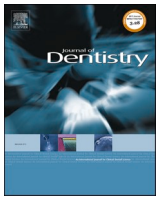
Journal of Dentistry 144 (2024) 104928

Contents lists available at ScienceDirect

Journal of Dentistry

journal homepage: www.elsevier.com/locate/jdent



Review article

The influence of laser-activated irrigation on post-operative pain following root canal treatment: A systematic review

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ARTICLE INFO

Keywords:
Post-endodontic pain
Laser-activated irrigation
PIPS
SWEEPS
Diode laser
Systematic review

ABSTRACT

Objectives: Synthesise evidence on post-endodontic pain (PEP) in adult teeth undergoing primary root canal treatment with the adjunctive use of laser-activated irrigation (LAI) as compared with conventional needle irrigation (CNI) during the first post-operative week.
Data: An electronic search was performed; no language constraints or restriction on the year of publication were applied.
Sources: Medline, Scopus, Cochrane and PubMed on 04 June 2023
Study selection: Randomised clinical trials (RaCTs) that evaluated PEP after LAI of endodontic irrgants were included. Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were used. PEP was analysed at various time intervals until 1 week after treatment, related to the type of LAI used and the need for analgesia.
Reults: Of the 793 articles identified through the electronic database search, 6 RaCTs were included. Qualitative review was favoured over meta-analysis due to substantial methodological heterogeneity between studies. Five studies were at high risk for bias determined by the Cochrane Risk-of-Bias 2 tool. Diode LAI demonstrated superior efficacy to needle irrigation in reducing pain 6–48 h post-treatment. The impact of LAI by photon-induced photoacoustic streaming (PIPS) was unclear and no difference was observed between PIPS and needle irrigation. However, PIPS mitigated PEP better than manual dynamic activation, sonic and ultrasonic activation. There was no difference in analgesia intake between LAI and needle irrigation groups.
Conclusions: LAI may help reduce PEP in the first 48 h. Methodological standardisation of future RaCTs on LAI would be beneficial in allowing a more accurate review with the possibility of quantitative synthesis.
Clinical significance: This unique synthesis used stringent criteria to reduce confounding factors and provided valuable evidence regarding PEP with different types of LAI. It helps clinicians choose an appropriate LAI technique as compared with CNI and predicts a time frame for reducing PEP.

1. Introduction

Elimination of the microbial bio-burden from the root canal system is widely considered to be one of the most important steps in determining the success of root canal treatment (RCT). The root canal system often comprises complex morphological features, including isthmi, accessory canals, fins, deltas, C-shaped canals and anastomoses [1]. Mechanical debridement is therefore not effective in the complete removal of bacteria and necrotic tissue and approximately 35 % of the canal surface area remains unaltered following instrumentation [2]. Therefore, irrigants are essential in combination with mechanical instrumentation to achieve more complete microbial reduction within the root canal system, hence mitigating the risk of persistent post-treatment periradicular disease. Sodium hypochlorite (NaOCl) is the most commonly used irrigant in endodontics due to its antimicrobial properties and ability to dissolve organic tissue [3].

Experimental evidence indicates that even after mechanical shaping and conventional passive needle-based irrigation, a significant proportion of the root canal surface area remains untouched by irrigants [4]. Further methods are therefore required to enhance the penetration of irrigants into the root canal system, allowing them to reach previously inaccessible regions. Several methods of activating endodontic irrigants are available to enhance root canal disinfection and smear layer removal. Among the most well documented are manual dynamic

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https://doi.org/10.1016/j.jdent.2024.104928
Received 15 January 2024; Received in revised form 29 February 2024; Accepted 5 March 2024
Available online 13 March 2024

activation (MDA), sonic activation, passive ultrasonic irrigation (PUI) and laser-activated irrigation (LAI) [5].

Light amplification by stimulated emission of radiation (laser), has demonstrated numerous applications in endodontics, most notably enhancing root canal debridement and disinfection. A number of laser types are currently available for the purpose of LAI, most commonly Erbium-doped: Yttrium Aluminium Garnet (Er:YAG), Neodymium-doped: Yttrium Aluminium Garnet (Nd:YAG), and diode lasers [6]. The operative wavelength of Er:YAG lasers (2940 nm) coincides with the absorption spectrum of water, thus interacting with the aqueous irrigant to generate cavitation bubbles that subsequently implode at high velocity to produce large-amplitude shockwaves, a phenomenon known as photon-induced photoacoustic streaming (PIPS) [7,8].

Further, carefully timed consecutive energy pulses can cause cavitation bubbles to collapse faster, thereby increasing the efficacy of the PIPS technique. This is known as shockwave-enhanced emission photoacoustic streaming (SWEEPS). The result of PIPS and SWEEPS is increased irrigant flow rate and generation of physical forces against the canal walls capable of removing the smear layer, even in conservatively prepared canals [9,10].

Nd:YAG is a solid-state laser with a wavelength of 1064 nm which is well-absorbed by pigmented tissues such as melanin and haemoglobin [11]. Such lasers have been used to activate endodontic irrigants clinically [12] and demonstrate bactericidal effects by local absorption in bacteria-specific chromophores or via photothermal effects [13,14]. The diode lasers are traditionally used for soft tissue ablation and have limited hard tissue absorption [15]. This is advantageous during root canal treatment where the economical hand-held laser devices have been used at near-infrared wavelengths (810 nm, 830 nm, 940 nm and 980 nm) to produce cavitation bubbles in the endodontic irrigants which enhances disinfection [16–18].

