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Comparative Efficacy of Different Irrigant Activation Techniques for Irrigant Delivery Up to the Working Length of Mature Permanent Teeth: A Systematic Review and Meta-Analysis

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ABSTRACT

This systematic review aimed to establish whether various irrigant activation techniques (IATs) result in greater penetration of irrigant up to the working length. The MEDLINE, Scopus and Cochrane Library electronic databases were searched to determine the difference in irrigant penetration depth in the main canal following the use of manual dynamic activation (MDA), sonic irrigation (SI), passive ultrasonic irrigation (PUI), and apical negative pressure irrigation technique (ANP) in comparison with conventional needle irrigation technique (CNI) in mature permanent teeth. Meta-analysis was performed for straight canals as well as curved canals in addition to subgroup analyses for a) Individual IATs in comparison with CNI, b) Comparison of PUI v ANP and SI v ANP in the straight canals, c) comparison of different IATs performed in straight and curved canals. The outcome was presented as effect size: standardized mean difference (SMD) and percentage difference (% diff) of irrigant penetration up to the working length (WL) alongside 95% confidence intervals using chi-square analysis. Of the 840 records screened, 20 studies were included in the systematic review and 17 studies were included in the meta-analysis. It revealed IATs had significant improvement in irrigant delivery up to the WL in straight (% diff: 51.94%, 95% CI: 39.20–64.67%) and curved canals (SMD: 1.08, 95% CI: 0.64–1.52) over CNI. The subgroup analysis revealed ANP was the most effective and significant technique followed by PUI, SI and MDA techniques in straight canals (% diff: 91.70%, 95% CI: 75.63–107.77%) and curved canals (SMD: 1.45, 95% CI: 0.77–2.13). IATs improve irrigant penetration when compared to CNI technique. In both straight and curved canals, ANP is the most effective in delivering the irrigant up to the WL followed by PUI, SI and MDA techniques. Hence adaptation of recent IATs in routine endodontic practice is recommended.

Keywords: Apical negative pressure, irrigant penetration, passive ultrasonic irrigation, root canal therapy, sonic irrigation, ultrasonics

HIGHLIGHTS

- The irrigant penetration shows vast improvement with IATs when compared to CNI.
- In both straight and curved canals, ANP is the most effective IAT in delivering the irrigant up to the WL followed by PUI, SI and MDA techniques.
- It is beneficial to incorporate IATs in routine endodontic practice.

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INTRODUCTION

The focus of successful endodontic therapy is dependent on the complete elimination of microorganisms which is the main aetiology for pulpitis and apical periodontitis (1). The goals of endodontic therapy are to shape the canal, eliminate infected dentine, permit an adequate supply of irrigant to the entire root canal system, promote apical healing in infected root canals and maintain the integrity of the tooth (2). The anatomy of the curved root canal impairs the cleaning efficiency (3). Hence, various irrigant activation techniques (IATs) aim to enhance the cleaning process and lower the microbial load (4).

There are two factors typically linked with effective irrigation - the irrigant and the delivery method (5). Ideal requisites of root canal irrigants are broad antimicrobial spectrum, neutralization of endotoxins, smear layer removal and dissolution of vital pulp and necrotic pulpal remnants (6). Although sodium hypochlorite (NaOCl) is the gold standard for its antimicrobial activity and tissue dissolving characteristics, it does not remove the smear layer (7). Thus, NaOCl has been utilized in combination with ethylenediamine tetra acetic acid (EDTA), which helps to remove the smear layer generated during instrumentation (8).

Root canal irrigation methods can be classified into two major types: manual techniques and machine-assisted irrigation activation techniques (9). Manual techniques include conventional needle irrigation technique (CNI) and manual dynamic activation (MDA) with gutta-percha (GP) cones or files (10). Most extended machine-assisted irrigation activation techniques are sonic irrigation technique (SI), passive ultrasonic irrigation technique (PUI), and apical negative pressure irrigation technique (ANP) (10).

The use of these techniques enhances the flow and distribution of irrigating solutions and results in better canal debridement when compared with CNI (9). CNI is not efficient in cleaning the apical third of the canal as it is confined to the level of needle penetration (11). MDA is a simple as well as a cost-effective method of activating irrigants. It uses a well-fitting GP cone that is repeatedly inserted into an instrumented root canal in order to eliminate the apical vapour lock (9). SI is based on sonic energy which helps break smear layer and biofilm through hydrodynamic phenomenon producing cavitation and acoustic streaming. This results in extensive cleaning and disinfection (12, 13). PUI also promotes cavitation by the transfer of microcurrents through ultrasonic waves with its blunt tip (14). It eliminates microorganisms, smear layer, and debris without exceeding the apical constriction (15). ANP is a new technique of delivering irrigants into the root canal that minimizes the risk of irrigant extrusion (16). Irrigants are delivered by a master delivery tip within the pulp chamber, and a small suction tip placed up to the working length (WL) creates the necessary apical negative pressure to drive the irrigant all along the extent of the root canal (16–18).

Effective irrigation is assured only when the irrigant is activated upon contact with the whole root canal system (9). The essential requirements of successful endodontic therapy include dissolution of pulpal remnants and thorough removal of microorganisms and their by-products from the root canal system especially the apical third (19). As a consequence, mechanical instrumentation in conjunction with chemical disinfection will lead to improved canal debridement (20). Therefore, complete disinfection before obturation needs to be ensured. Nonetheless, controversy remains about the effectiveness of the above-mentioned IATs in the apical third of straight and curved canals. Thus, it is essential to know which among the various IATs could be used effectively to deliver the irrigant up to the WL.

Objectives

The aim of the systematic review was to establish the effectiveness of different IATs and their irrigant delivery up to the WL of mature permanent teeth when compared to CNI. Moreover, this review also aimed to identify the efficacy of individual IATs and their irrigant delivery up to the WL in straight and curved canals.

Review question

Are IATs more effective than the conventional method of irrigation for the irrigant delivery up to the WL for mature permanent teeth?

Null hypothesis: There is no difference in the irrigant penetration in main canal up to the WL when compared to CNI with current IATs.

MATERIALS AND METHODS

Protocol and Registration

The current systematic review was prepared in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (The PRISMA 2020 statement: an updated guideline for reporting systematic reviews) (21). This systematic review was prepared and registered in the PROSPERO (International Prospective Register of Systematic Reviews) with the registration number - CRD42021247430.

PICOST Format

Population (P): Studies on mature permanent maxillary or mandibular teeth.

Interventions (I): Manual dynamic activation (MDA), Sonic irrigation (SI), Passive ultrasonic irrigation (PUI), and Apical negative pressure irrigation technique (ANP).

Comparison (C): Conventional needle irrigation technique (CNI).

Outcome (O): Penetration of irrigant up to the WL as assessed using the direct observation/radiographic method.

Study designs (S): *In vivo*, *ex vivo* and *in vitro* studies.

Timeframe (T): Studies published between 1st January 2000 and 31st May 2022.

Eligibility Criteria

Inclusion criteria:

1. Interventional studies inclusive of at least one of the IATs as the trial arm.

2. Studies evaluating the efficacy of irrigant penetration up to the WL, following the use of any of the aforementioned IATs using the direct observation/radiographic method.

3. Studies using NaOCl with or without EDTA as an irrigant.

4. *In vivo* studies inclusive of patients undergoing primary endodontic therapy.

5. *Ex vivo*/*in vitro* studies including extracted human teeth.

Exclusion criteria:

1. Studies conducted on root-filled teeth, resin blocks, animal teeth, and open canal systems.
2. Studies inclusive of retreatment cases.
3. Case reports, case series, review articles, animal studies, commentaries, and letters to the editor.

Information Sources

Formally published research in endodontics was searched in all the electronic databases with no language constraints, which included the following: MEDLINE (via PubMed), Scopus, and Cochrane Library. The additional search methods featured reference list follow-up on all included articles, Clinical Trials Registry- India (CTRI), Google Scholar, and hand searches of the Journal of Endodontics and International Endodontic Journal. The literature search was performed by two independent reviewers namely RSK and MP.

Search Strategy

The search strategy structure adopted was based on a PICO-style approach with medical subject headings (MeSH) and text words related to the PICO format and research question. Synonyms, keywords and indexed terms were selected using the authors' knowledge, current literature, and indexed databases to build on these headings. The search strategy was then devised using truncations and boolean operators ('OR', 'AND') and modified for each database, taking into account both sensitivity and specificity (Table 1).

Selection Process

Two reviewers (RSK and MP) independently compared the search results to ensure completeness. Zotero reference management software for Windows, Version 5.0.96 (Corporation for Digital Scholarship, Virginia, USA) was utilized as a reference manager. The reviewers identified, screened, and read the full-text articles to decide on the eligibility criteria. An inter-examiners agreement was calculated using Cohen's kappa statistics (0.92). Disagreements among the reviewers were resolved by a third reviewer (AA). No automation tool was used in the selection process.

Data Collection Process

Predetermined data items were extracted and prepared by RSK in Microsoft Excel, version 16.43 (Microsoft Corp., Redmond, WA, USA) and assessed by the other reviewer (MP). Any disagreement between the reviewers was resolved through discussion.

Data Items

Data extraction was based on a previously published systematic review (22). It was later adapted for evaluating the irrigant penetration depth in the main canal as per PE Căpută et al. (22). The Data items pertaining to study design, specimen selection, randomization, instrumentation, irrigation and IATs used, and outcome assessment were extracted. All data are summarized in Table 2.

