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REVIEW ARTICLE

Effectiveness of various irrigant activation techniques on the penetration of sodium hypochlorite into lateral canals of mature permanent teeth: A systematic review and meta-analysis

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KEYWORDS

Apical negative pressure;
Irrigant penetration;

Abstract *Objective:* This review aimed to systematically review the effectiveness of various irrigant activation techniques (IATs) on the penetration of sodium hypochlorite (NaOCl) into the lateral canals of mature permanent teeth.

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Lateral canal;
Passive ultrasonic irrigation;
Root canal therapy

Methods: Electronic databases including MEDLINE (via PubMed), Scopus, ProQuest, and Cochrane Library were searched to identify laboratory studies evaluating the penetration of NaOCl into lateral canals following the use of apical negative pressure irrigation (ANP), passive ultrasonic irrigation (PUI), sonic irrigation (SI), and/or manual dynamic activation (MDA) techniques. Meta-analysis was performed for individual IATs in comparison with CNI into the lateral canals of both straight and curved root canals. On the basis of the previous literature and parameters, the risk of bias of the selected studies was evaluated with the help of a customized tool.

Results: Of the 983 records screened, 12 studies were selected to include in the systematic review, and 10 studies were selected for the *meta*-analysis. The total quality assessment across the included studies indicated a high quality (83.3%). Overall, the *meta*-analysis demonstrated IATs had significant improvement in the penetration of NaOCl into the lateral canals of straight canals (34.3%) over CNI. The subgroup analysis of individual IATs demonstrated PUI (60.9%) to be superior in the penetration into lateral canals of straight canals.

Conclusions: IATs improved the irrigant penetration into lateral canals and therefore their use during routine endodontic practice is recommended. In straight canals, PUI is the most effective IAT followed by ANP, SI, and MDA techniques.

Contents

1. Introduction

The success of endodontic therapy depends on the extensive removal of microorganisms and the thorough clearance of their by-products from the root canal system including lateral canals. Infection is unaffected by inadequately instrumented, irrigated, medicated or obturated canals, leading to endodontic therapy failing most often (Siqueira and Rôças, 2022). Even though biomechanical preparation contributes to effective disinfection of the main canal, in a majority of failure cases, bacteria in lateral canals, dentinal tubules, deltas, and isthmi may remain unaffected. Moreover, instruments cannot reach into the lateral canals owing to the obvious physical constraints, thus retaining the infection (Carr et al., 2009; Nair et al., 1990; Vieira et al., 2012).

The irrigant and its method of delivery are the two elements linked with optimal irrigation. The ideal requirements of a root canal irrigant are broad antimicrobial activity, endotoxin neutralization, smear layer removal, and necrotic pulpal remnants and vital pulp dissolution (Zehnder, 2006). Sodium hypochlorite (NaOCl) is the gold standard for antibacterial activity and tissue dissolution. However, it does not remove the smear layer (Baumgartner and Mader, 1987). Thus, NaOCl is being used in combination with ethylenediamine tetraacetic acid (EDTA), which aids in the smear layer removal (Çalt and Serper, 2002).

To address the constraints of conventional needle irrigation (CNI), various irrigant activation techniques that have been aided by machines are introduced. The most common are apical negative pressure irrigation (ANP), passive ultrasonic irrigation (PUI), sonic irrigation (SI), and manual dynamic activation (MDA) techniques.

ANP is a new technique of delivering irrigants into the root canal that minimizes the risk of irrigant extrusion (Nielsen et al., 2007). A master delivery tip is utilized to deliver NaOCl within the pulp chamber, and a small suction tip is placed up to the working length (WL), providing a negative pressure that draws NaOCl (de Gregorio et al., 2010; Nielsen et al., 2007; Spoorthy et al., 2013). PUI promotes cavitation by the transfer of microcurrents through ultrasonic waves with its blunt tip (Huffaker et al., 2010). It eliminates microorganisms, smear layer, and debris without violating the apical constriction (Munoz and Camacho-Cuadra, 2012). SI is based on sonic energy, which helps break down the smear layer and biofilm through hydrodynamic phenomena that produce cavitation and acoustic streaming. This results in extensive cleaning and disinfection (Helmy et al., 2016; Kanumuru et al., 2015). MDA is a simple and cost-effective method of activating irrigants. It uses a well-fitting gutta percha (GP) cone that is repeatedly inserted into an instrumented root canal to get rid of the vapour lock (Gu et al., 2009).

There is a strong positive correlation between the healing of periapical lesion and the obturation of lateral canals (Seltzer et al., 1967). Therefore, lateral canals must be completely disinfected before obturation (Weine, 1984). Moreover, the anatomy of the curved root canal also impairs cleaning efficiency. As a consequence, mechanical instrumentation in conjunction with chemical disinfection will lead to improved canal cleanliness (Jaju S and Jaju P, 2011). Despite the vast availability of literature illustrating the effectiveness of the aforementioned techniques, the penetration of NaOCl into lateral canals is varied and often contradictory. There is uncertainty over the effectiveness of the IATs in the lateral canals. Therefore, it is crucial to investigate which of the IATs could be used effectively to introduce NaOCl into the lateral canals. The present review aimed to evaluate the effectiveness of various IATs on the penetration of NaOCl into the lateral canals of mature permanent teeth when compared to CNI. A secondary objective was to evaluate the effectiveness of individual IATs on the irrigant penetration at various levels short of the WL and the overall penetration into the lateral canals of both straight and curved canals.

2. Methods

2.1. Protocol and registration

The present review was registered in PROSPERO (CRD42022304534) and adopted a PRISMA 2020 statement for conducting the review. This research is a part of the concurrent research projects of various IATs in the main and lateral canals.

2.2. PICO question

Are IATs more effective than CNI in the penetration of NaOCl into the lateral canals of mature permanent teeth?

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

Interventions (I):

1. Apical negative pressure irrigation technique (ANP),
2. Passive ultrasonic irrigation technique (PUI),
3. Sonic irrigation technique (SI),
4. Manual dynamic activation technique (MDA).

Comparison (C): Conventional needle irrigation technique.

Outcome (O): Improvement in the penetration of NaOCl into the lateral canals using direct observation and/or radiographic methods.

Study designs (S): Ex vivo and in vitro studies.

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

2.3. Selection criteria

2.3.1. Inclusion criteria

Laboratory studies with at least one irrigation technique as the trial arm; Studies employing a direct observation and/or radiographic approach to assess the effectiveness of the aforementioned IATs; Studies using NaOCl as an irrigant with or without EDTA and studies including extracted human teeth.

2.3.2. Exclusion criteria

Studies conducted on animal teeth, resin blocks, root-filled teeth, and open canal systems. Review articles, case series, and case reports.

2.4. Sources of information and Search strategy

The literature search was conducted by independent reviewers (R.S.K. and R.M.S.). The sources included Endodontic research in databases like MEDLINE (via PubMed), Scopus, ProQuest, and Cochrane Library (CENTRAL) with no language constraints. Additional search methods included Google Scholar, grey literature, hand searching of the International Endodontic Journal and the Journal of Endodontics, and the reference list from the included studies.

The PICO-style approach was adopted. All the indexed terms, medical subject headings (MeSH), keywords, and synonyms were selected using the current literature, reviewers' knowledge, and indexed databases. The search strategy was built for individual databases by employing truncations, and boolean operators with an emphasis on specificity and sensitivity (Appendixes A1–A4).

2.5. Selection Process, data Items, and collection process

The reviewers (R.S.K. and R.M.S.) independently screened the records to verify the search results. Zotero reference management software 5.0.96 (Corporation for Digital Scholarship, USA) was used in the selection process as a reference manager and to eliminate duplicate records as well. The reviewers located, filtered, screened, and read the full-text articles to determine the criteria for eligibility. Cohen's kappa statistics were used to calculate inter-examiner agreement (0.91). A third reviewer (A.V.A) settled disagreements among the reviewers. Both reviewers independently collected, assessed, extracted, and prepared the data in the Excel sheet. Any disagreement between the reviewers was settled through conversation.

2.6. Quality assessment and Risk of Bias

Each article was critically assessed independently by the reviewers using a predefined set of criteria based on the published systematic review (Căpută et al., 2019). The bias tool contained 28 questions, which were divided into four major domains. Each domain had a specific set of questions that were to be answered with a "yes" response, scoring 1 point, or a "no or unclear" response scoring 0 point. A summary score of the checklist was generated for individual studies on the basis of the quality and requirements fulfilled by the studies, which were further graded as high quality (score > 75 %), medium quality (score 50–75 %), or low quality (score < 50 %). The requirements employed to evaluate the quality and risk of bias of the included studies are shown in Appendix B.

2.7. Effect measures and synthesis method

In order to facilitate direct comparisons across the studies, *meta*-analysis was carried out using STATA® SE16.1, StataCorp LLC, Texas, USA. Outcomes were presented as effect size, which included standardized mean differences (SMD)/percentage differences (% diff) of the irrigant penetration into lateral canals alongside 95 % confidence interval (CI). The I^2 index and Cochran's Q-test were used in identifying heterogeneity across the studies. Sub-group analyses were also performed to explore heterogeneity. The significance level was set at $p \leq 0.05$. Funnel plot analysis was performed to identify any signs of publication bias. The certainty of evidence was assessed by Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) using the GRADEpro software, McMaster University, Canada (Guyatt et al., 2011).