Post-endodontic pain (PEP) is a relatively common occurrence, with reported incidence between 3- 58 % [19]. A systematic review [20] found that 40 % of patients experienced pain within the first 24 h after endodontic treatment. The likely cause is periapical inflammation due to chemo-mechanical disinfection and microbial irritants, which usually subsides over time [21]. PEP is an important outcome used to determine patients' quality of life after RCT, and efforts should be made to ensure patient comfort wherever possible.

The aim of this systematic review was to evaluate and collate existing evidence relating to the effect of LAI during primary RCT on pain reported by patients at various time intervals up to 7 days post-operatively.

2. Materials & methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic reviews and Meta Analysis (PRISMA) [22] and the protocol was registered with PROSPERO (CRD42023437185).

The **PICOTS** question for this study was:

P (population): Human adult patients undergoing primary RCT of mature permanent teeth which have been diagnosed with any of the following conditions or combinations thereof, as per the American Association of Endodontics criteria: irreversible pulpitis, pulpal necrosis, symptomatic or asymptomatic apical periodontitis, condensing osteitis and chronic apical abscess.
I (intervention): RCT with adjunctive LAI (including PIPS, SWEEPS, Nd:YAG laser, Er:YAG laser and diode LAI).
C (control): RCT utilising conventional needle irrigation (CNI).
O (outcome): Self-assessed intensity of pain reported using a visual analogue scale (VAS) or numerical rating scale (NRS) following RCT
T (time): A series of time intervals from 6, 8, 12, 24, 48, 72 h, and 7 days post-operatively.
S (study): Randomised clinical trials (RaCT).

The following research question was subsequently generated:

In adult patients undergoing primary RCT on mature permanent teeth, does the adjunctive use of LAI influence the intensity of PEP reported at incremental time periods from 6 h up to 7 days when compared with CNI?

This review also aimed to secondarily compare the effects of different laser types on PEP and assess their effects on post-operative analgesia intake.

2.1. Information sources and search strategy

The search was conducted on 04 June 2023 by two reviewers (AM and AD) via an electronic search of the following databases: Medline via Ovid, Scopus, Cochrane Library and PubMed. No date restrictions were applied. The search carried out on Medline via Ovid was as follows:

Endodontics OR endodont*.tw OR "root canal treatment" OR "root canal therapy".tw OR "root canal".tw
AND
sterilis*.tw OR disinfect*.tw OR adjunct*.tw OR irrigat*.tw OR irrigant*.tw OR activat*.tw OR lasers OR "PIPS" OR "photon-induced photoacoustic streaming".tw OR SWEEPS.tw OR "shockwave-enhanced emission photoacoustic streaming".tw OR "Nd:YAG".tw OR "neodymium-doped yttrium aluminium garnet".tw OR "Er:YAG".tw OR "erbium-doped yttrium aluminium garnet".tw OR diode.tw OR phototherapy.tw OR photodynamic.tw
AND
Pain.tw OR discomfort.tw OR "post-operative".tw
AND
Randomized.tw OR randomised.tw

The search was adapted for the remaining databases (Scopus, Cochrane Library and PubMed) and was run as follows:

endodont* OR "root canal therapy" OR "root canal treatment" OR "root canal"
AND
sterilis* OR disinfect* OR adjunct* OR irrigat* OR irrigant* OR activat* OR laser* OR PIPS OR "photon induced photoacoustic streaming" OR SWEEPS OR "shockwave enhanced emission photoacoustic streaming" OR "Nd:YAG" OR "neodymium-doped yttrium aluminium garnet" OR "Er:YAG" OR "erbium-doped yttrium aluminium garnet" OR diode OR phototherapy OR photodynamic
AND
pain OR discomfort OR "post-operative"
AND
randomized OR randomised

A search of grey literature was also conducted but no relevant articles were found.

2.2. Study selection & eligibility criteria

All articles identified through the search were screened by two reviewers (AM and AD) against selection criteria, initially by title and then by abstract. The articles remaining were evaluated by full text and subsequently excluded if they did not meet the eligibility criteria. Where further information or clarification was needed, authors were contacted by email and given two weeks to provide a response. A further reminder email was sent out following the two-week deadline if the author had not responded to the initial request. Articles were excluded if the author failed to provide information or clarification.

The inclusion criteria were as follows:

1. RaCTs;
2. Permanent human teeth with completely formed root apices requiring primary RCT diagnosed with any of the following conditions or a combination thereof: irreversible pulpitis, pulpal

necrosis, symptomatic or asymptomatic apical periodontitis, condensing osteitis and chronic apical abscess.
3. Presence or absence of pre-operative pain;
4. RCT protocol between the intervention and control groups would be the same with the exception of adjunctive LAI (PIPS/ SWEEPS/ Nd:YAG/ Er:YAG/ diode LAI);
5. Irrigant activated must include NaOCl or EDTA or both;
6. Treatment completed in single or multiple visits;
7. Treatment performed under rubber dam;
8. 27-gauge needle or finer used for irrigation;
9. Follow-up time periods up to 7 days post-operatively;
10. Patient-reported pain scores on VAS or NRS;
11. Articles published in English.

The exclusion criteria were as follows:

1. Follow-up period of >7 days post operatively;
2. Cohort studies, case reports, *in vitro* and *ex vivo* studies;
3. Root canal re-treatment procedures;
4. Deciduous teeth or immature permanent teeth;
5. Use of photobiomodulation (PBM)/ low level laser therapy (LLLT);
6. Use of phototherapy/ antimicrobial photodynamic therapy (aPDT).

The screening process was undertaken independently by the two reviewers and differences were resolved by discussion.