Study Risk of Bias Assessment

Each study was critically assessed independently by two reviewers (RSK and MP) as per a predetermined set of criteria based on the previously published systematic review (22). It was later adapted for evaluating the irrigant penetration depth in the main canal as per PE Căpută et al. (22). It consists of 28 questions under four major subheadings with a yes or no/unclear response scoring 1 or 0 points, respectively. The checklist for a summary score was tabulated for each study and the risk of bias was graded as potentially high risk (score <50%), medium risk (score 50%–75%), and low risk (score >75%). The quality requirements during the risk of bias assessment of included studies are presented in Appendix 1.

Effect Measures

The main effect measures were

1. The mean distances between the WL and the maximal irrigant penetration.
2. The percentage of irrigant penetration depth up to the WL.

The outcome waspresented as standardized mean differences (SMD)/percentage difference (% diff) of the irrigant penetration up to the WL alongside 95% confidence interval (CI) using chi-square analysis.

Synthesis Methods

Data synthesis: A Meta-analysis was performed using the STATA® SE 16.1 for Windows (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC, Texas, USA), in order to facilitate direct comparisons across the studies. The Cochran's Q test and I^2 index were used for the identification of heterogeneity across the studies. In addition to this, subgroup meta-analyses were also conducted to explore heterogeneity. Significance was set at $P \leq 0.05$.

a) Subgroup analysis and comparison of individual IATs with CNI
   i. In straight canals
   ii. In curved canals
b) Subgroup analysis and comparison of ANP with PUI and with SI in straight canals.
c) Subgroup analysis and comparison of IATs performed in both straight and curved canals.

Due to the high heterogeneity, the random effect model was used to conduct a meta-analysis. The weight for each study and estimates with upper and lower CI was obtained. Egger's regression test and funnel plot analysis with a 95% CI were carried out to identify any evidence of publication bias by determining the number of studies that could be missing using the trim and fill procedure.

RESULTS

Study Selection

A total of 840 records were found from the initial search using a combination of an electronic and manual search. There were 586 duplicates removed, and 254 studies evaluated against the inclusion criteria (Fig. 1). Following a screening of the title and abstract, 43 studies (6 *in vivo*, 6 *ex vivo* and 31 *in vitro*) were eligible for full-text assessment. Finally, 20 studies [4 *in vivo* (15, 23–

TABLE 1. PubMed database search

Search found	PICO	Search strategy input query	No. of items
#1	P	(patients[Title/Abstract]) OR (mature permanent teeth[Title/Abstract]) OR (mature permanent tooth [Title/Abstract]) OR (mature apex[Title/Abstract]) OR (mature apices[Title/Abstract]) OR (permanent molar* [Title/Abstract]) OR (permanent premolar*[Title/Abstract]) OR (permanent canine*[Title/ Abstract]) OR (permanent incisor*[Title/Abstract]) OR (incisor[MeSH Terms]) OR (bicuspid[MeSH Terms]) OR (cuspid[MeSH Terms]) OR (Molar[MeSH Terms]) OR (dentition, permanent[MeSH Terms]) AND (Root Canal Therapy[MeSH Terms]) AND ("2000/01"[Date - Publication]: "2022/05"[Date - Publication])	5,120
#2	Ia	(passive ultrasonic irrigation[Title/Abstract]) OR (ultrasonic irrigation[Title/Abstract]) OR (continuous ultrasonic[Title/Abstract]) OR (PUI[Title/Abstract]) OR (intermittent ultrasonic[Title/Abstract]) OR (ultrasonics [MeSH Terms]) OR (Ultrasonic Therapy[MeSH Terms]) AND ("2000/01"[Date - Publication]: "2022/05"[Date-Publication])	20,480
#3	Ib	(sonic irrigation[Title/Abstract]) OR (endoactivator[Title/Abstract]) OR (sonication[MeSH Terms]) AND ("2000/01"[Date - Publication]: "2022/05"[Date - Publication])	
#4	Ic	(apical negative pressure[Title/Abstract]) OR (endovac[Title/Abstract]) OR (suction[MeSH Terms]) OR (vacuum[MeSH Terms]) AND ("2000/01"[Date - Publication]: "2022/05" [Date - Publication])	4,751
#5	Id	(manual dynamic activation[Title/Abstract]) OR (manual dynamic irrigation[Title/Abstract]) OR (gutta-percha[MeSH Terms]) AND ("2000/01"[Date - Publication]: "2022/05" [Date - Publication])	11,114
#6	C	(conventional needle irrigation[Title/Abstract]) OR (needle irrigation[Title/Abstract]) OR (positive pressure irrigation[Title/Abstract]) OR (conventional irrigation[Title/Abstract]) OR (positive pressure irrigation[Title/Abstract]) OR (passive irrigation[Title/Abstract]) OR (syringe irrigation[Title/Abstract]) OR (conventional syringe irrigation[Title/Abstract]) OR (syringe[MeSH Terms]) OR (Needles[MeSH Terms])AND (therapeutic irrigation[MeSH Terms]) AND ("2000/01"[Date - Publication]: "2022/05" [Date-Publication])	1,660
#7	O	(apical third[Title/Abstract]) OR (irrigant penetration[Title/Abstract]) OR (working length[Title/ Abstract]) OR (patency[Title/Abstract]) OR (Radiography, Dental, Digital[MeSH Terms]) OR (dye [Title/Abstract]) OR (contrast media[Title/Abstract]) OR (contrast solution[Title/Abstract]) AND (Tooth Apex[MeSH Terms]) AND ("2000/01"[Date - Publication]: "2022/05"[Date - Publication])	377 678
#8		#1 AND #2	205
#9		#1 AND #3	43
#10		#1 AND #4	46
#11		#1 AND #5	530
#12		#1 AND #6	72
#13		#1 AND #7	234
#14		#2 AND #7	40
#15		#3 AND #7	14
#16		#4 AND #7	19
#17		#5 AND #7	91
#18		#6 AND #7	29
#19		#2 AND #3 AND #4	25
#20		#3 AND #4 AND #5	5
#21		#4 AND #5 AND #6	7
#22		#5 AND #6 AND #2	11
#23		#6 AND #2 AND #3	43
#24		#2 AND #3 AND #4 AND #5	5
#25		#2 AND #3 AND #4 AND #5 AND #6	3
#26		#1 AND #2 AND #3 AND #4 AND #5 AND #6	1
#27		#1 AND #2 AND #3 AND #4 AND #5 AND #6 AND #7	0

P: population, Ia: intervention a – passive ultrasonic irrigation, Ib: intervention b – sonic irrigation, Ic: intervention c – apical negative pressure irrigation, Id: intervention d - manual dynamic activation, C: comparator – conventional needle irrigation, O: outcome

25), 3 *ex vivo* (26–28) and 13 *in vitro* (12, 13, 29–37, 17, 18)] were included in the systematic review, thus qualifying for inclusion and 23 studies were excluded (the reasons for the exclusion are outlined in Appendix 2). In the included studies, thirteen studies reported the irrigant penetration up to the WL in terms of percentage (12, 17, 34–36, 18, 24, 25, 28–30, 32, 33). Seven studies (13, 15, 23, 26, 27, 31, 37) reported the irrigant penetration in terms of mean and standard deviation. Retrieving the raw data from the authors was attempted through e-mail communication, but only Sáinz-Pardo et al. (27) responded with the raw data. Hence a total of 17 studies [4 *in vivo* (15, 23–25), 2 *ex vivo* (27, 28) and 11 *in vitro* (12, 17, 37, 18, 29, 30, 32–36)] were included in the meta-analysis (Fig. 1). No automation tools were used for the inclusion and exclusion of records.

Study Characteristics

Table 2 summarizes the characteristics of the 20 included studies. All the studies were published between the years 2010 and

TABLE 2. Summary of study characteristics of all the included studies that evaluated the irrigant penetration up to the working length