3. Results

3.1. Study selection

The initial search, which included both electronic and manual searches resulted in a total of 983 records. Out of this, 739 records were found to be duplicates and were removed, leaving 244 to be assessed against the selection criteria. Following a title and abstract screening, 23 studies were found to be eligible for full-text evaluation. A total of 12 studies were selected to include in the systematic review (Castelo-Baz et al., 2021, 2016,2012; de Gregorio et al., 2012, 2010,2009; Kanumuru et al., 2015; Khare et al., 2017; Pawar et al., 2013; Souza et al., 2019; Spoorthy et al., 2013; Yaghi and Kaloustian, 2016), with the omission of 11 studies. The reasons for the exclusion are outlined in Appendix C. A total of 10 studies were qualified for inclusion in the *meta*-analysis (Castelo-Baz et al., 2021, 2016,2012; de Gregorio et al., 2012, 2010; Khare et al., 2017; Pawar et al., 2013; Souza et al., 2019; Spoorthy et al., 2013; Yaghi and Kaloustian, 2016) (Fig. 1).

3.2. Study characteristics

The characteristics of the included studies are summarized in Appendix D. All twelve included studies performed CNI for comparison with other IATs. A total of ten studies were performed on PUI of which IrriSafe® [Satelec, France] was the most commonly used passive ultrasonic device among the included studies. Four studies were performed on ANP using EndoVac® [Discus Dental, USA]. Four studies performed SI using EndoActivator® [Dentsply, USA], and two studies were performed on MDA. The characteristics of CNI and various IATs in the included studies are summarized in Appendix E.

Irrigating contrast solution (ICS) was prepared by mixing contrast/dye solution with NaOCl at a concentration ranging from 10 to 40 %. There was a lack of information about the concentration of ICS in the study by Pawar et al., 2013. In all of the investigations, the outcome was evaluated using the direct observation method, except for de Gregorio et al., 2009 who utilized both direct observation and radiographic methods. Nine out of twelve studies represent the outcome of irrigant penetration in terms of percentage in both straight and curved canals.

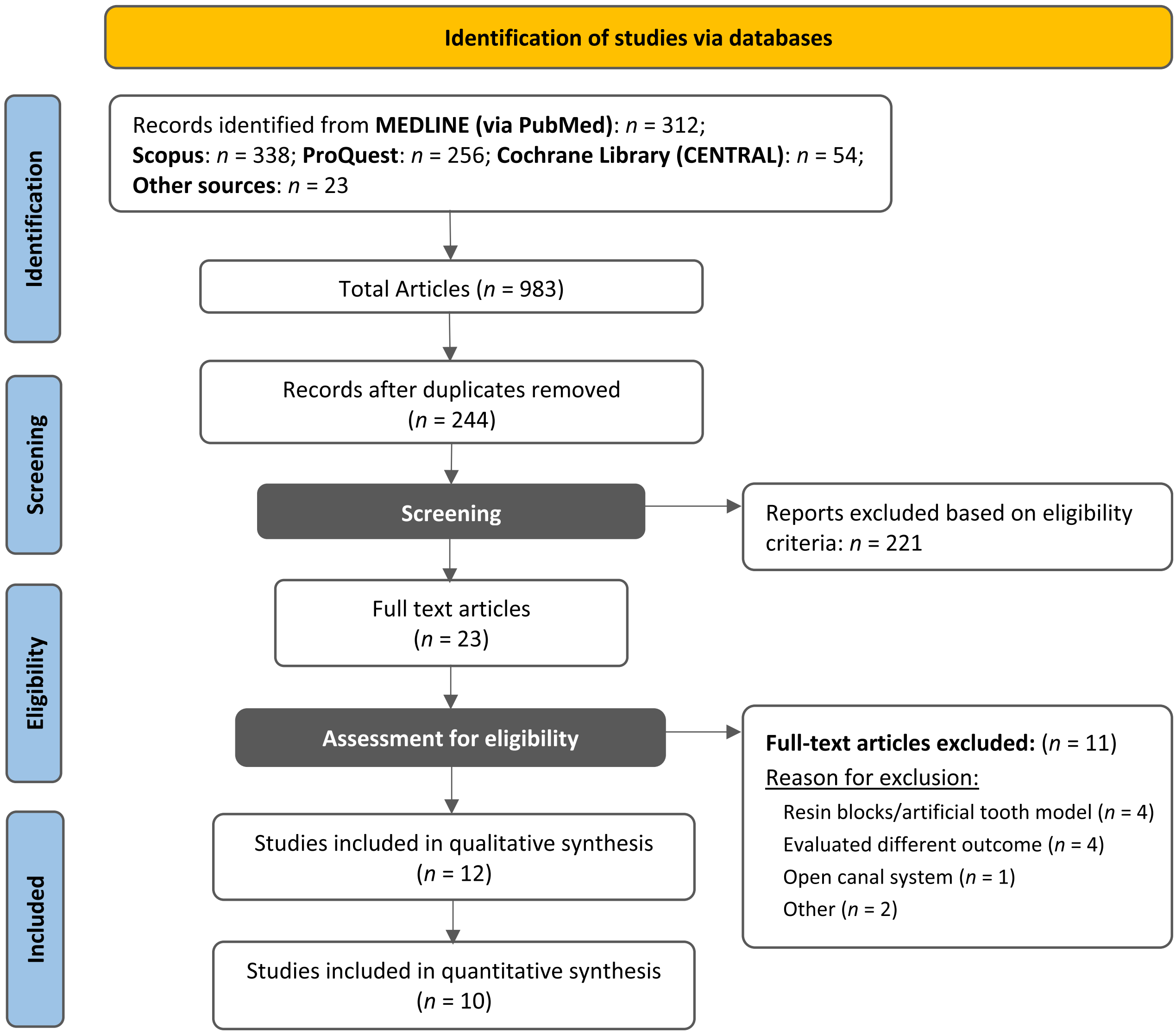


Fig. 1 PRISMA flow diagram.

The remaining three studies demonstrated as mean in straight canals. Table 1 summarizes the results of individual studies.

3.3. Risk of bias and quality assessment

The Kappa score for the interrater analysis was 0.89. The overall quality assessment across the included studies indicated a high quality, i.e., 83.3 % (61–93 %). Fig. 2a, Fig. 2b, and Appendix F summarize the risk of bias and quality assessment of the included studies.

3.4. Results of individual studies and meta-analysis

3.4.1. Straight canals

The *meta*-analyses with outcome presented as % diff demonstrated IATs to have a significant penetration of NaOCl into lateral canals over CNI at 2 mm [26.03 %] (Fig. 3a), 4 mm/4.5 mm [35.63 %] (Fig. 3b), 6 mm [39.90 %] (Fig. 3c) short of the WL, and the overall penetration into lateral canals [34.34 %] (Fig. 3d). Similarly, the *meta*-analysis with outcomes presented as SMD demonstrated IATs to have a significant penetration of NaOCl over CNI at various levels short of the WL and the overall penetration into lateral canals [SMD: 0.33] (Appendix Fig. A1).

The subgroup analysis of individual IATs with outcome presented as % diff demonstrated the most effective and significant penetration of NaOCl at various levels short of the WL and the overall penetration into lateral canals was found in PUI (Fig. 3a-3d). The outcome of subgroup analyses of individual IATs presented as SMD demonstrated the most effective and significant penetration of NaOCl (overall) to be PUI [SMD: 0.40] (Appendix Fig. A1).

3.4.2. Curved canals

The *meta*-analysis demonstrated that IATs have significant penetration of NaOCl into lateral canals over CNI at 2 mm [29.89 %], 4 mm [33.64 %], 6 mm short of the WL

Table 1 Summary of the results of individual studies for the number of lateral canals that were penetrated with the irrigant by using the various IATs.

