias from incomplete outcome data.

## Publication bias assessment

No publication bias was observed based on Egger's test for the LLLT group ($p$ = .2989 for 24 h in Figure 6a and

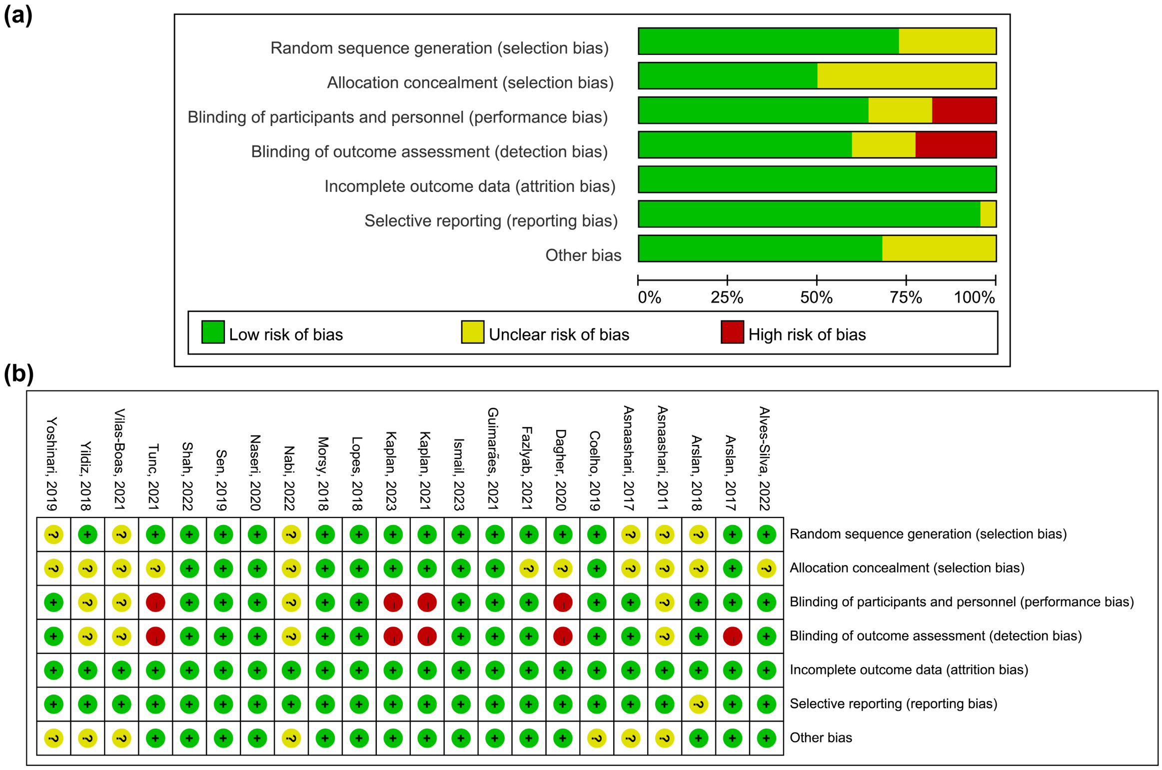


**FIGURE 5** Risk of bias evaluated by the Cochrane risk of bias assessment tool. (a) risk of bias graph; (b) risk of bias summary.

$p=.0775$ for 48 h in Figure 6b) and the diode laser therapy group ($p=.7510$ for 24 h in Figure 6c and $p=.3715$ for 48 h in Figure 6d). A symmetric funnel plot was observed in both the LLLT and diode laser therapy groups (Figure 6).

## DISCUSSION

This study reported a reduction in PEP intensity in the LLLT, diode laser therapy and PDT groups and a reduction in the incidence of PEP in the PDT group. As the first meta-analysis to assess laser adjuvant therapy for PEP management, this study included the most extensive list of laser adjuvant therapies, including LLLT, diode laser therapy and PDT as interventions and treated VAS pain level and PEP incidence rate as outcomes. The inclusion of a wide array of laser adjunctive treatments provides a comprehensive overview of the existing clinical applications. A meticulous evaluation was conducted to assess the quality of the 22 eligible studies, which provided credibility for data synthesis. With rigorous overall subgroup and sensitivity analyses of different laser types, LLLT, diode laser therapy and PDT were found to be efficacious in diminishing PEP intensity across a 24- to 48-h window post-treatment. PDT can be distinguished by the significant attenuation of the incidence of PEP.

However, the presence of methodological bias in some studies introduces uncertainties that may affect the interpretation of our results. First, studies with nonpositive SD values in the laser exposure and control groups were excluded. SD = 0 and mean = 0 mostly appeared in the experimental group (Coelho et al., 2019; Kaplan et al., 2022; Morsy et al., 2018), possibly due to the clinical benefits of laser adjuvant therapy for pain management. Second, the leave-one-out approach failed to determine the source of heterogeneity. Third, the PEP scores evaluated using the VAS may have lacked normality. We performed normality tests on studies with median and range of VAS score data and found that the results did not follow a normal distribution (Alves-Silva et al., 2022; Vilas-Boas et al., 2021). Furthermore, they were not included in the meta-analysis. Additionally, four studies without fake laser controls were considered to have a high risk of bias owing to the possibility of blinding the patients.