Study	Study design	Control group - CNI (*n*)	Test groups (*n*)	Other groups evaluated	Sample (Curvature)	Working length (mm)	Method used to simulate periapical tissues	Patency with 10 K-file	File system	Apical preparation size/taper	Irrigation (mL)	Contrast solution preparation	Method of assessment
S DPA et al., 2022 (37)	*In vitro*	(15)	SI (15) MDA (15)	SVN	Single-rooted premolars (20°- 40°)	16	Wax	Y	ProFit S3 rotary	30/.06	3% NaOCl (2 mL)	Iohexol (Omnipaque), Ireland (45:55)	Radiographic
Castelo-Baz et al., 2021 (29)	*In vitro*	St. canal (20), Curved canal (20)	PUI St. canal (20) PUI curved canal (20)	CANUI-St, CANUI-Curved	Incisors (St.+Curved 20°-30°)	16	Wax	Y	ProTaper Next (Dentsply)	40/.06	5% NaOCl (3 mL) 17% EDTA (3 mL)	20% Chinese ink, Germany	Direct observation
Abrar S et al., 2019 (23)	*In vivo*	(20)	ANP (20)	SAF	Mandibular molars (Curved)	Unclear	NA	Unclear	Mtwo (VDW)	35/.04	5% NaOCl (2 mL)	Iohexol (Omnipaque), Ireland	Radiographic
Souza et al., 2019 (30)	*In vitro*	(20)	PUI (20)	CUI, EC	Single rooted (NR)	15	Wax	Y	ProTaper universal (Dentsply)	40/.05	5.25% NaOCl (3 mL) EDTA (3 mL)	20% Nankin ink, Netherlands	Direct observation
Khare et al., 2017 (31)	*In vitro*	(12)	PUI (12) MDA (12)	_	Single-rooted (Straight)	14	Wax	Y	ProTaper universal (Dentsply)	25/.08	5.25% NaOCl (3 mL) 17% EDTA (3 mL)	10% ink marker, USA	Direct observation
Dhaimy S et al., 2016 (26)	*Ex vivo*	(60)	MDA (60)	PI with endodontic needle	Maxillary incisors (straight)	Unclear	Mixture of plaster and sawdust	Y	iRace	25/.04	2.5% NaOCl (NR)	TELEBRIX 35	Radiographic
Helmy et al., 2016 (13)	*In vitro*	(10)	SI (10)	_	Mandibular molars (25° or more)	Unclear	Wax	Unclear	Micro-Mega REVO-S™	35/.06	5.25% NaOCl (2 mL)	Optiray TM 320, USA	Radiographic
Kamra et al., 2016 (24)	*In vivo*	(15)	PUI (15)	Without patency PUI & CNI	Mandibular molars (straight)	Unclear	NA	Y	ProTaper (Dentsply)	30/.09	5.25% NaOCl (1 mL)	IV contrast medium containing iodine (Iopamidol)	Radiographic
Castelo-Baz et al., 2016 (32)	*In vitro*	(20)	PUI (20)	CUI	Incisors (20°-30°)	16	Wax	Y	GTX (Dentsply)	30.06	5% NaOCl (3 mL) 10% EDTA (3 mL)	20% Chinese ink, Germany	Direct observation
Kanumuru et al., 2015 (12)	*In vitro*	(15)	PUI (15) SI (15)	25/.02 RACE	Single rooted (Straight)	_	Elastomer	Y	ProTaper (Dentsply)	30/.09	5.25% NaOCl (1.5 mL)	40% Indian ink (2:3)	Direct observation
Sáinz-Pardo et al., 2014 (27)	*Ex vivo*	(10)	SI (10) PUI (10)	CNI, SI, PUI (Open system)	Incisors (Straight)	17	Paste-paste adhesive	Y	ProFile (Dentsply)	30/.06	4.25% NaOCl (1.5 mL) 17% EDTA (3 mL)	40% Iomeron 300®, Italy	Radiographic
Merino et al., 2013 (36)	*In vitro*	(4)	PUI.04 taper (15), SI .04 taper (15)	PUI.08, SI.08, CNI (open system)	Mandibular molars (30°-40°)	13.5	Wax	Y	GT rotary (Dentsply)	30/.04	5.25% NaOCl (1.5 mL)	60% Radialar-280 (Spain)+5.25% NaOCl (50:50)	Radiographic
Pawar et al., 2013 (33)	*In vitro*	(20)	PUI (20), SI (20), MDA	AI (F-file)	Single rooted (NR)	Unclear	Wax	Y	WaveOne (Dentsply)	25/.08	5% NaOCl (NR)	Methylene blue	Direct observation

TABLE 2. Cont.

Study	Study design	Control group - CNI (*n*)	Test groups (*n*)	Other groups evaluated	Sample (Curvature)	Working length (mm)	Method used to simulate periapical tissues	Patency with 10 K-file	File system	Apical preparation size/taper	Irrigation (mL)	Contrast solution preparation	Method of assessment
Spoorthy et al., 2013 (18)	*In vitro*	(16)	PUI (16), ANP (16)	ANP+PUI	Incisors (Straight)	Unclear	Wax	Unclear	ProTaper universal (Dentsply)	40/.05	5.25% NaOCl (3 mL) 17% EDTA (3 mL)	40% Indian ink, India	Direct observation
Castelo-Baz et al., 2012 (34)	*In vitro*	(20)	PUI (20)	CUI	Incisors (Straight)	16	Wax	Unclear	ProTaper (Dentsply)	30/.09	5% NaOCl (3 mL) 10% EDTA (3 mL)	20% Chinese ink, Germany	Direct observation
de Gregorio et al., 2012 (35)	*In vitro*	(15)	ANP (15)	SAF	Canines (Straight)	17	Wax	Y	K- Flexofiles (Dentsply)	35/.02	5.25% NaOCl (5 mL) 17% EDTA (NR)	10% ink marker, France	Direct observation
Munoz and Camacho-Cuadra., 2012 (15)	*In vivo*	(10)	PUI (10), ANP (10)	–	Mandibular molars (25°)	–	NA	Unclear	Mtwo (VDW)	35/.04	5.25% NaOCl (2 mL)	Iohexol (Omnipaque), Ireland	Radiographic
Vera et al., 2011 (25)	*In vivo*	(21)	PUI (21)	PUI without patency	Maxillary posteriors, mandibular molars (NR)	Between 19 and 21	NA	Y	ProTaper (Dentsply)	30/.09	5.25% NaOCl (1 mL)	IV contrast medium containing ioversol (Claritrast 300) (45:55)	Radiographic
de Gregorio et al., 2010 (17)	*In vitro*	(20)	SI (20), PUI (20), ANP (20)	AI (F file)	Single-rooted (Straight)	15	Wax	Y	Profile rotary (Dentsply)	40/.06	5.25% NaOCl (3 mL) 17% EDTA (3 mL)	10% Kuraray caries detector solution, Japan	Direct observation
Bronnec F et al., 2010 (28)	*Ex vivo*	(30)	MDA (30)	–	Mandibular molars (33.7°)	19	Wax	Y	ProTaper rotary (Dentsply)	20/.07	3% NaOCl (1 mL)	Hypaque Sodium 50% (Amersham Health Inc, USA)	Radiographic

NR: Not reported, NA: Not applicable, Y: Yes, St: Straight, CNI: Conventional needle irrigation technique, PUI: Passive ultrasonic irrigation, SI: Sonic irrigation, ANP: Apical negative pressure irrigation, CANUI: Continuous apical negative ultrasonic irrigation, MDA: Manual dynamic activation, SVN: Side-vented needle, AI: Active irrigation, PI: Passive irrigation, CUI: Continuous ultrasonic irrigation, EC: Easy clean, SAF: Self-adjusting files, NaOCl: Sodium hypochlorite, IV: Intravascular