Study	IATs	No. of teeth	Number of lateral canals *n* (%)				
			2 mm	4 mm	4.5 mm	6 mm	Overall
Straight canals							
Castelo-Baz et al., 2021	CNI	20	0 (0)	0 (0)	–	0 (0)	0 (0)
	PUI	20	15 (37.5)	10 (25)	–	15 (37.5)	40 (33.3)
Souza et al., 2019	CNI	20	2 (5)	–	4 (10)	13 (32.5)	19 (15.8)
	PUI	20	26 (65)	–	29 (72.5)	34 (85)	89 (74.2)
Kanumuru et al., 2015	CNI	15	0 (0)	8 (26.6)	–	16 (53.3)	24(26.7)
	PUI	15	30 (100)	30 (100)	–	30 (100)	90 (100)
	SI	15	14 (46.7)	18 (60)	–	30 (100)	62 (68.9)
Pawar et al., 2013	CNI	20	0 (0)	–	0 (0)	0 (0)	0 (0)
	PUI	20	28 (70)	–	40 (100)	40 (100)	108 (90)
	SI	20	0 (0)	–	4 (10)	6 (15)	10 (8.3)
	MDA	20	0 (0)	–	2 (5)	0 (0)	2 (5)
Spoorthy et al., 2013	CNI	16	0 (0)	0 (0)	–	0 (0)	0 (0)
	PUI	16	8 (25)	22 (68.8)	–	30 (93.8)	60 (62.5)
	ANP	16	0 (0)	4 (12.5)	–	8 (25)	12 (12.5)
Castelo-Baz et al., 2012	CNI	20	0 (0)	0 (0)	–	0 (0)	0 (0)
	PUI	20	13 (32.5)	8 (20)	–	15 (37.5)	36 (30)
de Gregorio et al., 2012	CNI	15	0 (0)	–	0 (0)	0 (0)	0 (0)
	ANP	15	1 (3.33)	–	0 (0)	0 (0)	1 (3.3)
de Gregorio et al., 2010	CNI	20	0 (0)	–	0 (0)	0 (0)	0 (0)
	PUI	20	30 (75)	–	40 (100)	40 (100)	110 (91.7)
	ANP	20	4 (10)	–	6 (15)	2 (5)	12 (10)
	SI	20	0 (0)	–	4 (10)	6 (15)	10 (8.3)
Curved canals							
Castelo-Baz et al., 2021	CNI	20	0 (0)	0 (0)	–	0 (0)	0 (0)
	PUI	20	10 (25)	13 (32.5)	–	20 (50)	43 (35.8)
Castelo-Baz et al., 2016	CNI	20	0 (0)	0 (0)	–	0 (0)	0 (0)
	PUI	20	14 (35)	14 (35)	–	18 (45)	46 (38.3)
Straight canals			**Mean ± SD**				
			2 mm	**4 mm**	**4.5 mm**	**6 mm**	**Overall**
Khare et al., 2017	CNI	12	0.7 ± 0.3	1.3 ± 0.1	–	1.6 ± 0.2	1.2 ± 0.4
	PUI	12	1.2 ± 0.7	1.7 ± 0.1	–	1.9 ± 0.1	1.6 ± 0.5
	MDA	12	1.1 ± 0.1	1.5 ± 0.1	–	1.9 ± 0.1	1.5 ± 0.35
Yaghi and Kaloustian, 2016	CNI	18	0.3 ± 0.3	–	0.4 ± 0.5	0.4 ± 0.5	0.37 ± 0.4
	ANP	20	0.8 ± 0.6	–	0.8 ± 0.7	0.7 ± 0.6	0.77 ± 0.6
de Gregorio et al., 2009							
a) Direct observation method	CNI	20	0.1 ± NR	–	0.3 ± NR	1.2 ± NR	0.53 ± NR
	PUI	20	0.6 ± 0.8	–	1.43 ± 0.7	1.6 ± 0.8	1.21 ± 0.9
	SI	20	1.0 ± 0.8	–	1.2 ± 0.8	1.83 ± 0.4	1.34 ± 0.8
b) Radiographic method	CNI	–	–	–	–	–	–
	PUI	20	0.1 ± 0.2	–	0.45 ± 0.6	0.55 ± 0.9	0.35 ± 0.7
	SI	20	0.1 ± 0.3	–	0.45 ± 0.6	0.75 ± 0.9	0.43 ± 0.7

Nine out of 12 studies represent the number of lateral canals (*n*) in terms of percentage (in parentheses) that were penetrated with the irrigant by using various IATs at 2, 4, 4.5 and 6 mm short of the working length, and its overall penetration in both straight and curved canals. The remaining three studies are demonstrated as the mean number of lateral canals successfully penetrated by the irrigant in straight canals (score range, 0–2).

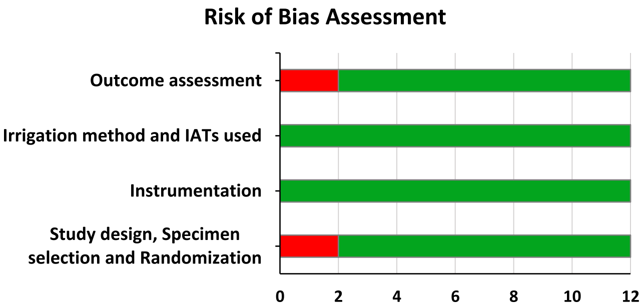
[47.40 %], and overall penetration into lateral canals [36.97 %] (Appendix Fig. A2).

3.4.3. Straight canals versus curved Canals- PUI

A significant decrease in the efficacy of PUI was observed in the lateral canal of curved canals [36.97 %] (Appendix Fig. A2) when compared to the lateral canal of straight canals [60.91 %] (Fig. 3d).

3.5. Heterogeneity Test and reporting bias

The *meta*-analyses of the straight and curved canals indicated significant heterogeneity. The chi-square tests ranged from 0-100 % and 55.4–98.3 % of heterogeneity for straight canals and curved canals, respectively. Therefore, the random-effects model was used (Fig. 3a–3d, Appendix Fig. A1 and Fig. A2). To look for any publication bias, the funnel plot



	Study design, Specimen selection and Randomization	Instrumentation	Irrigation method and IATs used	Outcome assessment
High Risk	2	0	0	2
Low Risk	10	12	12	10

Fig. 2a Risk of bias assessment.

Fig. 2b Violin plot showing quality assessment of the included studies; The overall quality assessment across the included studies indicated a high quality i.e., 83.3%.

analysis was conducted. Analysis revealed the presence of publication bias (Appendix Fig. A3).

3.6. Certainty of evidence

Table 2 presents a summary of the findings based on the GRADE approach. In the present review, the outcome of lateral canals of straight and curved canals assessed was attributed to low certainty and very low certainty of the evidence, respectively.

4. Discussion

The efficacy of irrigation is assured once the irrigant is in contact with the entire root canal system. The optimum penetration of NaOCl into the lateral canals is essential for effective debridement, dissolution, and disinfection where mechanical instrumentation cannot be established. Hence, several IATs were established for better distribution of NaOCl throughout the canals, resulting in the success of root canal therapy.

4.1. IATs versus CNI

Overall, the *meta*-analysis findings revealed that IATs considerably improved the penetration of NaOCl into lateral canals when compared to CNI. This notion is strengthened by computational fluid dynamic studies conducted by Boutsioukis et al., 2009 and Chen et al., 2014 who reported that CNI generated an increase in localized hydrodynamic pressure and shear stress when compared with IATs. When employing CNI alone, vapour lock is formed by the organic dissolution of NaOCl into bubbles of ammonium and carbon dioxide, which may restrict irrigant replenishment between 1 and 1.5 mm apical to the tip of the needle, especially in the apical third, leading to a drastic reduction in the debridement efficacy of CNI (Tay et al., 2010). The percentage formation of vapour lock for CNI (70 %) was higher when compared with SI (60 %) and PUI (30 %) (Sáinz-Pardo et al., 2014). The irrigant penetration depth of CNI on its own was restricted to the depth of needle penetration. High heterogeneity observed across studies must be viewed with caution, in order to consider the conclusion of *meta*-analyses as a reliable interpretation. The authors do accept the constraints of the data. However, the consistency of the findings and the surrounding literature support the conclusion that IATs have improved penetration of NaOCl into lateral canals than CNI.

4.2. Efficacy of individual IATs

MDA involves the activation of NaOCl hydrodynamically by the repeated movements of master GP cone using short vertical strokes, creating high intracanal pressure. This change in pressure aids in the displacement of the apical vapour lock, resulting in maximum irrigant penetration (Machtou, 2018). The major drawback of MDA is that it is operator-dependent and cannot be standardized. Additionally, the frequency of irrigant extrusion is higher, resulting in postoperative pain (Topçuoğlu et al., 2018).

The activation with SI generates mechanical oscillation at the file tip, combining acoustic waves with the chemical activity of NaOCl with a frequency ranging from 1 to 6 $\times$ 10^3 Hz, whereas PUI generates higher frequencies ranging from 40 to 45 $\times$ 10^3 Hz (Ahmad et al., 1988). SI aids in the removal of pulpal remnants, dentine debris and breaking of apical vapour locks thereby helping in the penetration of irrigants apically and laterally (de Gregorio et al., 2009; Souza et al., 2019). However, these also pose drawbacks, such as inadvertent contact of file tip with the canal wall due to the intricate anatomy of root canal structure (Peters, 2004), loss of cleansing efficiency (Ahmad et al., 1987), and excessive dentine removal (Lea et al., 2009).

Previous studies reported that ANP has better irrigant penetration in the main canal in comparison with PUI, SI, and MDA (de Gregorio et al., 2012, 2010; Munoz and Camacho-Cuadra, 2012; Abrar et al., 2019; Spoorthy et al., 2013). It aids in the removal of pulp debris (Nielsen et al., 2007) and ensures adequate disinfection in the apical third (Cohenca et al., 2010). Furthermore, ANP decreases the irrigant extrusion when compared to CNI (Mitchell et al., 2010). Nonetheless, ANP demonstrated decreased penetration and limited activation of irrigant in the non-instrumented areas, represented by lateral canals. The osmotic pulling effect reported by Pashley et al. possibly explains this limitation (Pashley et al., 1985).