2.3. Data extraction

Data was extracted by one author (AM) and reviewed by the second author (AD). From the articles that met the inclusion criteria, data were extracted regarding methodology [Author, year, effect size, number of participants, type of teeth, diagnoses, groups, root canal (RC) instrumentation, irrigant(s) used during preparation, final irrigation, and number of visits], laser parameters used [Author, year, laser type, wavelength, irrigant(s) activated, mode, frequency, total energy, energy per pulse, power/ average power, irradiation time, pause time, number of cycles, tip diameter and tip position] and outcome data in terms of mean or median VAS/NRS scores at different time intervals.

2.4. Quality assessment of evidence

All selected articles were subjected to critical appraisal by a single reviewer (AM) using the revised version of the Cochrane risk of bias tool for randomised trials (RoB2) [23]. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) [24] approach was to be used in the event of conducting a meta-analysis.

3. Results

3.1. Study selection

A total of 793 articles were retrieved from the search (Cochrane: 306, Medline: 98, PubMed: 194, Scopus: 195). Following electronic deduplication, 456 articles remained which were then subjected to manual deduplication, yielding 403 articles. Three-hundred-and-fifty-two articles were excluded by title, and 25 were excluded by abstract. The remaining 26 articles were screened by full text. For articles where further information or clarification was needed [25–36], the corresponding authors were contacted by email and requested to provide additional data. Further reminder emails were sent two weeks later in case the author had not responded. A total of five responses were received [30,31,33-35]. Whilst no responses were received from five authors [26-29,32], sufficient data was present in the papers to merit inclusion in this systematic review.

With this final information, a further 20 articles were excluded (Fig. 1), and the rationale for exclusion was noted (Table 1). Reasons for exclusion included protocols for unpublished articles, absence of VAS/ NRS, laser irradiation without the presence of an irrigant and the use of irrigation needles larger than 27 gauge.

3.2. Study characteristics

A total of six RaCTs met the inclusion criteria [26-29,32,33]. Data regarding study design and methodology (Table 2) and laser parameters (Table 3) were extracted. While one study included all teeth [32], the remainder focused on the posterior dentition. The pulpal diagnoses included irreversible pulpitis [26,28] and pulpal necrosis [26,27,32,33] and all studies included teeth with apical periodontitis, except one [28].

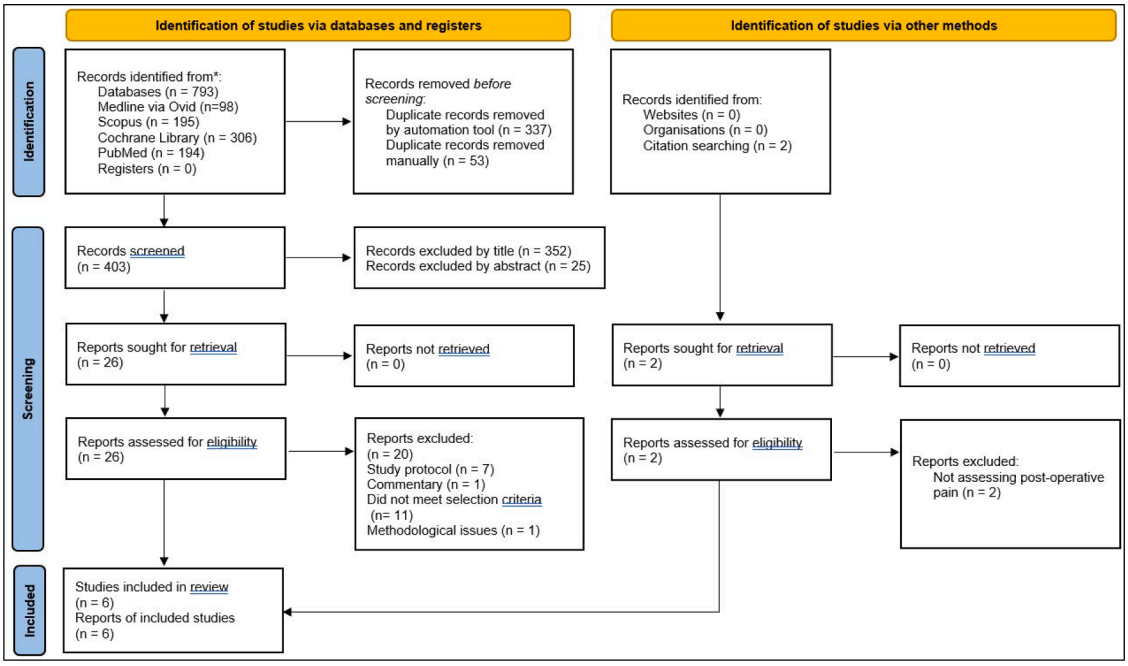

Fig. 1. PRISMA flowchart outlining the selection process for study inclusion.

Table 1
Excluded studies from the systemic reviews and meta-analysis based on full text assessment and reasons for exclusion.