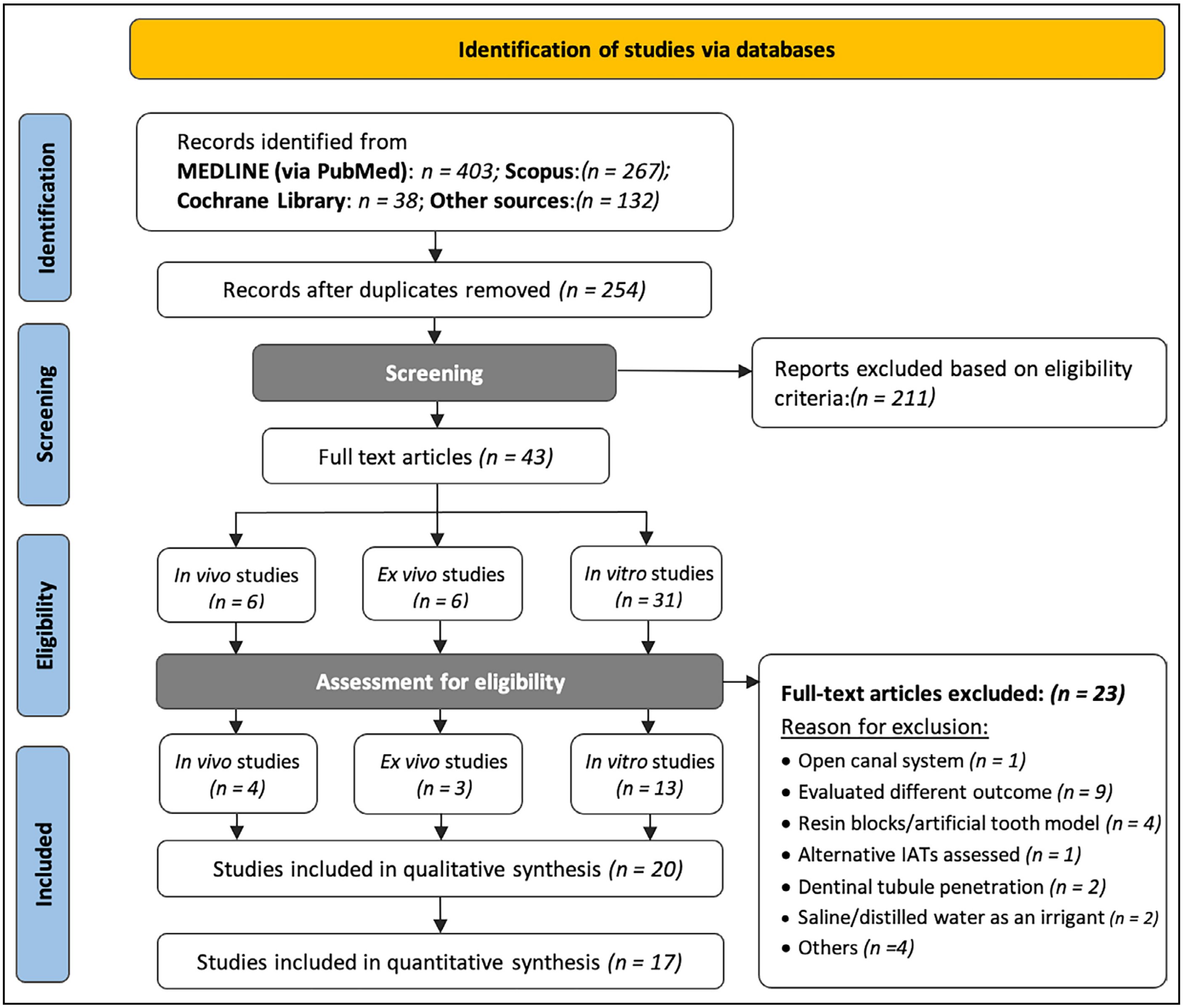

Figure 1. PRISMA flow diagram

2022. Studies were interventional type in which 4 studies were *in vivo* (15,23–25), 3 studies were *ex vivo* (26–28) and the remaining 13 studies were of *in vitro* design (12, 13, 35–37, 17, 18, 29–34). The evaluation of outcome was done using direct observation method in 10 studies (12, 17, 18, 29–35), and using radiographic observation method in 10 studies (13, 15, 23–28, 36, 37). In the direct observation method, the assessment of the outcome is based on direct visualization of the penetration of the dye into the main canal. Standardized decalcification, clearing, and re-hardening protocol for the samples by Robertson and Leeb (38) and a modified approach of the same by de Gregorio et al., (39) were used. The samples were evaluated by direct observation of images obtained under the operating microscope and the orientation of the recording microscope was standardized to reproduce the same image in all groups, using the criteria described by de Gregorio et al., (17). In the radiographic observation method, a digital radiographic image was attained with the irrigating contrast solution (ICS) inside the canal. The penetration of ICS was then measured using various image editing tools. A summary of the characteristics of CNI and IATs in the included studies is presented in Tables 3 and 4, respectively.

Risk of Bias in Studies

The Kappa score for the interrater analysis was 0.87. A summary of the risk of bias assessment of the included studies is presented in Table 5. None of the included studies met all of the criteria. The average quality of the evidence provided by the included articles was found to be moderate. The overall risk of bias in the included studies was 81.4% (61%–93%) indicating a 'low risk of bias'.

Results of Individual Studies

Table 6 summarizes the results of all the individual studies. The results of six studies (13, 15, 23, 26, 31, 37) were presented in terms of mean. Among these, five studies (13, 15, 23, 31, 37) presented the distance between the WL and the maximum irrigant penetration in terms of mean in straight and curved

TABLE 3. Characteristics of conventional needle irrigation technique used

Study	Characteristics of use					
	Manufacturer	**Gauge**	**End type**	**Volume (mL)**	**Duration (s)**	**Insertion depth from the WL (mm)**
S DPA et al., 2022 (37)	NR	26	Open-ended	NR	NR	2
Castelo-Baz et al., 2021 (29)	ProRinse, Dentsply Sirona, USA	30	Side vented	6	60	2
Abrar S et al., 2019 (23)	Miraject Endotec Duo, Germany	27	Side vented	2	120	Deep without binding
Souza et al., 2019 (30)	Ultradent, USA	30	NR	6	60	1
Khare et al., 2017 (31)	Vishal Dentocare, India	31	Double-Side vented	3	60	2
Dhaimy S et al., 2016 (26)	2.5 cc syringe	21	Open-ended	NR	NR	Deep without binding
Helmy et al., 2016 (13)	Vista-Probe TM, Inter-Med, Inc., USA	NR	Side vented	1	NR	Deep without binding
Kamra et al., 2016 (24)	Ultradent, USA	27	Side vented	1	20	2
Castelo-Baz et al., 2016 (32)	ProRinse, Dentsply Sirona, USA	30	NR	6	60	2
Kanumuru et al., 2015 (12)	NR	30	Side vented	1	30	2
Sáinz-Pardo et al., 2014 (27)	Max-i-Probe, Dentsply-Rinn	30	NR	1	30	2
Merino et al., 2013 (36)	NR	30	Side vented	1.5	30	2
Pawar et al., 2013 (33)	NR	25	End vented	NR		2
Spoorthy et al., 2013 (18)	NaviTip, Ultradent, USA	30	Open-ended	1.5	30	2
Castelo-Baz et al., 2012 (34)	ProRinse, Dentsply Sirona, USA	30	Side vented	6	60	2
de Gregorio et al., 2012 (35)	ProRinse, Dentsply Sirona, USA	30	Side vented	NR	30	2
Munoz and Camacho-Cuadra., 2012 (15)	Monoject, Hampshire, UK	27	Side vented	1	30	2
Vera et al., 2011 (25)	Endo-EzeTM, Ultradent, USA	27	Side vented	1	NR	2
de Gregorio et al., 2010 (17)	ProRinse, Dentsply Sirona, USA	30	Side vented	1.5	30	2
Bronnec F et al., 2010 (28)	Monoject, Hampshire, UK	27	Notched tip	1	NR	3

NR: Not reported, WL: Working length

canals. Dhaimy et al. (26) calculated the irrigant penetration in straight canal using an index of irrigant penetration (penetration length of the irrigant divided by the WL). The study concluded that MDA using a GP cone permits better penetration of the irrigant over CNI.

Results of Syntheses

IAT vs CNI

In the overall meta-analyses of straight canals, the pooled estimate (% diff) of irrigant delivery up to the WL by the different IATs when compared to CNI was 51.94%, 95% CI: 39.20–64.67% (Fig. 2). In curved canals, the pooled estimate was SMD: 1.08, 95% CI: 0.64–1.52 (Fig. 3a); % diff: 34.29%, 95% CI: 20.83–47.75% (Fig. 3b). These results revealed significant improvement in the irrigant delivery up to the WL in IATs over CNI.

Subgroup Analysis

a) Subgroup analysis and comparison of individual IATs with CNI in straight canals: ANP was the most effective and significant IAT for irrigant delivery up to the WL (% diff: 91.70%, 95% CI: 75.63–107.77%) followed by PUI, SI and MDA technique (Fig. 2).

b) Subgroup analysis and comparison of ANP with PUI and with SI in straight canals: In both of the above, ANP revealed a significant difference in the irrigant penetration (% diff: 52.35%, 95% CI: 35.10–69.59%) (Fig. 4).

c) Subgroup analysis and comparison of individual IATs with CNI in curved canals: ANP was the most effective and significant IAT for irrigant delivery up to the WL (SMD: 1.45, 95% CI: 0.77–2.13) followed by PUI, SI and MDA technique (Fig. 3a).

d) Subgroup analysis and comparison of IATs performed in both straight and curved canals: The irrigant penetration of PUI in both straight canals (% diff: 47.96%, 95% CI: 33.10–62.82%) and curved canals (% diff: 41.78%, 95% CI: 26.30–57.27%) did not reveal a significant difference thus attributing to the efficacy of PUI. However, a significant difference was observed in the irrigant penetration of SI in curved canals (% diff: 19.90%, 95% CI: 9.56–30.24%) when compared to straight canals (% diff: 38.40%, 95% CI: 245 27.17–49.62%) (Fig. 5).

Heterogeneity Tests

The overall meta-analyses of the straight canals (I^2=99.87%, P<0.001) and the curved canals (I^2=96.41%; I^2=97.43%, P<0.001) revealed significant heterogeneity. Similarly, significant heterogeneity also existed within the subgroup analyses for irrigant penetration up to the WL. Therefore, the random-effects model was used (Figs. 2-5).

Reporting Biases

To look for the presence of publication bias, funnel plot analysis was carried out which included the irrigant penetration up to the WL in straight canals. Funnel plot analysis revealed

TABLE 4. Characteristics of different irrigant activation techniques used

Irrigant activation techniques used	Study	Characteristics of use					
		File size [manufacturer]	**Mounting device [Manufacturer]**	**Activation time for each cycle (s)**	**Power setting**	**No. of cycles**	**Insertion depth from the WL (mm)**
Passive ultrasonic irrigation technique	Castelo-Baz et al., 2021 (29)	ISO 15 [ESI file]	EMS, Nyon, Switzerland	20	4	3	1
	Souza et al., 2019 (30)	20/.01 [Irrisonic]	Jet Sonic, Brazil	20	20%	3	2
	Khare et al., 2017 (31)	ISO 10 [IrriSafe, Satelec]	Satelec, Acteon, France	20	3	3	2
	Kamra et al., 2016 (24)	NR[U-Mani]	Top selector, APOZA	20	5	NR	3
	Castelo-Baz et al., 2016 (32)	ISO 15 [ESI file]	EMS, Nyon, Switzerland	20	6	3	1
	Kanumuru et al., 2015 (12)	ISO 20 [IrriSafe, Satelec]	Suprasson Newtron XS	20	5	NR	2
	Sáinz-Pardo et al., 2014 (27)	25/.01 [Irri-S (VDW)]	VDW, Germany	30	25	NR	2
	Merino et al., 2013 (36)	ISO 25 (untapered) [Irri-S (VDW)]	VDW, Germany	30	25	NR	2
	Pawar et al., 2013 (33)	ISO 20	NR	30	3	NR	0
	Spoorthy et al., 2013 (18)	ISO 25 [IrriSafe, Satelec]	Suprasson P5 Booster, Satelec, Acteon, France	30	5	NR	1
	Castelo-Baz et al., 2012 (34)	ISO 15 [IrriSafe, Satelec]	Satelec, Acteon, France	20	6	3	1
	Munoz and Camacho-Cuadra., 2012 (15)	ISO 20 and 25 [Irrisafe, Satelec]	NSK, Japan	30	NR	NR	0
	Vera et al., 2011 (25)	NR [SybronEndo]	MiniEndo, SybronEndo	20	5	NR	3
	de Gregorio et al., 2010 (17)	ISO 20 [IrriSafe, Satelec]	Satelec, Acteon, France	30	3	NR	0
		Volume (mL)	**Activation time (s)**	**Macrocannula depth from the WL**		**Microcannula depth from the WL (mm)**	
Apical Negative pressure technique (EndoVac®, Discus Dental, Culver City, CA)	Abrar S et al., 2019 (23)	NR	NR	Middle third of the canal		0	
	Spoorthy et al., 2013 (18)	1.5	30	Pulp chamber		0	
	de Gregorio et al., 2012 (35)	NR	30	Coronal third of the canal		0	
	Munoz and Camacho-Cuadra., 2012 (15)	1	30	Pulp chamber		0	
	de Gregorio et al., 2010 (17)	1.5	30	NR		0	
		Power setting (cpm)	**Activation time (s)**	**File size/taper**		**Insertion depth from the WL (mm)**	
Sonic Irrigation technique (Dentsply, USA)	S DPA et al., 2022 (37)	10,000	60	15/.02		2	
	Helmy et al., 2016 (13)	NR	30	25/.04		Deep without binding	
	Kanumuru et al., 2015 (12)	10,000	30	25/.04		2	
	Sáinz-Pardo et al., 2014 (27)	10,000	30	25/.04		2	
	Merino et al., 2013 (36)	10,000	30	25/.04		2	
	Pawar et al., 2013 (33)	NR	30	25/.04		0	
	de Gregorio et al., 2010 (17)	10,000	30	35/.04		0	
		Vertical strokes	**Activation time (s)**	**Gutta-percha cone size/taper**	**Amplitude (mm)**		**Insertion depth from WL (mm)**
Manual dynamic Activation	S DPA et al., 2022 (37)	NR	NR	NR	NR		1
	Khare et al., 2017 (31)	100	60	25/.06	2 to 3		NR
	Dhaimy S et al., 2016 (26)	3	3	25/.04	5		1
	Pawar et al., 2013 (33)	NR	30	NR/.06	NR		2
	Bronnec F et al., 2010 (28)	3	NR	20/.06	5		NR