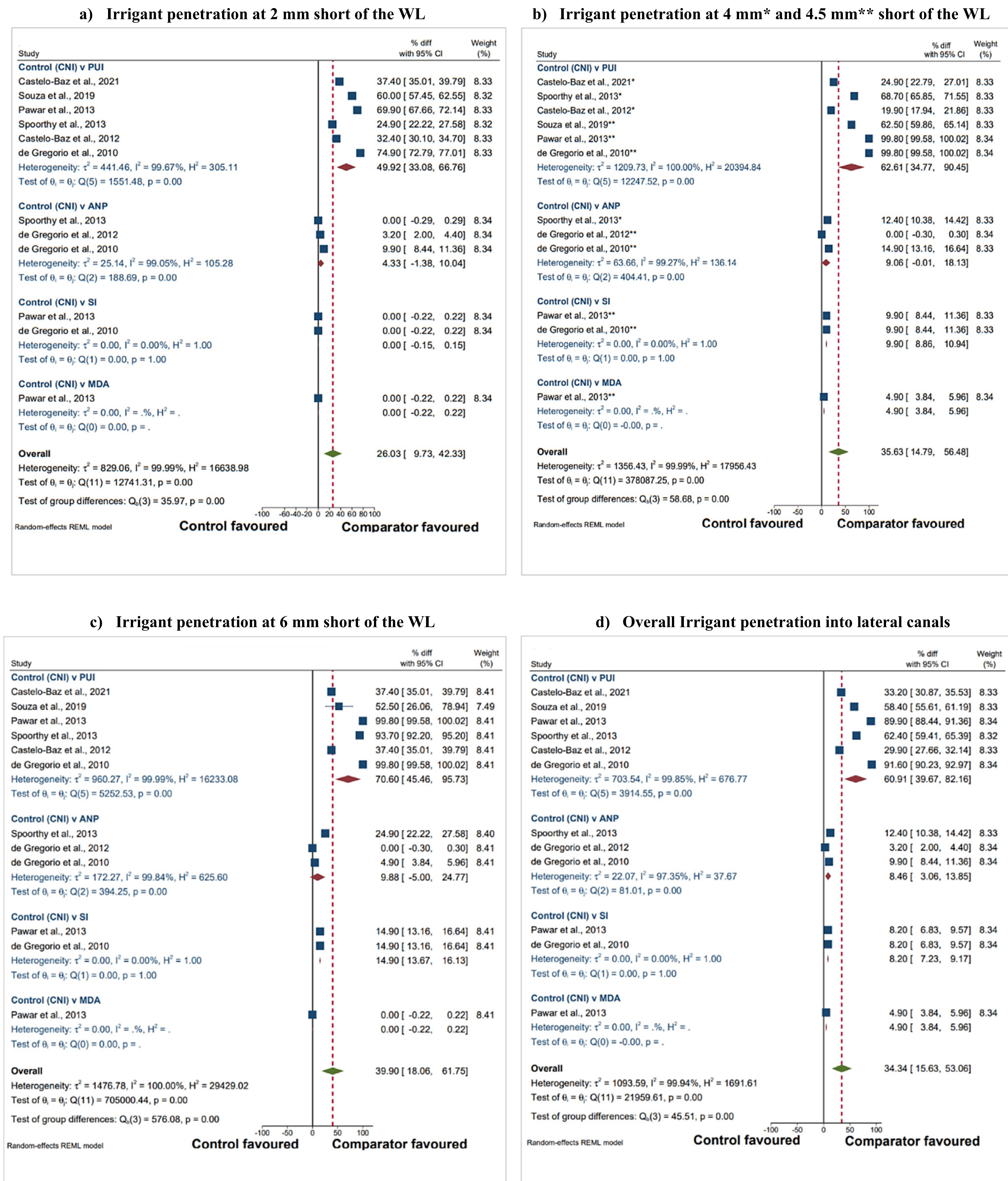


Fig. 3 Penetration of sodium hypochlorite into the lateral canals of straight canals using PUI, ANP, SI or MDA at **a)** 2 mm, **b)** 4 and 4.5 mm, **c)** 6 mm short of the WL and **d)** its overall penetration in comparison to CNI; Effect size: percentage difference (% diff).

PUI was more effective in lateral canal penetration because NaOCl was activated with adequate force in breaking the apical vapour lock (Castelo-Baz et al., 2012; de Gregorio et al., 2009). The file oscillation created cavitation and acoustic streaming effects (Sluis et al., 2007; Van Der Sluis et al., 2005). Moreover, PUI has the benefit of synergistic effect on the tissue-dissolving capabilities of NaOCl due to enhanced wetting of pulp tissue remains following activation (Cheung and Stock, 1993). In uninstrumented areas represented by lateral canals, the efficient penetration of NaOCl correlates directly with previous studies that

Table 2 GRADE summary of findings.

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**IATs**	**CNI**	**Relative (95 % CI)**	**Absolute (95 % CI)**		
Straight canals with effect size in terms of % diff												
7	Ex vivo and in vitro	Not serious	Serious[a]	Not serious	Not serious	Serious[b]	454	454	–	% diff 34.34 Irrigant penetration higher (15.63 higher to 53.06 higher)	⊕⊕○○ Low	Critical
Straight canals with effect size in terms of SMD												
2	Ex vivo and in vitro	Not serious	Not serious	Not serious	Serious[c]	Serious[d]	88	84	–	SMD 0.36 SD higher (0.22 higher to 0.49 higher)	⊕⊕○○ Low	Critical
Curved canals with effect size in terms of % diff												
2	Ex vivo and in vitro	Not serious	Serious[e]	Not serious	Serious[f]	Serious[g]	240	240	–	% diff 36.97 higher (29.77 higher to 44.17 higher)	⊕○○○ Very low	Critical

Abbreviations: CI, confidence interval; % diff, percentage difference; SMD, standardized mean difference.

[a] See Fig. 3d, substantial statistical heterogeneity: $I^2 = 99.94$ %, $p < .001$. Therefore, inconsistency was downgraded by one level.

[b] See Appendix Fig. A3, presence of publication bias. Therefore, inconsistency was downgraded by one level.

[c] Small sample size and hence not enough power to attain a reliable level of certainty. Therefore, inconsistency was downgraded by one level.

[d] Presence of publication bias. Therefore, inconsistency was downgraded by one level.

[e] See Appendix Fig. A2, substantial statistical heterogeneity: $I^2 = 98.27$ %, $p < .001$. Therefore, inconsistency was downgraded by one level.

[f] Small sample size and hence not enough power to attain a reliable level of certainty. Therefore, inconsistency was downgraded by one level.

[g] Presence of publication bias. Therefore, inconsistency was downgraded by one level.

assessed the effectiveness of PUI for smear layer and debris removal, debridement, and disinfection (Guerisoli et al., 2002; Gutarts et al., 2005; Lee et al., 2004). The combination of PUI and ANP resulted in an overall level of 85.4 % lateral canal penetration, which was higher than PUI (62.5 %) and ANP (12.5 %) when used alone. This combination facilitated irrigant penetration in both main canals and lateral canals (Spoorthy et al., 2013). The possible reason is the elimination of debris from the main canal by the resulting negative pressure created by ANP when employed in the beginning. This ensured optimum irrigant penetration up to the WL. On the subsequent use of PUI, an adequate volume of irrigant is maintained which may aid in the significant increase of the irrigant penetration into lateral canals (Spoorthy et al., 2013).

4.3. Factors implying the degree of irrigant penetration

A change in the needle-insertion depth (Boutsioukis et al., 2010), degree of root canal curvature (Ahmad et al., 1988; Boutsioukis et al., 2013; Castelo-Baz et al., 2021, 2016), activation of NaOCl and its continual replenishment (Pashley et al., 1985; Stojicic et al., 2010; Zehnder, 2006), and anatomic variations of the lateral canals (Ricucci et al., 2013). Other factors such as power intensity (Jiang et al., 2011), renewal rate, concentration, volume (Ricucci et al., 2013), flow rate (Pereira et al., 2021), and activation time (Retsas et al., 2022) of the irrigant in the lateral canals also have a great implication on the degree of irrigant penetration. The addition of EDTA did not show any significant enhancement of NaOCl penetration into lateral canals (de Gregorio et al., 2009).

The surface tension, density, and viscosity of the ICS should be almost identical to those of NaOCl. Dissimilarities in the physical characteristics may affect the irrigant penetration depth (Spoorthy et al., 2013). The radiographic evaluation method evidenced less penetration of ICS into lateral canals because the concentration of ICS may not facilitate detection radiographically when compared to the direct observation method visually, thus proving the direct observation method to be more sensitive and reliable (de Gregorio et al., 2009).