Author and Year	Reason(s) for Exclusion
Koba et al. 1999a [68]	Included teeth with no pulpal pathology VAS not used Irrigant not present during laser irradiation
Koba et al. 1999b [61]	VAS not used Canals dried prior to irradiation
Karakov et al. 2017 [69]	Photodynamic therapy
Nct 2017 [70]	Protocol for unpublished article
ISRCTN 2018 [71]	Protocol for unpublished article
Morsy, Negm, Diab and Ahmed [51]	25 gauge needle used during irrigation protocol
Nct 2019a [72]	Protocol for unpublished article
Nct 2019b [73]	Protocol for unpublished article
Aggarwal and Dewan 2020 [25]	Methodology describes laser application in "wet canal", no mention of irrigant presence in the canal. Did not respond to follow-up emails.
Nct 2020a [74]	Protocol for unpublished article
Nct 2020b [75]	Protocol for unpublished article
Dedania et al. 2021 [76]	Photoactivated disinfection
Kaplan et al. 2021 [30]	Irrigant not present in root canal during laser irradiation
Moghadam et al. 2021 [34]	Irrigant not present in root canal during laser irradiation
Tunc, Yildrim and Alacam 2021 [35]	Irrigant likely not present during laser irradiation. No mention of rubber dam isolation. No mention of needle gauge. Did not respond to follow-up questions
ISRCTN [77]	Protocol for unpublished article
Kaplan et al. 2022 [31]	Irrigant not present in root canal during laser irradiation
Rao et al. 2022 [36]	Irrigant likely not present during laser irradiation. No mention of needle gauge. Did not respond to follow-up emails.
Mittal et al. 2023 [39]	Conducted VAS telephonically, therefore not a visual scale
Simpson et al. 2023 [78]	Commentary on Kaplan et al., 2022

Four studies used PIPS [26,28,32,33], two used diode laser [27,29] and only one study used SWEEPS [28]. Laser irradiation times ranged from 20 to 30 s over 2–6 cycles. The position of the laser tip varied with respect to the position within the root canal. For the diode lasers, the tip of the laser was 1–3 mm short of the working length (WL) within the root canal [27,29]. In contrast, for studies that used PIPS and SWEEPS, the laser tip was present in the coronal part of the pulp space, often within the pulp chamber only [28,32,33]. All included studies activated NaOCl except one [29]. Only two studies did not report using EDTA irrigant [27,32].

Three studies did not report the effect size [26,32,33] and three studies reported a small effect size between 0.3–0.4 [27–29].

3.3. Risk of bias in studies

Five of the six studies [26-28,32,33] were deemed at high risk of bias in measurement of the outcome due to the lack of placebo in the comparator group(s). The remaining article [29] had 'some concerns' (Fig. 2).

3.4. Results of individual studies

VAS results were extracted from each study and presented as a percentage (Table 4). All results were mean pain scores at varying time intervals post-operatively with the exception of one study which presented results as a median score [28]. Raw mean data for Mandras et al. [33] were not available in the article but were provided at request through correspondence with the author.

The study design and parameters between studies were very heterogenous and thus a qualitative review was favoured over meta-analysis. Major sources of heterogeneity included: VAS interval selection, types of teeth, types of laser, irrigants activated, baseline pathoses, number of appointments, presence or absence of pre-operative pain and other procedural discrepancies such as occlusal adjustment following treatment.

3.5. Qualitative summary

Four of the six included studies [26,27,29,33] directly compared LAI with CNI, whereas two studies [28,32] compared LAI with other methods of irrigant activation such as ultrasonically activated irrigation (UAI) and MDA. Data for LAI was nevertheless useful from the latter two studies, even though meta-analyses could not be performed with this data owing to lack of homogeneity between studies.

Of the six articles included, four [27-29,32] reported a statistically significantly lower mean VAS score in the LAI group for at least one time interval, though of these, Liapis et al. [32] reported the result as clinically irrelevant. Two studies [26,33] found no significant difference between the LAI group and the control.

Of the four studies comparing LAI with needle irrigation, two [27, 29] found VAS scores to be lower in the LAI group. Elmawallany et al. [27] concluded that VAS was lower at all time points from 6 to 48 h with the use of a diode laser. At 7 days, the difference was not considered significant. The results of the paper by Ismail et al. [29], showed a lower mean VAS score in the diode laser group at 24 and 48 h, with no significant difference between the groups at 72 h. Therefore, as compared with needle irrigation, diode LAI produced a significant reduction in pain during the early post-endodontic period (6–48 h) [27,29] (Fig. 3). Two studies detected no statistically significant difference between the PIPS protocol and CNI during any time interval in the first post-operative week [26,33] whereas none of the included studies directly compared SWEEPS with CNI.

However, when compared with ultrasonic [28,32], MDA and sonic activation [28], lesser PEP was noted with PIPS [28,32] or SWEEPS [28] in the early post-treatment period (6–48 h) which was not clinically significant in one study [32]. At seven days, there were no differences in any study, irrespective of the irrigation or irrigant activation modality. When comparing the reduction in PEP with different LAI modalities, no significant difference was reported between the groups activated with PIPS and SWEEPS [28].

With regards to analgesia, Ismail et al. [29] excluded study participants in the event of analgesia intake. Elmallawany et al. [27] discouraged analgesia intake except in the case of severe pain. One study [33] assessed analgesia intake, but did not include the data, nor analysis in the study. The remaining three [26,28,32] found no significant difference in quantity of analgesia between the LAI and comparator group (s).

4. Discussion

The complete disinfection of the root canal system has remained challenging for the dental profession and the search for newer technologies to enhance the reduction in microbial biofilm has led to the introduction of lasers for activating endodontic irrigants. LAI also carries the benefit of enhancing debris removal from the walls of the root canals. PEP has been extensively studied in endodontic literature and recent RaCTs have become available assessing PEP after LAI. This systematic review was therefore undertaken to evaluate the effect of LAI on PEP experienced by patients in the first seven days following operative intervention. It also evaluated the relationship between the type of laser used for irrigant activation and PEP, as also the intake of analgesia.