NR: Not reported, WL: Working length

TABLE 5. Risk of bias assessment of the included studies

Study	Study design	Risk of Bias assessment				Total	Percentage (%)	Risk of bias
		Study design, specimen selection & randomization	Instrumentation	Irrigation and IATs used	Outcome assessment			
S DPA et al., 2022 (37)	*In vitro*	7/8	3/3	8/13	3/4	21/28	75	Low risk
Castelo-Baz et al., 2021 (29)	*In vitro*	6/8	3/3	13/13	4/4	26/28	93	Low risk
Abrar S et al., 2019 (23)	*In vivo*	5/8	2/3	8/13	3/4	18/28	64	Medium risk
Souza et al., 2019 (30)	*In vitro*	5/8	3/3	13/13	4/4	25/28	89	Low risk
Khare et al., 2017 (31)	*In vitro*	3/8	3/3	13/13	4/4	23/28	82	Low risk
Dhaimy S et al., 2016 (26)	*Ex vivo*	4/8	3/3	12/13	3/4	22/28	79	Low risk
Helmy et al., 2016 (13)	*In vitro*	6/8	2/3	9/13	4/4	21/28	75	Medium risk
Kamra et al., 2016 (24)	*In vivo*	4/8	3/3	12/13	4/4	23/28	82	Low risk
Castelo-Baz et al., 2016 (32)	*In vitro*	7/8	3/3	12/13	4/4	26/28	93	Low risk
Kanumuru et al., 2015 (12)	*In vitro*	6/8	3/3	12/13	4/4	25/28	89	Low risk
Sáinz-Pardo et al., 2014 (27)	*Ex vivo*	7/8	3/3	11/13	4/4	25/28	89	Low risk
Merino et al., 2013 (36)	*In vitro*	8/8	3/3	11/13	3/4	25/28	89	Low risk
Pawar et al., 2013 (33)	*In vitro*	3/8	3/3	9/13	2/4	17/28	61	Medium risk
Spoorthy et al., 2013 (18)	*In vitro*	5/8	2/3	12/13	4/4	23/28	82	Low risk
Castelo-Baz et al., 2012 (34)	*In vitro*	6/8	2/3	13/13	4/4	25/28	89	Low risk
de Gregorio et al., 2012 (35)	*In vitro*	5/8	3/3	9/13	4/4	21/28	75	Medium risk
Munoz and Camacho-Cuadra., 2012 (15)	*In vivo*	4/8	2/3	11/13	4/4	21/28	75	Medium risk
Vera et al., 2011 (25)	*In vivo*	5/8	3/3	12/13	4/4	24/28	86	Low risk
de Gregorio et al., 2010 (17)	*In vitro*	4/8	3/3	12/13	4/4	23/28	82	Low risk
Bronnec F et al., 2010 (28)	*Ex vivo*	6/8	3/3	10/13	3/4	22/28	79	Low risk

The numbers represent how many of the requirements were met by each study. High risk of bias (score <50%), medium risk 614 (score 50%–75%), or low risk (score >75%). The overall risk of bias was 81.4% indicating a 'low risk of bias' across studies

the presence of publication bias (Fig. 6). Additionally, Egger's regression test also suggested the presence of publication bias (P<0.001).

DISCUSSION

Overall, the meta-analyses revealed that IATs considerably improved the irrigant penetration up to the WL when compared to CNI. The narrative synthesis does support the hypothesis that IATs result in more irrigant penetration than CNI. This notion is further strengthened by Tay et al. (40) who reported that the irrigation with CNI did not reach up to the WL owing to the presence of an apical vapour lock generated by the organic decomposition of NaOCl into bubbles of carbon dioxide and ammonium that severely impacts the debridement efficiency of CNI. Sáinz-Pardo et al. (27) reported that the percentage of vapour lock formation for CNI (70%) is greater than SI (60%) and PUI (30%).

The effectiveness of individual IATs on an irrigant penetration was analyzed further using subgroup analysis. MDA creates higher intracanal pressure changes by using vertical strokes of a GP cone in the canal which leads to the displacement of the apical air bubble that is responsible for the vapour lock effect resulting in better irrigant penetration (41). However, the major drawback of this method was operator-dependent which could not be standardized, and the frequency of irrigant extrusion was higher, resulting in postoperative pain (42). SI helps in eliminating pulp tissue remnants and dentine debris, breaking vapour locks and transferring solutions apically and laterally (27,39). PUI has a synergistic effect on the tissue-dissolving capabilities of NaOCl (43). However, both pose shortcomings like inadvertent contact of the tip to the canal wall due to the size and complex anatomy of the root canal system (44), loss of cleaning efficacy (45), and excessive removal of dentine (46). To overcome the above-mentioned drawbacks, ANP was introduced as it has the maximum irrigant delivery up to the WL, helps eliminate pulp debris (16, 47), and ensures effective disinfection in the apical third (43). This can be accredited to the design of the microcannula of the EndoVac® (Discus Dental, Culver City, CA, USA). The micropores in the cannulae ensure that the canal walls are thoroughly cleaned and thus prevent clogging (17). A negative pressure created by the positioning of the microcannula up to the WL helps pull the irrigant supplied by the master delivery tip (17). Thus a steady flow of fresh irrigants is sustained, thereby permitting the efficient exchange of irrigants in the apical third (16, 17). Moreover, ANP minimizes apical irrigant extrusion as compared to CNI (48).

All the included studies were performed in direct comparison with CNI. Apical patency was maintained in the majority of the studies. Vera et al. (25) reported that improved irrigant

TABLE 6. Summary of the results of the individual studies

Study	Study design	IATs	Sample size	Straight canal *n* (%)	Curved canal *n* (%)
	Irrigant penetration reached up to the WL				
Castelo-Baz et al., 2021 (29)	*In vitro*	CNI	20	0 (0)	0 (0)
		PUI	20	13 (65)	7 (35)
Souza et al., 2019 (30)	*In vitro*	CNI	20	12 (60)	-
		PUI	20	16 (80)	-
Kamra et al., 2016 (24)	*In vivo*	CNI	15	7 (46.7)	-
		PUI	15	12 (80)	-
Castelo-Baz et al., 2016 (32)	*In vitro*	CNI	20	-	0 (0)
		PUI	20	-	8 (40)
Kanumuru et al., 2015 (12)	*In vitro*	CNI	15	9 (60)	-
		PUI	15	15 (100)	-
		SI	15	15 (100)	-
Sáinz-Pardo et al., 2014 (27)	*Ex vivo*	CNI	10	2 (20)	-
		PUI	10	7 (70)	-
		SI	10	4 (40)	-
Merino et al., 2013 (36)	*In vitro*	CNI	4	-	0 (0)
		PUI	15	-	10 (66.7)
		SI	15	-	3 (20)
Pawar et al., 2013 (33)	*In vitro*	CNI	20	0 (0)	-
		PUI	20	15 (75)	-
		SI	20	10 (50)	-
		MDA	20	5 (25)	-
Spoorthy et al., 2013 (18)	*In vitro*	CNI	16	4 (25)	-
		PUI	16	6 (37.5)	-
		ANP	16	16 (100)	-
Castelo-Baz et al., 2012 (34)	*In vitro*	CNI	20	0 (0)	-
		PUI	20	14 (70)	-
de Gregorio et al., 2012 (35)	*In vitro*	CNI	15	0 (0)	-
		ANP	15	15 (100)	-
Vera et al., 2011 (25)	*In vivo*	CNI	21	-	6 (28.6)
		PUI	21	-	12 (57.1)
de Gregorio et al., 2010 (17)	*In vitro*	CNI	20	0 (0)	-
		PUI	20	13 (65)	-
		ANP	20	20 (100)	-
		SI	20	8 (40)	-
Bronnec F et al., 2010 (28)	*Ex vivo*	CNI	30	-	24.4 (81.4)
		MDA	30	-	30 (100)
	Distance between the WL and maximum irrigant penetration (mean±SD)				
S DPA et al., 2022 (37)	*In vitro*	CNI	15	-	1.23±0.25
		SI	15	-	0.50±0.18
		MDA	15	-	0.71±0.04
Abrar S et al., 2019 (23)	*In vivo*	CNI	20	-	1.88±0.35
		ANP	20	-	0.10±0.14
Khare et al., 2017 (31)	*In vitro*	CNI	12	2.94±0.48	-
		PUI	12	0.50±0.48	-
		MDA	12	1.38±0.46	-
Helmy et al., 2016 (13)	*In vitro*	CNI	10	-	3.04±2.01
		SI	10	-	0.06±0.12
Munoz and Camacho-Cuadra., 2012 (15)	*In vivo*	CNI	10	-	1.51±0.43
		PUI	10	-	0.21±0.25
		ANP	10	-	0.42±0.30
	Index of irrigant penetration (mean±SD)				
Dhaimy S et al., 2016 (26)	*Ex vivo*	CNI	60	0.68±0.11	-
		MDA	60	0.88±0.07	-