Alonaizan and other researchers (Alonaizan & AlFawaz, 2019; Anagnostaki et al., 2020; Chen et al., 2019) conducted systematic reviews to summarize the evidence of the effectiveness of laser adjuvant therapy for pain management after endodontic treatment. However, owing to data limitations, they failed to conduct a quantitative statistical analysis, and it remains debatable whether phototherapy reduces PEP after RCT.

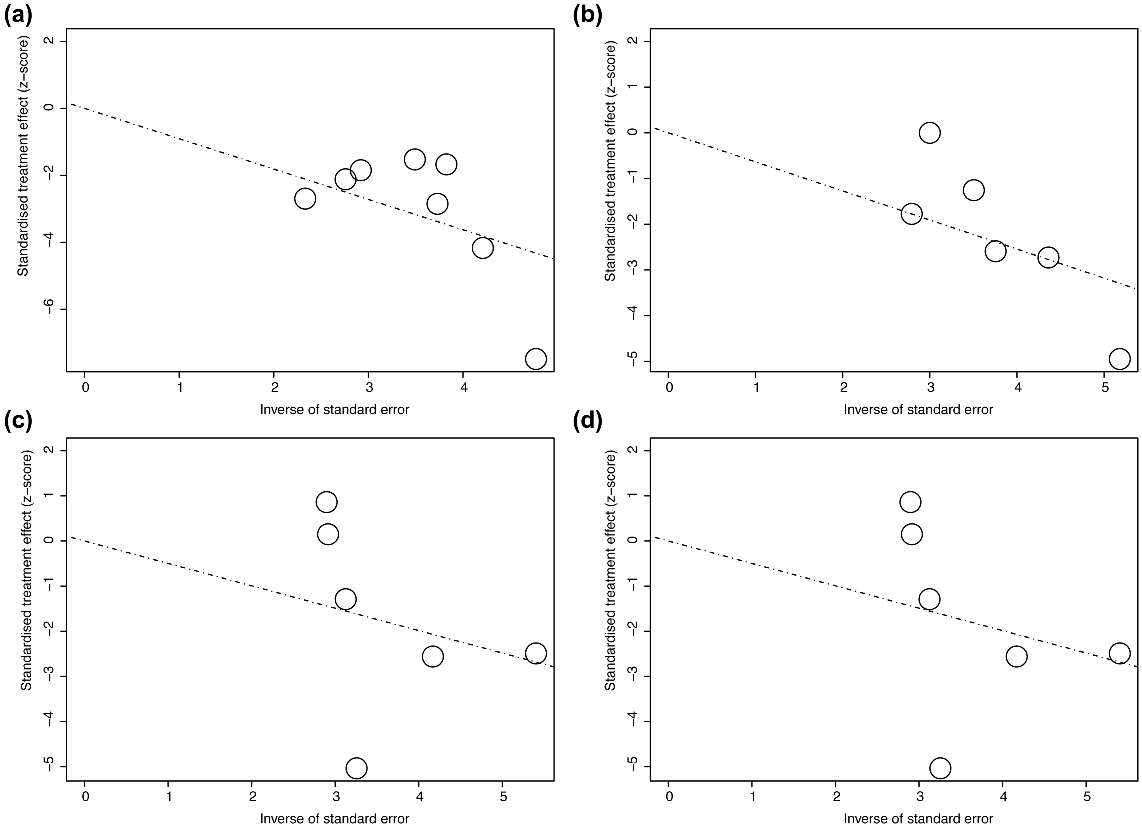


**FIGURE 6** Funnel plot of publication bias by Egger's test. (a) 24 h group for LLLT; (b) 48 h group for LLLT; (c) 24 h for Diode laser therapy; (d) 48 h for diode laser therapy.