4.4. Limitations

The results of the included studies are based on laboratory experiments. The existing data cannot be manifested in comparing individual IATs due to the heterogeneity present across the studies. The lack of essential information with respect to lateral canals in the *meta*-analysis of curved canals makes it difficult to compare CNI with individual IATs. The addition of a dye/radiopaque material to NaOCl alters its physical characteristics, perhaps reducing irrigant penetration. The usage of various concentrations of dye/radiopaque material across the studies may also affect the visual assessment of irrigant penetration depth. There is a paucity of volumetric data and a decreased spreading pattern of ICS throughout the canal in comparison to the prevailing data of NaOCl.

4.5. Future recommendations

1. Establishing a standard protocol for utilizing IATs with a robust experimental model to facilitate optimal cleaning of the root canals.
2. Standardization of the concentration of dye/radiopaque material used in conjunction with NaOCl to obtain accurate visual images of irrigant penetration.
3. Investigation of the efficacy of irrigant penetration of ANP, SI, MDA, and the synergistic impact of PUI and ANP techniques involving curved root canals.
4. Evaluating the extent of complete debridement, disinfection, and smear layer removal following the usage of IATs.

This review helps the clinician establish the importance of employing IATs to disinfect the lateral canals and gain greater success with the outcomes of endodontic therapy. The use of PUI technique for irrigant penetration into the lateral canals of straight canals is far superior for use in clinical practice.

5. Conclusions

Within the limitations, IATs improved the irrigant penetration into the lateral canals and therefore their use during routine endodontic practice is recommended. PUI is the most effective IAT followed by ANP, SI, and MDA techniques in the lateral canals of straight root canals. However, due to the lack of supporting information on IATs used in curved root canals, this review is unable to recommend the effective IAT in curved canals. Further investigations are required for any clinical recommendations, especially in studies involving curved root canals.

Ethical statement

The study did not require ethics approval because this study is exclusively based on published literature.

Conflict of interest

The authors declare that they have no known Conflict of interest that could influence the present research.

CRediT authorship contribution statement

Ram Surath Kumar: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing - original draft. **Anil V. Ankola:** Supervision, Validation, Conceptualization, Writing - review & editing. **Roopali M. Sankeshwari:** Supervision, Validation, Writing - review & editing. **Mamata Hebbal:** Validation, Writing - review & editing. **Vinuta Hampiholi:** Writing - Review & editing. **S. Lokesh Kumar:** Writing - review & editing. **Apurva Deshpande:** Data collection & processing, Literature search. **Abhra Roy Choudhury:** Supervision, analysis & interpretation. **Atrey J Pai Khot:** Literature search, Data collection & processing.

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Appendix A1. MEDLINE (via PubMed) database search

Search	PICO strategy	Search Strategy Input query	No. of items found
#1	P	((((((((((mature permanent teeth[Title/Abstract]) OR (mature permanent tooth[Title/Abstract])) OR (mature apex[Title/Abstract]))) OR (incisor[MeSH Terms])) OR (cuspid[MeSH Terms])) OR (bicuspid [MeSH Terms])) OR (molar[MeSH Terms])) OR (dentition, permanent[MeSH Terms])) OR (root canal therapy[MeSH Terms]))) AND ((“2000/01/01″[Date - Publication]: ”2022/01/31″[Date - Publication]))	43,697
#2	Ia	((((((passive ultrasonic irrigation[Title/Abstract]) OR (ultrasonic irrigation[Title/Abstract])) OR (IrriSafe [Title/Abstract])) OR (PUI[Title/Abstract])) OR (ultrasonics[MeSH Terms])) OR (Ultrasonic Therapy [MeSH Terms])) AND ((“2000/01/01″[Date - Publication]: ”2022/01/31″[Date - Publication]))	19,803
#3	Ib	(((sonic irrigation[Title/Abstract]) OR (endoactivator[Title/Abstract])) OR (sonication[MeSH Terms])) AND ((“2000/01/01″[Date - Publication]: ”2022/01/31″[Date - Publication]))	4,676
#4	Ic	((((apical negative pressure[Title/Abstract]) OR (endovac[Title/Abstract])) OR (suction[MeSH Terms])) OR (vacuum[MeSH Terms])) AND ((“2000/01/01″[Date - Publication]: ”2022/01/31″[Date - Publication]))	10,897
#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])	1346
#6	C	((((((((conventional needle irrigation[Title/Abstract]) OR (positive pressure irrigation[Title/Abstract])) OR (needle irrigation[Title/Abstract])) OR (passive irrigation[Title/Abstract])) OR (syringe irrigation [Title/Abstract])) OR (syringe[MeSH Terms])) OR (Needles[MeSH Terms])) OR (therapeutic irrigation [MeSH Terms])) AND ((“2000/01/01″[Date - Publication]: ”2022/01/31″[Date - Publication]))	43,283
#7	O	((((((((((((lateral canal*[Title/Abstract]) OR (simulated lateral canal*[Title/Abstract]) OR (2 mm[Title/Abstract])) OR (4 mm[Title/Abstract])) OR (4.5 mm[Title/Abstract])) OR (6 mm[Title/Abstract]))) OR (irrigant penetration[Title/Abstract])) OR (Radiography, Dental, Digital[Title/Abstract])) OR (dye[Title/Abstract])) OR (contrast media[Title/Abstract])) OR (contrast solution[Title/Abstract])) OR (Tooth Apex [MeSH Terms])) AND ((“2000/01/01″[Date - Publication]: ”2022/01/31″[Date - Publication]))	1,94,019
#8		#1 AND #2	705
#9		#1 AND #3	87
#10		#1 AND #4	166
#11		#1 AND #5	1,302
#12		#1 AND #6	694
#13		#1 AND #7	4,956
#14		#2 AND #7	924
#15		#3 AND #7	187
#16		#4 AND #7	195
#17		#5 AND #7	482
#18		#6 AND #7	1,012
#19		#2 AND #3 AND #4	22
#20		#3 AND #4 AND #5	4
#21		#4 AND #5 AND #6	9
#22		#5 AND #6 AND #2	21
#23		#6 AND #2 AND #3	78
#24		#2 AND #3 AND #4 AND #5	5
#25		#2 AND #3 AND #4 AND #5 AND #6	5
#26		#1 AND #2 AND #3 AND #4 AND #5 AND #6	3
#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.

Appendix A2. Scopus database search

Search	PICO strategy	Search Strategy Input query	No. of items found
#1	P	TITLE-ABS-KEY (patients OR "mature permanent teeth" OR "mature permanent tooth" OR "mature apex" OR "mature apices" OR "permanent molar*" OR "permanent premolar*" OR "permanent canine*" OR "permanent incisor*" AND "Root Canal Therapy" OR "root canal treatment") AND PUBYEAR > 2000 AND (LIMIT-TO (SUBJAREA, "DENT"))	2,426
#2	Ia	TITLE-ABS-KEY ("passive ultrasonic irrigation" OR "PUI" OR "ultrasonic irrigation" OR "continuous ultrasonic" OR "intermittent ultrasonic" OR "ultrasonics") AND PUBYEAR > 2000 AND (LIMIT-TO (SUBJAREA, "DENT"))	2,451
#3	Ib	TITLE-ABS-KEY ("sonic irrigation" OR "endoactivator" OR "sonication") AND PUBYEAR > 2000 AND (LIMIT-TO (SUBJAREA, "DENT"))	272
#4	Ic	TITLE-ABS-KEY ("apical negative pressure" OR "endovac" OR "suction" OR "vacuum") AND PUBYEAR > 2000 AND (LIMIT-TO (SUBJAREA, "DENT"))	961
#5	Id	TITLE-ABS-KEY ("manual dynamic activation" OR "manual dynamic irrigation" OR "gutta-percha") AND PUBYEAR > 2000 AND (LIMIT-TO (SUBJAREA, "DENT"))	2,551
#6	C	TITLE-ABS-KEY ("conventional needle irrigation" OR "needle irrigation" OR "conventional irrigation" OR "positive pressure irrigation" OR "passive irrigation" OR "syringe irrigation" OR "conventional syringe irrigation" OR "root canal irrigants") AND PUBYEAR > 2000 AND (LIMIT-TO (SUBJAREA, "DENT"))	2,526
#7	O	TITLE-ABS-KEY ("apical third" OR "tooth apex" OR "irrigant penetration" OR "working length" OR "dental radiography" OR "dye" OR "contrast media" OR "contrast solution" OR "patency file" OR "apical patency") AND PUBYEAR > 2000 AND (LIMIT-TO (SUBJAREA,"DENT"))	7,021
#8		#1 AND #2	53
#9		#1 AND #3	5
#10		#1 AND #4	15
#11		#1 AND #5	164
#12		#1 AND #6	138
#13		#1 AND #7	255
#14		#2 AND #7	369
#15		#3 AND #7	93
#16		#4 AND #7	126
#17		#5 AND #7	766
#18		#6 AND #7	784
#19		#2 AND #3 AND #4	26
#20		#3 AND #4 AND #5	4
#21		#4 AND #5 AND #6	15
#22		#5 AND #6 AND #2	48
#23		#6 AND #2 AND #3	89
#24		#2 AND #3 AND #4 AND #5	4
#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	1

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.