4.1. Search strategy

A detailed search using several key words and Boolean operators over multiple electronic databases was undertaken. Additionally, a supplementary search of grey literature via OpenGrey was carried out to identify potentially relevant unpublished material pertaining to the

Table 2
Study characteristics for included articles.

Author Year	Effect size	No. participants	Type of teeth	Diagnoses	Groups	Root Canal instrumentation (RCI)	Irrigants during RCI	Final irrigation	No. visits
Dagher et al. 2019	Not reported	56 (m+f)	Premolars and molars	Asymptomatic irreversible pulpitis Symptomatic irreversible pulpitis Symptomatic pulpal necrosis +/- apical periodontitis	1: Needle irrigation 2: PIPS protocol	ISO 10 C-PILOT file Reciproc R25	3 % NaOCl	10 mL 5.25 % NaOCl 5 mL 17 % EDTA Distilled water	1
Elmallawany et al. 2022	0.4	40 (m+f)	Mandibular molars	Pulp necrosis +/- apical periodontitis	1A: conventional needle 1B: Needle and diode laser 2A:Continuous ultrasonic irrigation (CUI) 2B: CUI with diode laser	ISO 10/15 K file Revo-S system	Saline, 2.5 % NaOCl	3 mL saline	1
Erkan et al. 2022	0.345	200 (m+f)	Single rooted mandibular premolars	Irreversible pulpitis	1: PIPS 2: SWEEPS 3: PUI 4: Sonic 5: MDA	ISO 10 K file Protaper Next	3 % NaOCl	3 mL 3 % NaOCl 2 mL 17 % EDTA	1
Ismail et al. 2023	0.322	180 (m)	Mandibular molars	Apical periodontitis	1: LAI 2: LLT 3: Needle irrigation	Protaper Next	2.5 % NaOCl	2 mL 17 % EDTA 3 mL saline	1
Liapis et al. 2021	Not reported	56 (m+f)	Any	Vital or necrotic (diagnosis not described) +/- radiographic apical rarefaction	1: UAI 2: LAI	Protaper Universal and Next	3 % NaOCl	2 mL 17% EDTA 3 % NaOCl	1
Mandras et al. 2020	Not reported	54 (m+f)	1st/2nd mandibular/ maxillary molars	Pulpal necrosis +/- apical periodontitis. Excluded abscesses, teeth with sinus tract drainage and cellulitis	A: Needle irrigation B: PIPS protocol	K files Protaper Next	5 % NaOCl, 10 % EDTA	Saline	2

study question. Whilst manual searching of relevant journals may have yielded more exhaustive results compared with electronic searching, this approach is time consuming and typically necessitates a team of reviewers. Consequently, a comprehensive manual search was deemed beyond the scope of this systematic review.

4.2. Inclusion and exclusion criteria

This review included RaCTs as these are widely regarded as the gold standard for study design when determining the effects of an intervention. The advantage of RaCTs includes superior internal validity due to reduced bias and control over confounding variables. Stringent inclusion criteria were applied to minimize ambiguity and the protocol was established and published *a priori* following review by one senior clinical academic. Clinical factors that may influence PEP such as the use of rubber dam to reduce microbial contamination of the root canal and the use of 27-gauge needle to adequately deliver endodontic irrigant to the root canal system were amongst the essential inclusion criteria.

In order to exclude studies that assessed laser irradiation of dry or damp canals, it was determined that laser activation of either NaOCl or EDTA, or both, must be present in the intervention group in order for the study to qualify for inclusion. This criterion was essential as the research question specifically addressed LAI, distinct from laser-assisted disinfection, which encompasses a broader array of laser applications to the root canal system. Furthermore, studies investigating the efficacy of aPDT and PBM were also excluded. The mechanism of action of aPDT involves the use of a photosensitizer which is placed inside the root canal and exposed to lasers leading to the creation of reactive oxygen species that are responsible for its antimicrobial action [37]. PBM utilises low-level laser therapy which is known to enhance biological responses by altering neural function which in turn leads to reduced pain perception [38]. While these represent important adjunctive procedures in mitigating PEP, owing to the variance in the mechanisms of action from LAI, aPDT and PBM-based studies were considered outside the scope of this review.

This review focused on the evaluation of self-reported pain outcomes, either via NRS or VAS. This choice was informed by the findings of the preliminary search, where the majority of articles assessed pain on either a visual or numerical scale. No articles were identified that utilised NRS while also satisfying the other selection criteria. Thus, only studies evaluating VAS were included in this review. One study identified through the search [39] recorded VAS telephonically, and was subsequently excluded due to the absence of a visual element- an essential aspect of a visual analogue scale.

4.3. Results

Significant heterogeneity between the articles negated the opportunity for meta-analysis. Pre-treatment diagnoses ranged from asymptomatic pulp necrosis to symptomatic irreversible pulpitis. Most articles also included teeth with apical periodontitis. The number of visits for RCT also varied, with one study [33] completing the treatment over two visits; applying calcium hydroxide to the root canals and obturating 7 days later following VAS measurements. Post-treatment occlusal reduction was performed in one study [26], which may act as a confounding factor as occlusal reduction is known to reduce PEP in teeth with irreversible pulpitis [40].

Two different types of laser were used across the selected studies; Er:YAG and diode lasers. Varying protocols were applied, with differences including tip position (coronal/apical), tip size (200–600 μm), number of cycles (2–6) and type of irrigant activated (saline/EDTA/NaOCl at varying concentrations). There appears to be no agreement in the

Table 3
Details of laser types and parameters.