Index of irrigant penetration = penetration length of the irrigant divided by the working length (WL); Summary of the results of 20 studies evaluated the irrigant penetration reached up to the WL; 14 out of 20 studies represent irrigant penetration up to the WL in the given number of samples (*n*) with percentages (in parentheses) in both straight and curved canals while the reminder of 6 studies' results is demonstrated in terms of mean±standard deviation (SD).

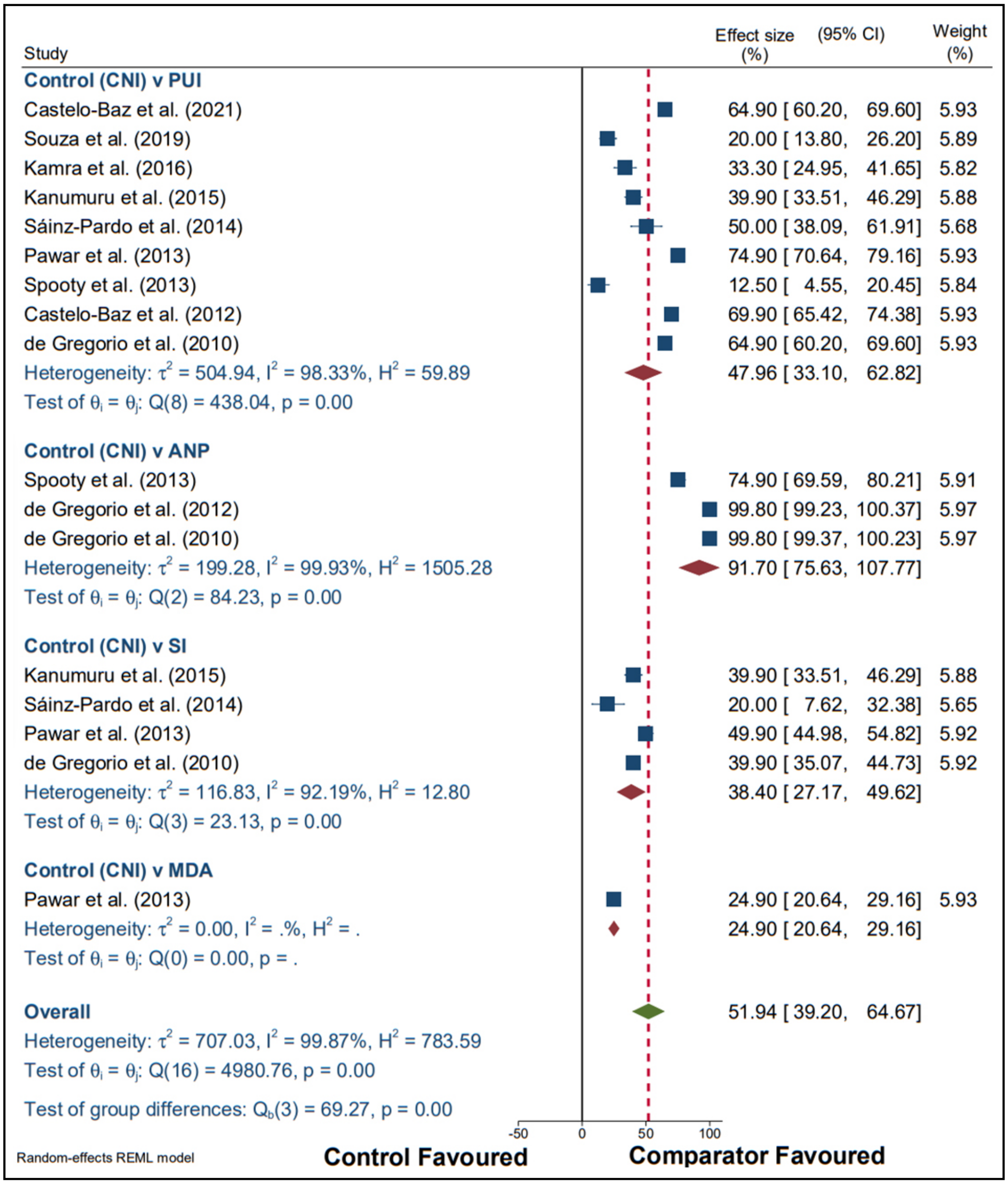

Figure 2. Forest plot evaluating the percentage difference (% diff) of irrigant penetration up to the working length in straight canals of the mature permanent teeth following the use of IATs when compared to CNI

IATs: Irrigant activation techniques, CNI: Conventional needle irrigation technique

penetration depth results from maintaining the apical patency thereby eliminating the vapour lock effect and inhibiting the collection of debris in the apical third of the canal. Furthermore, instruments with varied canal taper ranging from 2–8% with an average of 4% were used in all of the studies. Reduction in canal taper tends to influence the ability of SI to reach up to the WL, whereas it does not influence the ability of PUI in the curved canals (27, 36). Boutsioukis et al. (49) reported that apical preparation size can affect the irrigant penetration depth. Brunson et al. (50) observed that 40/.04 taper preparations resulted in a percentage gain of 44% irrigant penetration. According to Salzgeber RM and Brilliant JD (51), and Chow T (52), flaring of the root canal for greater irrigant penetration requires a minimum of ISO 30.

The ideal size of the needle (>27 gauge) facilitates greater penetration of irrigant up to the apical third of the canal (53). It is noteworthy that S DPA et al. (37), Dhaimy et al. (26) and Pawar et al. (33) used large needles (<27 gauge) which does not confer to current clinical standards (53). Majority of the included studies used side-vented needle for irrigation. Boutsioukis et al. (11) reported that an open-ended flat needle was capable of achieving maximum irrigant penetration up to the WL when compared to a side-vented needle. However, the use of the side-vented needle was safer to prevent irrigant extrusion (54). In the studies using PUI, the power setting ranged from 3 to 25 for three cycles, whereas SI was set at a constant of 10,000 cycles per minute for a period of 30–60 seconds. The information about the power settings used was not available in the studies of Helmy et al.(13) and Pawar et al. (33). Al-Jadaa