Appendix A3. ProQuest database search

Search	PICO strategy	Search Strategy Input query	No. of items found
1	P	('dental pulp cavity'/exp OR 'endodontic procedure'/exp OR endodont* OR tooth OR teeth)	319,689
2	Ia	('passive ultrasonic irrigation' OR 'ultrasonic irrigation' OR ultrasonics OR IrriSafe)	24,434
3	Ib	('sonic irrigation' OR endoactivator)	1,943
4	Ic	('apical negative pressure' OR endovac)	29,530
5	Id	('manual dynamic activation' OR 'manual dynamic irrigation' OR 'gutta-percha')	97,636
6	C	('conventional needle irrigation' OR 'positive pressure irrigation' OR 'passive irrigation' OR 'syringe irrigation' OR syringe OR needle)	621,850
7	O	(irrigant* OR irrigation OR rinse OR activation OR 'sodium hypochlorite' OR naocl OR edta OR 'simulated lateral canal*' OR 'irrigant penetration' OR radiograph OR dye OR 'contrast media' OR 'contrast solution' AND 'lateral canal*')	3,366,010
8		('irrigant activation technique*' OR 'irrigation activation technique*')	9,948
9		1 AND 2	3,476
10		1 AND 3	1,008
11		1 AND 4	3,261
12		1 AND 5	9,098
13		1 AND 6	27,895
14		1 AND 7	130,269
15		2 AND 7	16,756
16		3 AND 7	1,939
17		4 AND 7	22,873
18		5 AND 7	96,792
19		6 AND 7	347,608
20		2 AND 3 AND 4	264
21		3 AND 4 AND 5	184
22		4 AND 5 AND 6	1,457
23		5 AND 6 AND 2	1,172
24		6 AND 2 AND 3	675
25		20 AND 5	164
26		25 AND 6	161
27		1 AND 26	155
28		27 AND 7	155
29		28 AND 8	129

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.

Appendix A4. Cochrane Library (CENTRAL) database search

Search	Search Strategy Input query	No. of items found
#1	MeSH descriptor: [Dental Pulp Cavity] explode all trees	765
#2	MeSH descriptor: [Root Canal Therapy] explode all trees	680
#3	endodont*	4122
#4	tooth	27,630
#5	teeth	27,630
#6	‘‘irrigant activation’’ OR ‘‘irrigation activation’’	36
#7	‘‘passive ultrasonic irrigation’’ OR ‘‘ultrasonic irrigation’’ OR IrriSafe	109
#8	‘‘sonic irrigation’’ OR endoactivator	48
#9	‘‘apical negative pressure’’ OR endovac	39
#10	‘‘manual dynamic activation’’ OR ‘‘manual dynamic irrigation’’ OR ‘‘gutta-percha’’	573
#11	‘‘conventional needle irrigation’’ OR ‘‘positive pressure irrigation’’ OR ‘‘passive irrigation’’ OR ‘‘syringe irrigation’’ OR syringe OR needle	20,050
#12	Irrigant* OR irrigation OR rinse OR activation OR ‘‘sodium hypochlorite’’ OR NaOCl OR EDTA OR ‘‘lateral canal*’’ OR ‘‘simulated lateral canal*’’ OR ‘‘irrigant penetration’’ OR radiograph OR dye OR ‘‘contrast media’’ OR ‘‘contrast solution’’	50,183
#13	#1 OR #2 OR #3 OR #4 OR #5	2886
#14	#6 OR #7 OR #8 OR #9 OR #10	718
#15	#14 AND #11	120
#16	#14 AND #12	408
#17	#14 AND #11 AND #12	118
#18	#13 AND #17	113

Appendix B. Risk of bias and quality assessment of the included studies (expanded)

Sl. No.	Domain	Castelo-Baz et al., 2021	Souza et al., 2019	Khare et al., 2017	Castelo-Baz et al., 2016	Yaghi and Kaloustian, 2016	Kanumuru et al., 2015	Pawar et al., 2013	Spoorthy et al., 2013	Castelo-Baz et al., 2012	de Gregorio et al., 2012	de Gregorio et al., 2010	de Gregorio et al., 2009
		1.	**2.**	**3.**	**4.**	**5.**	**6.**	**7.**	**8.**	**9.**	**10.**	**11.**	**12.**
I	**Study design, specimen selection, & randomization**												
1.	Prior sample size estimation	0	0	0	0	0	0	0	0	0	0	0	0
2.	Type of teeth	1	1	0	1	1	1	0	1	1	1	0	0
3.	Working length/ Standardized root length	1	1	1	1	1	0	0	0	1	1	1	1
4.	Canal Curvature (straight/ curved)	1	0	0	1	1	1	0	1	1	0	0	0
5.	Inclusion & Exclusion criteria	0	1	0	1	0	0	0	0	0	0	0	0
6.	Random allocation to different groups	1	1	1	1	1	1	1	1	1	1	1	1
7.	Method used to simulate periapical tissues	1	1	1	1	1	1	1	1	1	1	1	1
8.	Verification of presence of single canal for anterior teeth/ separate canals for posterior teeth	1	0	0	1	1	1	1	1	1	1	1	1
II	**Instrumentation**												
1.	Patency	1	1	1	1	1	1	1	0	0	1	1	1
2.	Identical standardized instrumentation in all groups	1	1	1	1	1	1	1	1	1	1	1	1
3.	Apical root canal size and taper	1	1	1	1	0	1	1	1	1	1	1	1
III	**Irrigation method and IATs used**												
1.	Concentration of NaOCl used	1	1	1	1	1	1	1	1	1	1	1	1
2.	Type, conc., manufacturer of contrast solution	1	1	1	1	1	1	1	1	1	1	1	1
3.	Needle: Manufacturer, type and size (CNI group)	1	1	1	1	1	1	1	1	1	1	1	1
4.	Needle insertion depth (CNI group)	1	1	1	1	1	1	1	1	1	1	1	1
5.	Volume and duration/flow rate of irrigant delivered (CNI group)	1	1	1	1	1	1	0	1	1	1	1	1
6.	Device model and manufacturer (Test group/ groups)	1	1	1	0	1	1	0	1	1	1	1	1
7.	File/tip: type, size, length (Test group/ groups)	1	1	1	1	1	1	1	1	1	0	1	1
8.	File/tip: insertion depth (Test group/ groups)	1	1	1	1	1	1	1	1	1	1	1	1
9.	Power setting (Test group/ groups)	1	1	1	1	1	1	1	1	1	0	1	1
10.	Duration of activation (Test group/ groups)	1	1	1	1	1	1	1	1	1	1	1	1
11.	Volume of irrigant delivered (Test group/ groups)	1	1	1	1	1	1	0	1	1	0	1	1
12.	No. of cycles (Test group/ groups)	1	1	1	1	1	0	0	0	1	0	0	1
13.	Irrigation protocols identical in the compared groups except for activation cycles	1	1	1	1	1	1	1	1	1	1	1	1
IV	**Outcome assessment**												
1.	Blinding of outcome assessment	1	1	1	1	1	1	0	1	1	1	1	0
2.	Reliability of outcome measured	1	1	1	1	1	1	0	1	1	1	1	1
3.	Data summary (descriptive statistics)/ complete raw data	1	1	1	1	1	1	1	1	1	1	1	0
4.	Suitable statistical tests	1	1	1	1	0	1	1	1	1	1	1	1
	Total	26	25	23	26	24	25	17	23	25	21	23	22
	Percentage (%)	93	89	82	93	86	89	61	82	89	75	82	78
	Overall quality	High	High	High	High	High	High	Medium	High	High	Medium	High	High

NA, not applicable.

Yes:1 point; No and unclear: 0 point; the numbers represent how many of the requirements were met by each study; high (score > 75 %), medium (score 50 %– 75 %), or low (score < 50 %).

Appendix C. 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
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

Appendix D. Summary of study characteristics of all the included studies that evaluated the penetration of sodium hypochlorite into lateral canals