Author/Year	Laser Type	Wavelength (nm)	Irrigant(s) activated	Mode	Frequency (Hz)	Total energy (J)	Energy per pulse (mJ)	Power/ average power (W)	Irradiation time (s)	Pause time (s)	No. cycles	Tip diameter (µm)	Position of tip
Dagher et al. 2019	Er:YAG (PIPS)	2940	EDTA, distilled water, 5.25 % NaOCl	Pulsed	15	9	20	0.3	30	30	6	600	9 mm into pulp chamber
Elmallawany et al. 2022	Diode	810	2.5 % NaOCl	Continuous	Not recorded	Not recorded	Not recorded	0.8	20	20	4	200	1 mm short of WL, withdrawn during activation
Erkan et al. 2022	Er:YAG (PIPS &SWEEPS)	2940	3 % NaOCl, 17 % EDTA	Pulsed	15	Not recorded	20	0.3	20	Not recorded	6	600	In access cavity
Ismail et al. 2023	Diode	980	17 % EDTA, saline	Not recorded	100	Not recorded	Not recorded	2.5	20	10	3	Not stated	2–3 mm from WL withdrawn
Liapis et al. 2021	Er:YAG (PIPS)	2940	3 % NaOCl	Pulsed	15	Not recorded	20	Not recorded	30	Not recorded	2	400	Above canal entrance
Mandras et al. 2020	Er:YAG (PIPS)	2940	10 % EDTA, distilled water, 5 % NaOCl	Super short pulse	15	Not recorded	20	0.3	30	30	6	600	Coronal part of pulp chamber

literature on the most suitable protocol for LAI, even with the same type of laser. Four studies used PIPS and one study used SWEEPS. Both techniques used the same wavelength (2940 nm) in a pulsed mode which indicated that there was more consistency between studies in the usage protocols, though the tip size differed between studies. Three studies used a 600 µm tip [26,28,33] which was the equivalent of a size 60 endodontic file [International Standardisation Organisation (ISO) file standard] while one study used a 400 µm tip (size 40 ISO file) [32]. The position of the tip of the laser within the tooth during LAI varied between studies, but the results indicate that PIPS and SWEEPS were utilized within the pulp chamber only. This is advantageous from the dentist's perspective because LAI with PIPS or SWEEPS can be used even in teeth with minimally prepared root canals since the laser tip need not enter the root canal system. The trend for conservative root canal preparation techniques has been advocated in the recent past [41] and both PIPS and SWEEPS have been shown to effectively disinfect root canals prepared to small diameters and minimal tapers [42] even with the coronal placement of the laser tip. In contrast, the diode lasers required insertion into the root canal close to working length which was facilitated by using small laser tip sizes. One study included in the systematic review used a laser tip which corresponded to a size 20 ISO endodontic file that could be extended along the entire length of the root canal [27]. This indicated that the diode lasers could also be used for LAI in root canals prepared with a conservative approach resulting in reduced intracanal microbial loads and better periapical healing as compared with CNI [43]. No studies that used Nd:YAG lasers met the inclusion criteria of this systematic review. Whilst the beneficial properties of Nd:YAG lasers have included effective disinfection [44] and ability to achieve cleanliness in short and wide isthmi [45], these lasers are also known to alter the properties of root dentine including surface roughness, microhardness [46] and enhanced apical debris extrusion [47] which may be considered detrimental. From the PEP perspective, no relevant literature was found with respect of Nd:YAG laser. However a recent study indicated that Nd:YAG lasers used within a dry root canal after shaping and cleaning at a distance of 1 mm from working length resulted in reduction of pro-inflammatory cytokines [48]. While not representative of LAI, this finding suggests that Nd:YAG lasers may influence PEP experienced by patients and should be further investigated.

The results show that diode LAI helped reduce pain during the initial post-operative period (48 h). PEP is influenced by several factors that include the efficacy of canal disinfection, fluid dynamics of the irrigant (including extrusion) and debris extrusion. The antimicrobial action of diode LAI has been well documented through both *in vitro* [49] and clinical studies [50,51]. The reduction of the intra-radicular bacterial biofilm will have an impact on PEP, and this may explain the reduced pain score during the first two days that was reported through this systematic review. However, the extension of the diode laser tip deep within the root canal may also influence irrigant and apical debris extrusion because of concerns of vapour bubble generation several millimeters beyond the laser tip [52]. PIPS and SWEEPS represent a more modern approach for LAI in this context as the mechanism of action depends on generating high velocity liquids from the root canal orifice extending to the apical region of the root canal system via primary and secondary cavitation [53]. This may result in lesser pressure being created in the fluid within the root canal [54] and therefore lesser debris extrusion [55]. Er:YAG lasers also demonstrated enhanced biofilm eradication compared with UAI [56], and the results of this systematic review also show that when compared with UAI, MDA and sonic activation, PIPS appeared to be advantageous in mitigating PEP. This can be supported by clinical evidence that also shows better periapical healing when LAI was used as compared with PUI [57] and enhanced penetration ability of the root canal irrigants with PIPS [58]. Better canal cleanliness can also be achieved with SWEEPS and PIPS as compared with sonic activation techniques and this may also help explain the reduction in PEP with PIPS. None of the studies in this systematic review compared SWEEPS with CNI directly in terms of PEP and

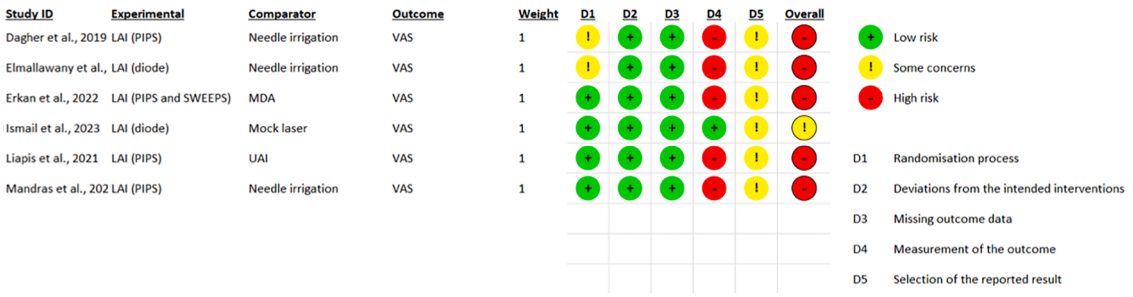

Fig. 2. Summary of RoB2 findings.