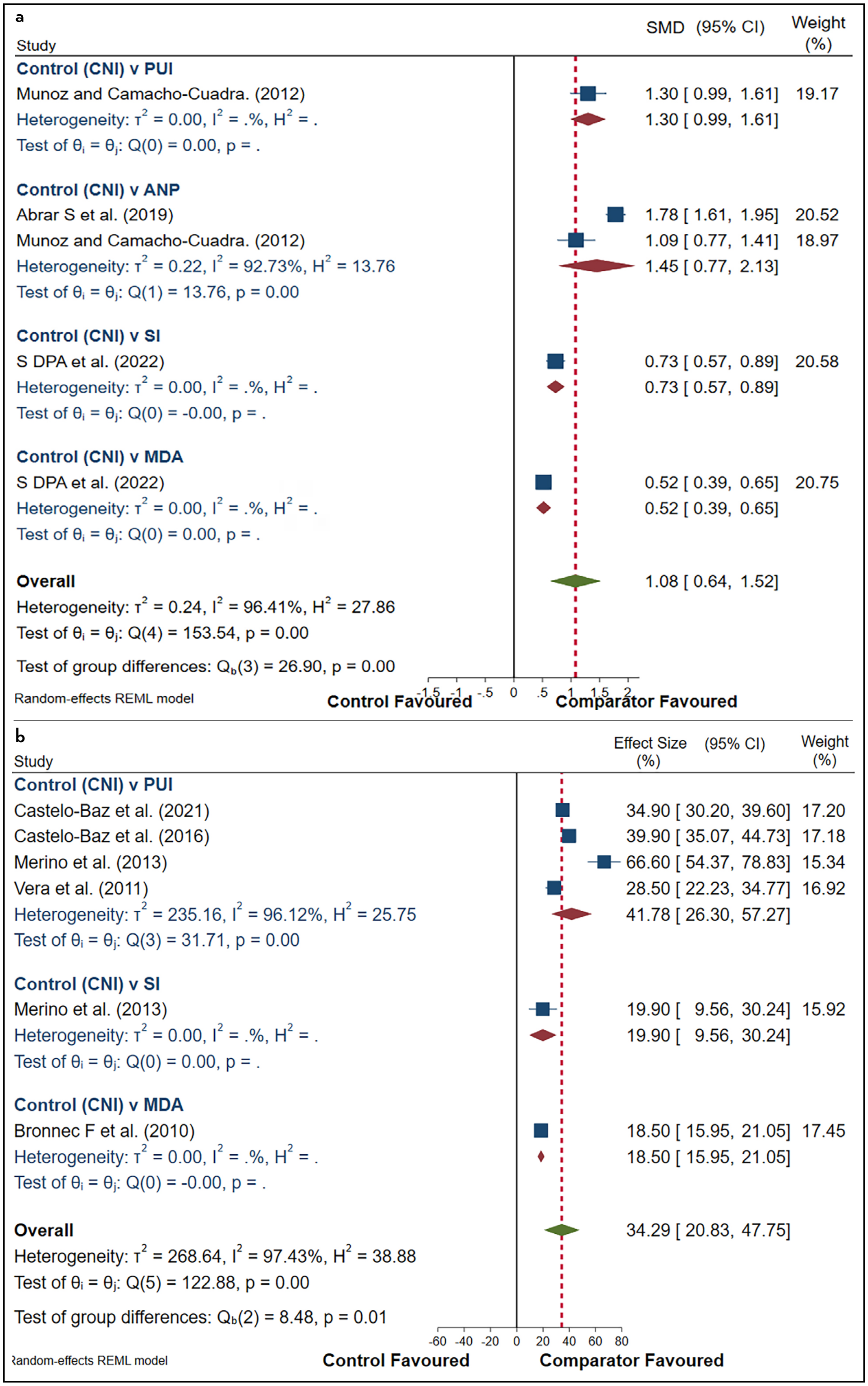

Figure 3. (a) Forest plot evaluating the standardized mean difference (SMD) of irrigant penetration up to the working length in the curved canals of the mature permanent teeth following the use of IATs when compared to CNI. (b) Forest plot evaluating the percentage difference (% diff) for irrigant penetration up to the working length in the curved canals of the mature permanent teeth following the use of IATs when compared to CNI.

SMD: Standardized mean difference, CI: Confidence interval, IATs: Irrigant activation techniques, CNI: Conventional needle irrigation technique

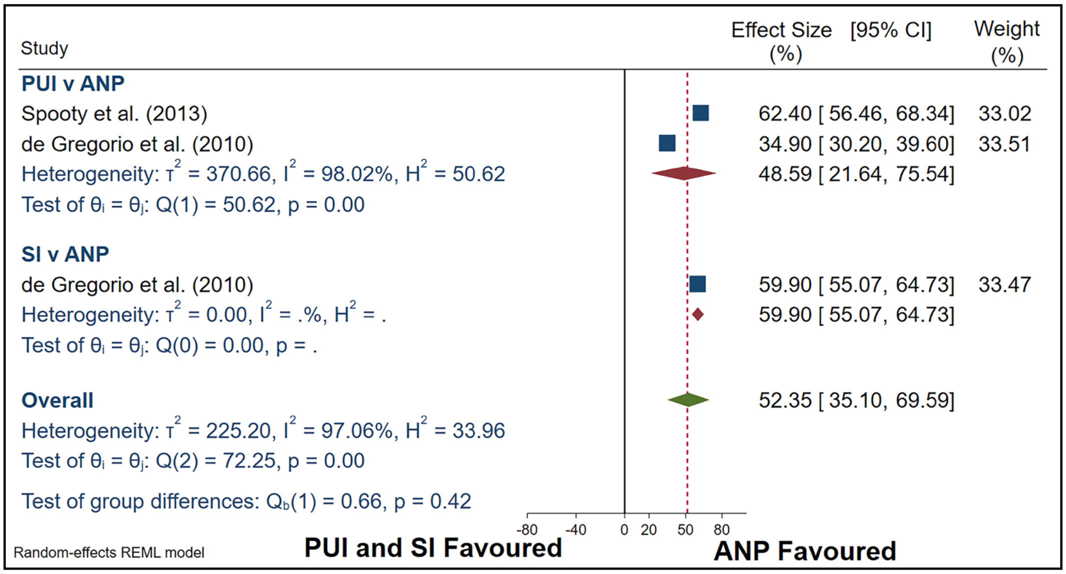

Figure 4. Forest plot evaluating the percentage difference (% diff) of irrigant penetration following the use of PUI and SI in comparison with ANP in the straight canals of mature permanent teeth

CI: Confidence interval, PUI: Passive ultrasonic irrigation, ANP: Apical negative pressure, SI: Sonic irrigation

et al. (55) observed that higher intensity of 29 x 10^3 hertz created by PUI promotes better irrigant penetration when compared to the lower intensity of 166 hertz created by SI. Jiang et al. (56) reported that power intensity has a great impact on the degree of irrigant penetration. In the studies using PUI, activation time for each cycle ranged from 20–30 seconds and for SI ranged from 30–60 seconds, whereas ANP was constant at 30 seconds. Nagendrababu et al. (57) and Retsas et al. (58) stated that activation time has a great implication on the degree of irrigant penetration. In PUI, the high flexibility of the ESI file (EMS, Nyon, Switzerland) when compared to the stainless steel ultrasonic tips, favours the irrigant penetration (29, 32). Various passive ultrasonic devices are commercially available of which IrriSafe® (Satelec, France) was the most commonly reported ultrasonic device among the included studies. Similarly, various manufacturers for sonic devices are commercially available. However, EndoActivator® (Dentsply, USA) was the only one to have been clinically evaluated and reported during the period of review. Studies employing ANP used EndoVac® (Discus Dental, Culver City, CA, USA). In all the studies that included ANP, microcannula was passively inserted to a depth equal to WL, whereas in the majority of studies using PUI and SI, tips were not inserted to a depth equal to the WL. In all the studies, the needle insertion depth in CNI was reported as being 2 mm or more short of the WL. This could be the reason that CNI is ineffective in cleaning the apical third of the canal due to the confined level of needle penetration (11). Studies reported that needle insertion depth has a great impact on the degree of irrigant penetration (11, 59, 60).

In the studies evaluated by the direct observation method, standardized decalcification, clearing and re-hardening protocols were used. ICS was prepared by mixing dye with NaOCl with a concentration ranging from 10–50%. Information about the concentration of ICS was lacking in number of studies [direct observation method (33) and radiographic method (13, 15, 23, 24, 26, 37)]. These two different types of assessing the outcome could also have introduced bias in the results. Diverse contrast solutions were employed across the studies with various concentrations of different manufacturers which may have introduced bias in the results. Studies by S DPA et al. (37), Kanumuru et al. (12), and Munoz and Camacho (15) found the density, viscosity, and surface tension of the ICS to be similar to that of NaOCl. However, Sáinz-Pardo et al. (27), Helmy et al. (13), Spoorthy et al. (18), and Dhaimy et al. (26) found that the above physical characteristics to be dissimilar which may affect irrigant penetration depth. According to de Gregorio et al. (39), when compared to the direct observation method visually, the radiographic evaluation method evidenced less penetration of ICS because the concentration of ICS may not facilitate detection radiographically. Thus proving the direct observation method to be more sensitive and reliable.

Methodological differences represent a likely source of bias due to one or more of the following reasons. i) Lack of adequate information or reported variations in irrigation procedure across the groups. ii) Varying concentrations of ICS of different manufacturers may have affected the radiographic evaluation of irrigant penetration up to the WL. iii) Other factors like teeth sampled, depth of penetration, size of the needle, concentration, volume and flowrate of irrigants used, variations in the apical size and canal taper could also introduce bias. In the majority of these studies, the outcome evaluators were blinded. Hence, assessment bias was minimized and did not influence the results.

Effective IATs with increased irrigant penetration promote greater cleaning and canal debridement (48). The systematic review conducted by Susila A and Minu J (61) consists of a single *in vivo* study (15) which does not provide concrete evidence of irrigant delivery up to the WL using IATs (PUI and ANP). The effectiveness of irrigation is assured only when the irrigant is activated upon contact with the whole root canal