We juxtapose our findings against the backdrop of the existing literature, noting congruence with prior research that ascribes PEP reduction to the intracanal antibacterial capabilities and extra-canal photobiomodulation of laser therapy. Bacteria are the most common cause of PEP (Alonaizan & AlFawaz, 2019; Chen et al., 2019). Intracanally, the optical fibre sends the laser to the working length, and the penetration of the laser allows it to pass through the dentin and reach the periapical tissue. Diode lasers, characterized by higher output power than LLLT, demonstrated antibacterial effects by direct thermal action on pigmented bacterial membranes of pulp pathogenic bacteria or by producing a short-term temperature increase in the bacterial microenvironment (da Costa Ribeiro et al., 2007; Gutknecht et al., 2000; López-Jiménez et al., 2015), whereas in antibacterial PDT the photosensitizer is activated by laser irradiation to produce reactive oxygen species to perform the role of anti-bacteria (Franco et al., 2023). Reducing the bacterial load can reduce bacterial excretion and retention, thereby decreasing pain perception. Extracanal analgesics can be attributed to photobiomodulation in LLLT and PDT, which can be summarized at the molecular, cellular and cyclic levels. During molecular events, laser irradiation can stabilize cyclooxygenase-2 mRNA levels, thus reducing prostaglandin release, inhibiting cyclooxygenase-2, and exerting anti-inflammatory properties while lowering the release of pain mediators such as histamine, and acetylcholine, serotonin, H+ and K+, thereby reducing pain (Ismail et al., 2023; Nabi et al., 2018). At the cellular level, the laser can regulate the inflammatory process, reduce inflammatory cell infiltration and remove pain-causing substances. In addition, laser therapy can reduce the permeability of the cell membrane to Na+ and K+, cause hyperpolarization of neurones and increase the pain threshold (Arslan et al., 2017). At the circular level, laser irradiation can increase blood flow and lymphatic drainage, thus accelerating the excretion of painful substances and reducing tissue oedema, leading to pain relief (Nabi et al., 2018). Furthermore, laser irradiation promotes the expression of genes associated with human cell healing, thereby promoting cell proliferation and neovascularization (Enwemeka et al., 2004). In addition, Chow et al. (2011) suggested that the laser absorbed by nociceptor (energy intensity above 300 mW/cm$^2$) can inhibit the conduction velocity of A$^\delta$ and C pain fibres, thereby reducing the amplitude of compound action potential and inhibiting neurogenic inflammation.

Medications such as ibuprofen are still the most routine option for PEP management. However, interestingly, two studies indicate that LLLT and diode laser therapy can significantly reduce pain within the first 24 h post-treatment (6 h: SMD = −4.82 (95%CI: −5.77, −3.88), 12 h: SMD = −4.62 (95%CI: −5.54, −3.71), 24 h: SMD = −1.12 (95%CI: −1.63, −0.61)), with effect sizes showing superior or comparable outcomes to those of ibuprofen (Nabi et al., 2018; Nunes et al., 2020). However, considering the low quality of these two studies, classified as moderate- and high-risk, respectively, and the scarcity of related comparative studies, the conclusions require further scrutiny. A study with a low risk suggests that the use of ibuprofen significantly reduces the intensity of PEP, with a mean reduction in VAS scores of 4.2 compared to the control group at 6 h (Mehrvarzfar et al., 2012), which is superior to the current laser adjunctive therapy, where the maximum mean reduction in VAS scores was 2.85. However, it cannot be denied that laser adjuvant therapies may provide an effective method for postoperative pain management with minimal side effects, particularly for patients with special conditions such as hepatic and renal metabolic dysfunction, allergies to NSAIDs, and pregnant women, thereby enhancing the patient's therapeutic experience.

Due to the limited number of studies on the incidence of pain, we believe that more studies should focus on the incidence of pain to confirm whether LLLT can reduce the incidence of PEP. For LLLT, no significant differences existed among the subgroups. Furthermore, direct comparative studies investigating the reduction of PEP with different types of laser adjuvant therapies are lacking. Future randomized clinical trials may provide answers to these questions.

## CONCLUSION

A clear PEP intensity reduction effect in the LLLT, diode laser therapy and PDT groups, as well as a PEP incidence reduction effect in the PDT group, was observed in the meta-analysis. Clinical evidence strongly supports laser adjuvant therapy as an effective and virtually side-effect-free treatment for postoperative pain management. This may encourage its application in endodontic treatment for patients, especially those with special conditions, and improve their therapeutic experience. However, the differences in PEP management effects between laser therapies are unknown, and no significant differences were observed among the subgroups. Therefore, there is still a need for more, larger and well-conducted randomized clinical trials evaluating the PEP level or incidence rate reduction effect of different laser adjuvant therapies to further identify the best combination of laser treatment and endodontic treatment for PEP relief.

## AUTHOR CONTRIBUTIONS

J. Chen and Z. Luo: conception and design, acquisition of data, analysis and interpretation of data, statistical analyses and drafting and revising of the manuscript. Y. He carried out the data extraction and quality assessment, analysed the data and drafted the manuscript. Y. Li: acquisition of data, analysis and interpretation of data and critical revision of the manuscript. H. Wu, L. Shen, L. He, L. Cheng and X. Zhou analysed and interpreted the data and critically revised the manuscript. All the authors have read and approved the manuscript.

## FUNDING INFORMATION

This work was supported by the Research Funding from West China School/Hospital of Stomatology Sichuan University, No. RCDWJS2022-5 (to JC).

## CONFLICT OF INTEREST STATEMENT

The authors declare no potential conflicts of interest.

## DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in Appendix S1 of this article.

## ETHICAL APPROVAL

This research did not require ethical approval since it did not involve any human and animal subjects.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Luo, Z., He, Y., Wu, H., Li, Y., Shen, L., Cheng, L. et al. (2024) Efficacy of laser adjuvant therapy in the management of post-operative endodontic pain: A systematic review and meta-analysis. *International Endodontic Journal*, 57, 1700–1716. Available from: https://doi.org/10.1111/iej.14140