Table 4
Mean/median pain scores on VAS for selected articles at commonly selected time intervals (*H*= hour, *D*= day, - = no data available).

Author and year	Group	No. teeth analysed (per group)	Mean/median pain score on VAS (0–100 scale) at various time intervals											
			D0	H6	H8	H12	D1	H36	D2	D3	D4	D5	D6	D7
Dagher et al. 2019	Er:YAG (PIPS)	25	7.1	–	–	–	13.2	–	9.7	6.1	2.3	1	0	0
	Needle irrigation	31	11.2	–	–	–	13.2	–	8.8	5.2	3.2	1.2	0	0
Elmallawany et al. 2022	Diode laser	10	–	58.9	–	39.7	25.7	17.6	9.3	–	–	–	–	1.2
	Needle irrigation	10	–	74.5	–	52.4	41.4	32.2	28.6	–	–	–	–	1.7
Erkan et al. 2022	Er:YAG (PIPS)	40	–	–	10	–	10	–	10	–	–	–	–	0
	Er:YAG (SWEEPS)	40	–	–	10	–	10	–	0	–	–	–	–	0
	PUI	40	–	–	10	–	20	–	20	–	–	–	–	0
	Sonic	40	–	–	10	–	20	–	20	–	–	–	–	0
	MDA	40	–	–	20	–	30	–	20	–	–	–	–	10
Ismail et al. 2023	Diode laser	60	–	–	–	–	38	–	27	13	–	–	–	–
	Needle irrigation	60	–	–	–	–	48	–	32	16	–	–	–	–
Liapis et al. 2021	Er:YAG (PIPS)	28	–	4.9	–	–	5.3	–	3.9	1.9	–	–	–	–
	UAI	27	–	13.9	–	–	7.7	–	4.3	3.2	–	–	–	–
Mandras et al. 2020	Er:YAG (PIPS)	27	–	–	–	–	19.6	–	11.1	8.9	4.4	4.1	3	2.6
	Needle irrigation	27	–	–	–	–	23	–	14.8	11.1	8.1	5.2	3.7	2.2

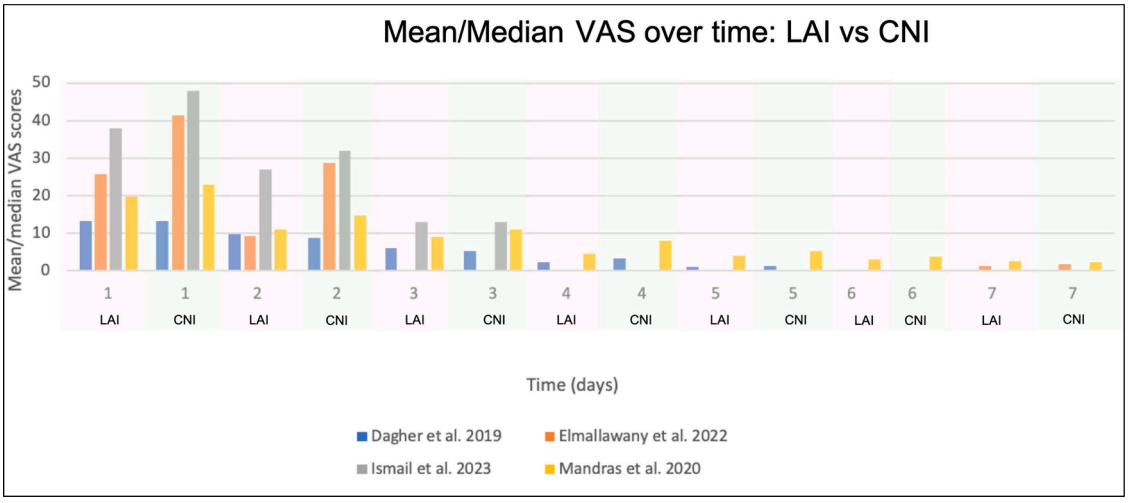

Fig. 3. Average VAS scores over 7 days for LAI and conventional needle irrigation (CNI) groups. Overall, pain scores lessened on each sequential day. In comparison with needle irrigation groups, PEP was significantly lower at days 1 and 2 in two studies [27,29], and the difference was negligible in two studies [26,33].

this requires further studies to be undertaken in the future. Contrasting results were noted in this systematic review between PIPS and CNI with two studies reporting no differences in PEP at 24 h [26,33] but with reduced PEP in one studying being reported at 48 h [33]. The reason for this discrepancy is unclear, though the variability in reported results observed between studies can likely be attributed to the methodological discrepancies such as a wider variety of pulpal and periapical diseases being treated by the same modalities, as also the inclusion of a variety of teeth (both anterior and posterior) with no criteria specified for root canal anatomy. In the future, an increase in methodological homogeneity between RaCTs may allow for more accurate statistical analyses of the effects of LAI.