Study	Control group-CNI (*n*)	Test group (*n*)	Other groups evaluated	Sample (Curvature)	Working length (mm)	Method used to simulate periapical tissues	Patency with 10 K-file	File system used	Apical preparation size/ taper	Irrigation (mL)	Preparation of ICS	Method of assessment
Castelo-Baz et al., 2021	St. canal (20), Curved canal (20)	PUI St. canal(20) PUI curved canal (20)	CANUI-St, CANUI-Curved	Incisors (Straight & 20°-30° curved)	16	Wax	Y	ProTaper Next (Dentsply)	40/0.06	5 % NaOCl (3 mL) 17 % EDTA(3 mL)	20 % Chinese ink, Germany	Direct observation
Souza et al., 2019	(20)	PUI (20)	CUI, EC	Single rooted (Straight)	15	Wax	Y	ProTaper universal (Dentsply)	40/0.05	5.25 % NaOCl (3 mL) EDTA (3 mL)	20 % Nankin ink, Netherlands	Direct observation
Khare et al., 2017	(12)	PUI (12)MDA (12)	–	Single-rooted (Straight)	14	Wax	Y	ProTaper universal (Dentsply)	25/0.08	5.25 % NaOCl (3 mL) 17 % EDTA (3 mL)	10 % ink marker, USA	Direct observation
Castelo-Baz et al., 2016	(20)	PUI (20)	CUI	Incisors (20°-30° curved)	16	Wax	Y	GTX (Dentsply)	30.06	5 % NaOCl (3 mL) 10 % EDTA (3 mL)	20 % Chinese ink, Germany	Direct observation
Yaghi and Kaloustian, 2016	(18)	ANP (20)	ANP + heat	Single-rooted (Straight)	15	Wax	Y	ProTaper (Dentsply)	NR	4.8 % NaOCl (3 mL) 17 % EDTA (3 mL)	40 % Iohexol (Omnipaque), Ireland & 10 % Red Detector	Direct observation
Kanumuru et al., 2015	(15)	PUI (15) SI (15)	25/0.02 RACE	Single rooted (Straight)	NR	Elastomer	Y	ProTaper (Dentsply)	30/0.09	5.25 % NaOCl (1.5 mL)	40 % Indian ink (2:3)	Direct observation
Pawar et al., 2013	(20)	PUI (20), SI (20), MDA (12)	AI (F-file)	Single rooted (Straight)	Unclear	Wax	Y	WaveOne (Dentsply)	25/0.08	5 % NaOCl (NR)	Methylene blue	Direct observation
Spoorthy et al., 2013	(16)	PUI (16), ANP (16)	ANP + PUI	Incisors (Straight)	Unclear	Wax	Unclear	ProTaper universal (Dentsply)	40/0.05	5.25 % NaOCl (3 mL) 17 % EDTA (3 mL)	40 % Indian ink, India	Direct observation
Castelo-Baz et al., 2012	(20)	PUI (20)	CUI	Incisors (Straight)	16	Wax	Unclear	ProTaper (Dentsply)	30/0.09	5 % NaOCl (3 mL) 10 % EDTA (3 mL)	20 % Chinese ink, Germany	Direct observation
de Gregorio et al., 2012	(15)	ANP (15)	SAF	Canines (Straight)	17	Wax	Y	K-Flexofiles (Dentsply)	35/0.02	5.25 % NaOCl (5 mL) 17 % EDTA (NR)	10 % ink marker, France	Direct observation
de Gregorio et al., 2010	(20)	SI (20), PUI (20) ANP (20)	AI (Rotary file)	Single-rooted (Straight)	15	Wax	Y	ProTaper rotary (Dentsply)	40/0.06	5.25 % NaOCl (3 mL) 17 % EDTA (3 mL)	10 % Kuraray caries detector solution, Japan	Direct observation
de Gregorio et al., 2009	(20)	SI (20), PUI (20)	Addition of EDTA in SI & PUI	Single-rooted (Straight)	15	Silicon	Y	ProTaper rotary (Dentsply)	25/0.08	5.25 % NaOCl (1.5 mL)	40 % of 76 % Pielograf (Brasil), & 10 % Kuraray caries detector, Japan	Both direct & radiographic method

NR, not reported; 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; AI, active irrigation; CUI, continuous ultrasonic irrigation; EC, easy clean; SAF, self-adjusting files; NaOCl, sodium hypochlorite; IV, intravascular; ICS, irrigating contract solution.

Appendix E. Characteristics of conventional needle irrigation and various irrigant activation techniques used

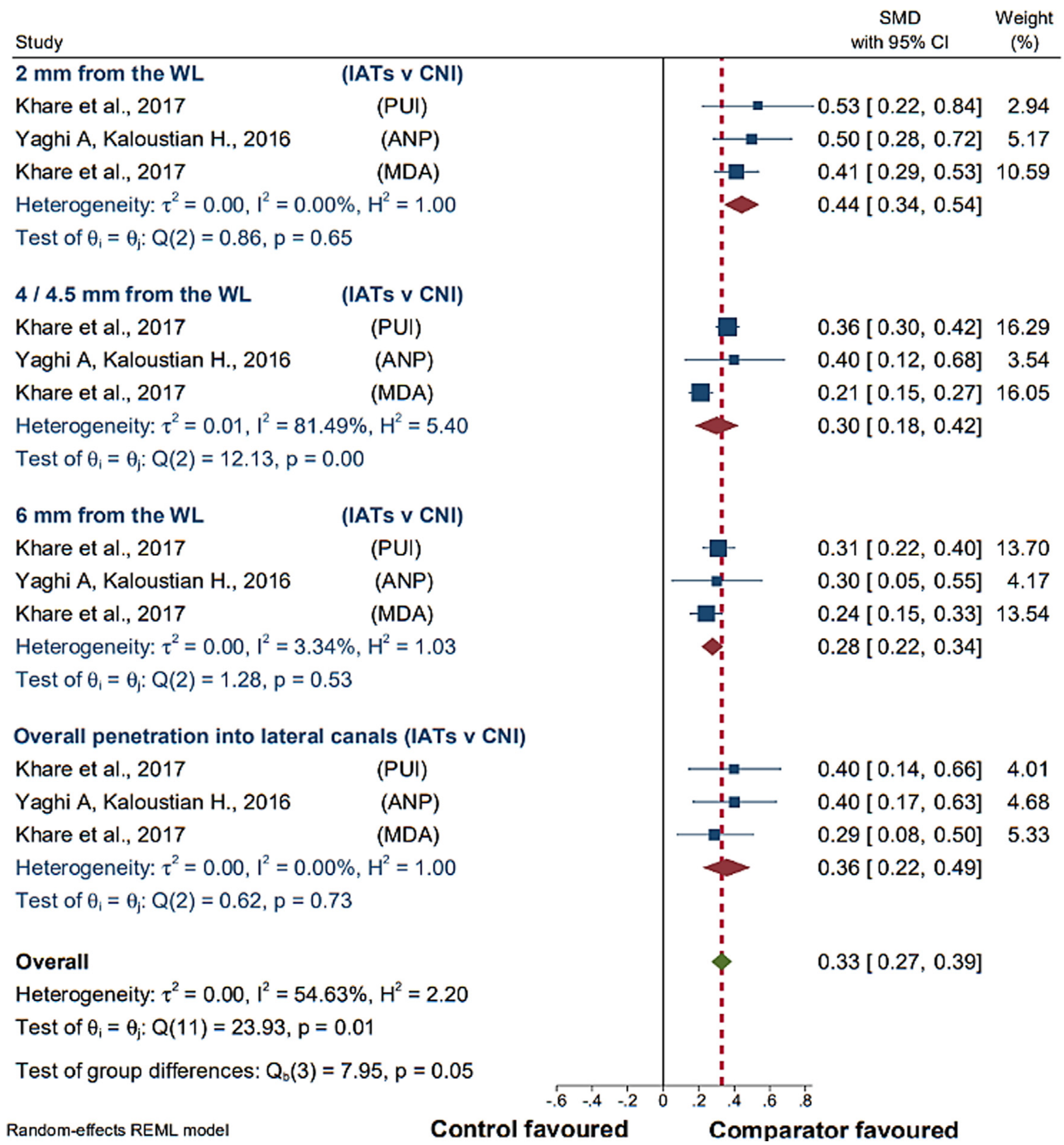
IATs used	Study	Characteristics of use					
		Manufacturer	**End type**	**Gauge**	**Volume (mL)**	**Duration (s)**	**Insertion depth short of the WL (mm)**
CNI	1. Castelo-Baz et al., 2021	ProRinse, Dentsply Sirona, USA	Side vented	30	6	60	2
	2. Souza et al., 2019	Ultradent, USA	NR	30	6	60	1
	3. Khare et al., 2017	Vishal Dentocare, India	Double-Side vented	31	3	60	2
	4. Castelo-Baz et al., 2016	ProRinse, Dentsply Sirona, USA	NR	30	6	60	2
	5. Yaghi and Kaloustian, 2016	Endo-Eze™, Ultradent, USA	NR	27	3	60	3
	6. Kanumuru et al., 2015	NR	Side vented	30	1	30	2
	7. Pawar et al., 2013	NR	End vented	25	NR	NR	2
	8. Spoorthy et al., 2013	NaviTip, Ultradent, USA	Open-ended	30	1.5	30	2
	9. Castelo-Baz et al., 2012	ProRinse, Dentsply Sirona, USA	Side vented	30	6	60	2
	10. de Gregorio et al., 2012	ProRinse, Dentsply Sirona, USA	Side vented	30	NR	30	2
	11. de Gregorio et al., 2010	ProRinse, Dentsply Sirona, USA	Side vented	30	1.5	30	2
	12. de Gregorio et al., 2009	Monojet (Sherwood Davis & Geck, St Louis, MO)	Side vented	27	3	60	2
		File size [manufacturer]	**Mounting device [manufacturer]**	**Activation time for each cycle (s)**	**Power setting**	**No. of cycles**	**Insertion depth short of the WL (mm)**
PUI	1. Castelo-Baz et al., 2021	ISO 15 [ESI file]	EMS, Nyon, Switzerland	20	4	3	1
	2. Souza et al., 2019	20/0.01 [Irrisonic]	Jet Sonic, Brazil	20	20 %	3	2
	3. Khare et al., 2017	ISO 10 [IrriSafe, Satelec]	Satelec, Acteon, France	20	3	3	2
	4. Castelo-Baz et al., 2016	ISO 15 [ESI file]	EMS, Nyon, Switzerland	20	6	3	1
	5. Kanumuru et al., 2015	ISO 20 [IrriSafe, Satelec]	Suprasson Newtron XS	20	5	NR	2
	6. Pawar et al., 2013	ISO 20 [NR]	NR	30	3	NR	0
	7. Spoorthy et al., 2013	ISO 25 [IrriSafe, Satelec]	Suprasson P5 Booster, Satelec, Acteon, France	30	5	NR	1
	8. Castelo-Baz et al., 2012	ISO 15 [IrriSafe, Satelec]	Satelec, Acteon, France	20	6	3	1
	9. de Gregorio et al., 2010	ISO 20 [IrriSafe, Satelec]	Satelec, Acteon, France	30	3	NR	0
	10. de Gregorio et al., 2009	ISO 10 [IrriSafe, Satelec]	Suprasson P5 Booster, Satelec, Acteon, France	20	3	3	2
		Volume (mL)	**Activation time (s)**	**Macrocannula depth short of the WL**		**Microcannula depth short of the WL (mm)**	
ANP	1. Yaghi and Kaloustian, 2016	3	60	12 mm		3	
	2. Spoorthy et al., 2013	1.5	30	Pulp chamber		0	
	3. de Gregorio et al., 2012	NR	30	Coronal third of canal		0	
	4. de Gregorio et al., 2010	1.5	30	NR		0	
		Power setting (cpm)	**Activation time (s)**	**File size/taper**		**Insertion depth short of the WL (mm)**	
SI	1. Kanumuru et al., 2015	10,000	30	25/0.04		2	
	2. Pawar et al., 2013	NR	30	25/0.04		0	
	3. de Gregorio et al., 2010	10,000	30	35/0.04		0	
	4. de Gregorio et al., 2009	10,000	60	35/0.04		2	
		Vertical strokes	**Activation time (s)**	**Gutta-percha cone size/taper**		**Amplitude (mm)**	**Insertion depth short of the WL (mm)**
MDA	1. Khare et al., 2017	100	60	25/0.06		2 to 3	NR
	2. Pawar et al., 2013	NR	30	NR/0.06		NR	2