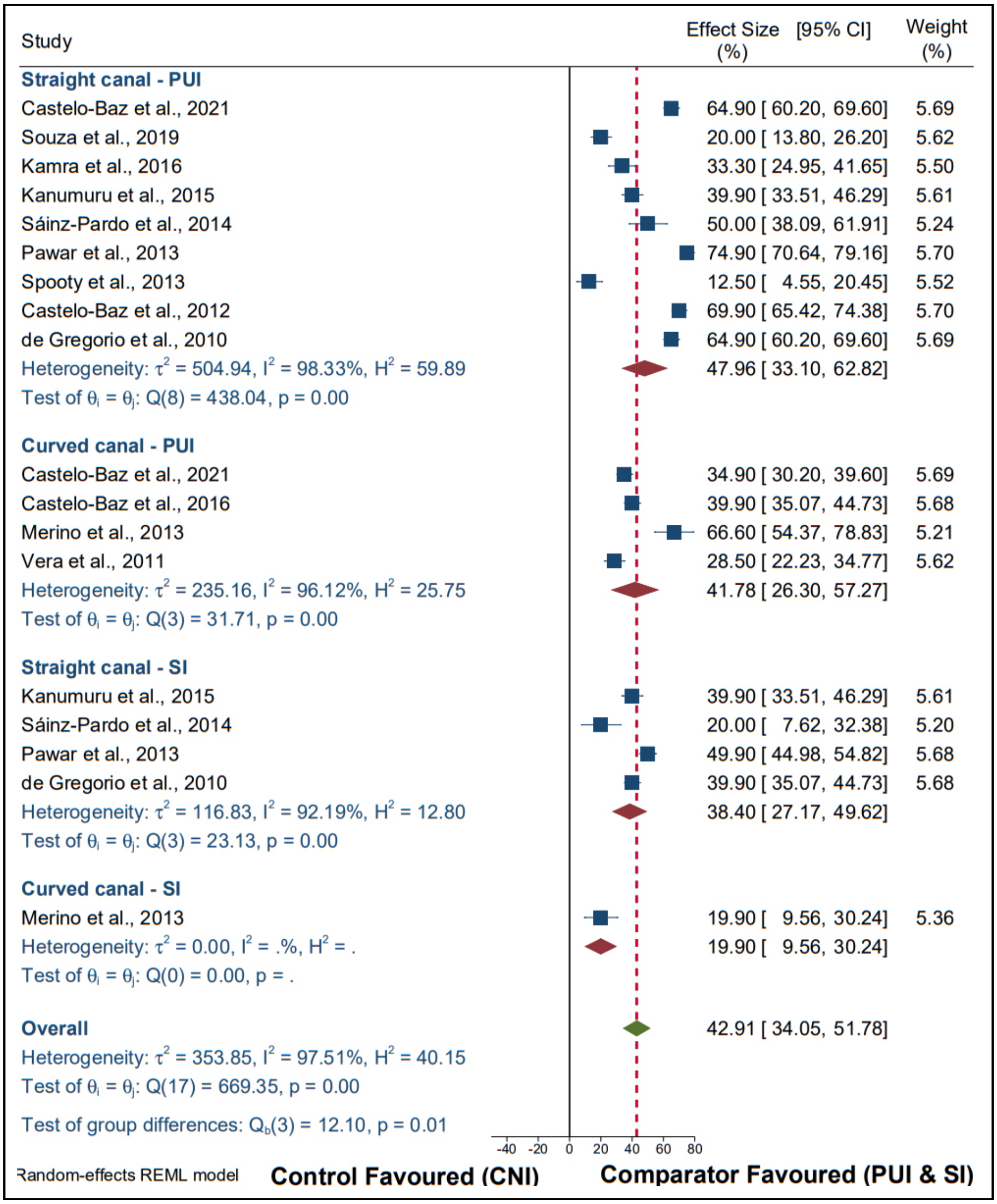

Figure 5. Forest plot evaluating the percentage difference (% diff) of irrigant penetration following the use of PUI v CNI and SI v CNI in the straight and curved canals of mature permanent teeth

CI: Confidence interval, CNI: Conventional needle irrigation technique, PUI: Passive ultrasonic irrigation, SI: Sonic irrigation

system (9). The mere presence of NaOCl in the apical third does not ensure thorough cleanliness and disinfection (62), as NaOCl requires adequate time, concentration, and contact to break down organic substances and affect the microbes protected by biofilm for the success of endodontic therapy. Even though the authors accept the limitations of the data, the consistency within the results and the existing literature support the hypothesis that IATs have better penetration depth up to the WL in straight and curved canals when compared to CNI. For all the above reasons, the null hypothesis is rejected.

Strength and Limitations

The key strengths of this systematic review and meta-analysis were: i) following a rigorous protocol, ii) testing a prior hypothesis. iii) low risk of bias across the included studies. The overall risk of bias was found to be 81.4% which symbolizes the true treatment effect.

The limitations of our review pertain to the following: i) High heterogeneity found across the studies, hence the conclusion of the meta-analysis as a reliable interpretation should be viewed with caution. ii) Lack of standardization prevents the comparison among the various IATs. iii) The findings in 16 of 20 studies are based on laboratory experiments. iv) Alterations in the physical characteristics of NaOCl due to the addition of radiopaque substances. v) The lack of quantitative volumetric data and the spreading pattern of ICS within the canal when compared to the existing data of NaOCl. vi)

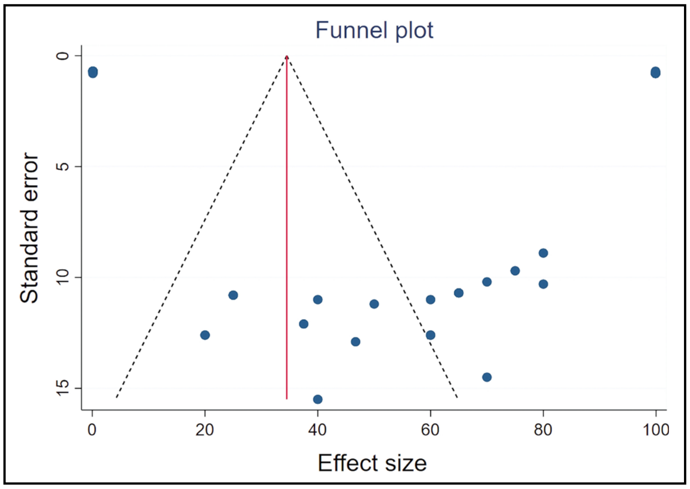

Figure 6. Funnel plot analysis with 95% CI for the irrigant penetration up to the working length in straight canals of matured permanent teeth

CI: Confidence interval

Anatomical barriers, variations in the procedures, and concentrations of radiopaque substances employed in the studies may also influence the visual radiographic assessment of irrigant penetration depth.

Future Research

An ideal protocol for assessing irrigant penetration does not exist, hence future research should address the following:

1. Maintaining a standardized protocol for using IATs with a robust experimental model.
2. Use of randomized controlled design.
3. Standardization of the concentration of radiopaque substance used with NaOCl to obtain accurate visual images of irrigant penetration.
4. *In vivo* procedures should include fluid irrigation dynamics assessment when using radiopaque substances with similar physical characteristics as that of NaOCl.
5. Apical extrusion of different IATs needs to be evaluated *in vivo*.
6. Evaluation of *in vivo* effect of PUI and ANP on disinfection and debridement.
7. Investigation of the synergistic impact of ANP and PUI irrigation on more complex root structures.

CONCLUSION

This review helps the clinician establish the importance of employing IATs to disinfect the main canal up to the WL and gain greater success with the outcomes of endodontic therapy. Within the limitations of the studies reviewed in this paper, the authors conclude that IATs improve irrigant penetration when compared to CNI and therefore their use during root canal therapy is recommended. In both straight and curved canals, ANP is the most effective IAT in delivering the irrigant up to the WL followed by PUI, SI and MDA techniques. Hence adaptation of recent IATs in routine endodontic practice is recommended.

Disclosures

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APPENDIX 1. Quality requirements during risk of bias assessment of included studies

Study design, specimen selection, & randomization

1. Prior sample size estimation
2. Type of teeth
3. Working length/ Standardized root length
4. Canal Curvature (straight/ curved)
5. Inclusion & Exclusion criteria
6. Random allocation to different groups
7. Method used to simulate periapical tissues
8. Verification of the presence of single canal for anterior teeth or separate canals for posterior teeth

Instrumentation

1. Patency
2. Apical root canal size and taper
3. Identical standardized instrumentation in all groups

Irrigation and IATs used

1. Concentration of NaOCl used
2. Type, concentration, manufacturer of contrast solution
3. Needle: Manufacturer, type and size (CNI group)
4. Needle insertion depth from the WL (CNI group)
5. Volume and duration/flow rate of irrigant delivered (CNI group)
6. Device model and manufacturer (Test group/groups)
7. File/GP cone: type, size, length (Test group/groups)
8. File/GP cone: insertion depth from the WL (Test group/groups)
9. Power setting (Test group/groups)
10. Duration of activation (Test group/groups)
11. Volume of irrigant delivered (Test group/groups)
12. No. of cycles (Test group/groups)
13. Irrigation protocols identical in the compared groups except for activation cycles

Outcome assessment

1. Blinded/observer-independent assessment of the results
2. Reliability of outcome measured
3. Data summary (descriptive statistics) or complete raw data
4. Suitable statistical tests

APPENDIX 2. List of excluded articles with reason after full-text evaluation

Study	Reason for exclusion
Maiti et al., 2021	Duplication of study results of Castelo-Baz et al., 2021
Nangia et al., 2020	Open canal system
Pacheco-Yanes et al., 2020	Different outcome evaluated
Wahjuningrum et al., 2020	Outcome measures were not mentioned clearly
Galler et al., 2019	Penetration depth of irrigants into root dentine
Landolo et al., 2019	Penetration depth of irrigants into root dentine
Lorono et al., 2019	Different outcome evaluated
Andrade et al., 2016	Resin block
Adorno et al., 2015	Artificial Tooth model
Tanomaru-Filho et al., 2015a	Resin tooth
Tanomaru-Filho et al., 2015b	Transparent artificial tooth
Chávez-Andrade et al., 2014	Different outcome evaluated
Kungwani et al., 2014	Debris removal from root canal
Chen et al., 2013	Different outcome evaluated
de Gregorio et al., 2013	Different outcome evaluated
Peeters et al., 2013	Saline as an irrigating solution
Guerreiro-Tanomaru et al., 2013	Distilled water as an irrigating solution
Vera et al., 2012a	Different outcome evaluated
Vera et al., 2012b	Different outcome evaluated
Bronnec et al., 2010	Alternative IATs assessed
Brunson et al., 2010	Different outcome evaluated
Nielsen et al., 2007	Assessing efficacy of canal debridement
Khademi et al., 2006	Different outcome evaluated