In addition to the variability in study design between the included studies, this systematic review has some additional limitations. Five of the six included studies failed to provide evidence of a placebo (by means of laser tip insertion into the tooth without activation) in the comparator group(s). This was reflected in the RoB2 scores, where a high risk of bias was assigned to studies where no evidence of sham laser application was mentioned. Given that the outcomes were assessed by study participants (via self-reported pain scores), it was determined that their knowledge of the intervention may have influenced the results. Blinding may have been difficult to achieve in some studies, notably

Erkan et al. [28] where five distinct irrigation procedures were assessed (PIPS, SWEEPS, MDA, sonic and ultrasonic activation), thus multiple different sham interventions would be required for each group to effectively blind participants. Due to the nature of the treatment involved, blinding of the clinician delivering the intervention was not attainable. This was not deemed to have a significant impact on the quality of results obtained as outcomes were reported by patients and therefore could not be influenced by the clinicians. In all studies, a questionnaire or pain diary was given to participants to complete at the respective time intervals which were then returned at a subsequent visit. It is possible that participants may not have complied with completing the questionnaire at appropriate time intervals, for example due to forgetfulness or not understanding the importance of the temporal element. Thus, the accuracy of the results may be called into question. The results of this systematic review are based on studies with a higher risk of bias and should be interpreted with caution. From a statistical perspective, only three studies reported a relatively small effect size (0.3–0.4) whereas the other three included studies did not report one at all. The results of all studies with respect to PEP experience should therefore be treated with caution, especially when significant differences were reported between experimental groups.

4.4. Comparison with existing studies

Two other recent systematic reviews have been reported in the field of laser application within the root canal system, but with marked differences from the current review [59,60]. To enhance homogeneity between included studies, the current review only focused on LAI whereas the other two systematic reviews have included aPDT [59,60] and PBM [59].

A qualitative systematic review by Elafifi-Ebeid et al. [60] evaluated the influence of different laser disinfection techniques on PEP. RaCTs were reviewed to analyse the efficacy of three techniques: LAI, dry canal irradiation and aPDT. The attempt to compare different modalities of laser application, including studies with dry canal irradiation [61], makes interpretation of results difficult from that systematic review. Elafifi-Ebeid et al. [60] also included studies [35,61] with Nd:YAG lasers which are also known to melt dentine that later resolidifies. This also indicates a departure from the LAI principles which were being evaluated through the current review since both studies applied the Nd:YAG laser to dry root canals. Additionally, the authors included both primary and retreatment cases [62] that utilised LAI which may be a confounding factor as pain levels vary between these two treatment modalities [63]. The inclusion criteria for the current systematic review only focused on primary endodontic treatment cases thereby enhancing the validity of this review. With regards to LAI, Elafifi-Ebeid et al. [60] determined that Er:YAG showed some efficacy in reduction of PEP over a short time period (6–24 h). This was comparatively similar to the current systematic review, which also identified a reduction in pain intensity reported in the laser groups in the short- term (6–48 h), whereas no significant differences were found from 72 h to 7 days post-operatively. Anagnostaki et al. [59] aimed to evaluate the clinical efficacy of laser use in endodontics over three domains: direct canal irradiation, aPDT and PBM. They found that 14/17 studies reported improved outcomes using one of these three forms of laser-assisted endodontics. These results, while important, were not comparable to the findings of the present systematic review as they were not specific to pain and only included one study that performed LAI.

The S3-level clinical practice guidelines by the European Society of Endodontology [64] analysed various adjunctive methods for treatment of apical periodontitis, including aPDT and laser canal irradiation [65]. These are a high-powered series of documents that guide endodontists and also influence teaching and practice amongst general dental practitioners. However, some of the criteria used for studies that evaluated adjunctive methods for enhancing canal disinfection using lasers have been suboptimal, resulting in the inclusion of studies which are not fit for purpose [30,51,61]. These studies have methodological issues which were identified in the current systematic review (Table 1) and are not truly representative of the potential of LAI. Additionally, the systematic review associated with the S3 guideline undertook a meta-analysis regarding PEP at seven days using two studies [30,51] with high statistical heterogeneity being noted (I^2= 84 %) [65]. A qualitative summary would have been preferable over meta-analysis. Several other papers that are included in the current review have not received mention in the S3 guideline since the search for articles was concluded on 01 October 2021, thereby missing out on the most contemporary articles published in this field [27-29,32]. The current review thus represents the most up to date information in this domain.

A number of articles evaluate the effects of photobiomodulation [66] and phototherapy [67] on PEP. To the knowledge of the authors, this is the only systematic review that specifically investigates LAI in relation to PEP for primary root canal treatment cases.

5. Conclusions

The results of this review suggest LAI with diode lasers may be an effective adjunct in the reduction of PEP between 6 and 48 h when compared with needle irrigation. With regards to Er:YAG lasers (specifically PIPS), the findings are unclear. Results suggest PIPS has advantages in mitigating PEP when compared with UAI, MDA and sonic activation, but demonstrated no difference when compared with needle irrigation. Quantity of analgesia intake was not significantly impacted by LAI. The limitations of this systematic review should be considered, specifically the lack of homogeneity and the high risk of bias between included studies.

Further RaCTs with more consistent selection criteria and procedural protocol would be beneficial to support a more robust analysis of the influence of LAI on PEP.

Registration

The protocol for this systematic review was registered with PROSPERO (CRD42023437185).

CRediT authorship contribution statement

Alex McGillivray: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Arindam Dutta:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Formal analysis, Conceptualization.

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.

Funding

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

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