IATs, irrigant activation techniques; CNI, conventional needle irrigation technique; PUI, passive ultrasonic irrigation technique; ANP, apical negative pressure technique; SI, sonic irrigation technique; MDA, manual dynamic activation; NR, not reported; WL, working length.

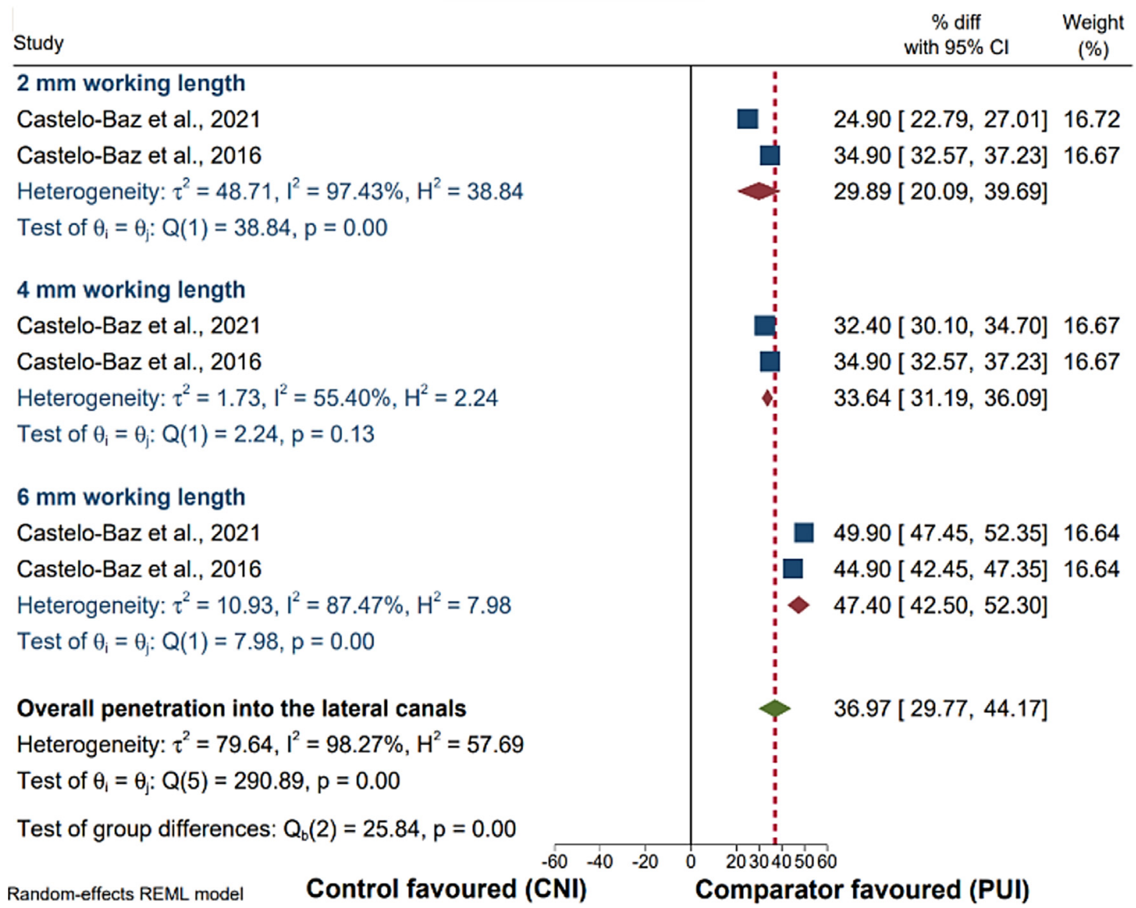
Appendix F. Quality assessment of the included studies

Study		Domain						
		1	2	3	4			
		Study design, specimen selection & randomization	Instrumentation	Irrigation and IATs used	Outcome assessment	Total	Percentage (%)	Overall quality
1.	Castelo-Baz et al., 2021	6/8	3/3	13/13	4/4	26/28	93	High
2.	Souza et al., 2019	5/8	3/3	13/13	4/4	25/28	89	High
3.	Khare et al., 2017	3/8	3/3	13/13	4/4	23/28	82	High
4.	Castelo-Baz et al., 2016	7/8	3/3	12/13	4/4	26/28	93	High
5.	Yaghi and Kaloustian, 2016	6/8	2/3	13/13	3/4	24/28	86	High
6.	Kanumuru et al., 2015	6/8	3/3	12/13	4/4	25/28	89	High
7.	Pawar et al., 2013	3/8	3/3	9/13	2/4	17/28	61	Medium
8.	Spoorthy et al., 2013	5/8	2/3	12/13	4/4	23/28	82	High
9.	Castelo-Baz et al., 2012	6/8	2/3	13/13	4/4	25/28	89	High
10.	de Gregorio et al., 2012	5/8	3/3	9/13	4/4	21/28	75	Medium
11.	de Gregorio et al., 2010	4/8	3/3	12/13	4/4	23/28	82	High
12.	de Gregorio et al., 2009	4/8	3/3	13/13	2/4	22/28	78	High

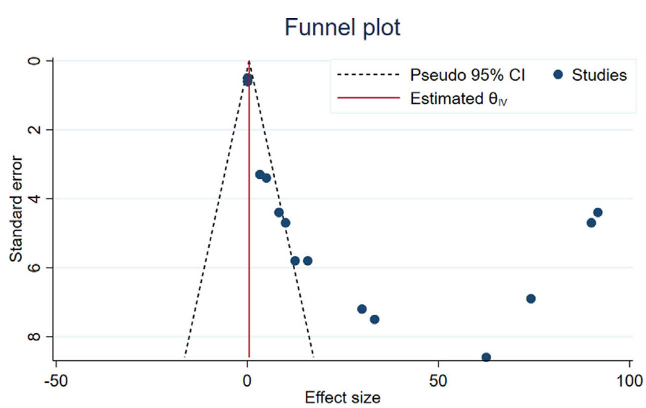
The numbers represent how many of the requirements were met by each study. high (score > 75 %), medium (score 50 %– 75 %), or low (score < 50 %).



Appendix Fig. A1 Penetration of sodium hypochlorite into the lateral canals of straight canals using PUI, ANP or MDA at 2, 4, 4.5 and 6 mm short of the WL, and its overall penetration in comparison to CNI; Effect size: standard mean difference (SMD).



Appendix Fig. A2 Penetration of sodium hypochlorite into the lateral canals of curved canals using PUI at 2, 4 and 6 mm short of the WL, and its overall penetration into the lateral canals in comparison to CNI; Effect size: percentage difference (% diff).



Appendix Fig. A3 Funnel plot analysis with 95% CI for the overall irrigant penetration into the lateral canals of straight canals of mature permanent teeth.

Ethical Statement

The study did not require ethics approval because this study is exclusively based on published literature.

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