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Self-perceived pain levels following irrigation with various concentrations of sodium hypochlorite solution and gels: A systematic review of randomized clinical studies

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Abstract

Background: Sodium hypochlorite, a prevalent root canal irrigation solution, valued for its antibacterial properties and tissue-dissolving abilities, varies in concentration (0.5% to 8.25%). However, its efficacy across formulations awaits systematic evaluation.

Aim: To evaluate self-perceived post-operative pain levels in a 5.25% concentration of NaOCl in gel or solution form.

Materials and Methods: An unrestricted search of indexed databases (PubMed, Embase, Scopus, Web of Science, and Cochrane) and a manual search were performed up to April 2023. Three randomized controlled trials (RCTs) compared a solution form of 5.25% NaOCl to other solution concentrations, whereas 2 RCTs compared a gel form of 5.25% NaOCl concentration to 5.25 % NaOCl solution form. The risk of Bias (RoB) assessment was conducted using the Cochrane tool.

Results: A total of 5 RCTs met the inclusion criteria and were included in the review. Four RCTs used the visual analog scale (VAS), whereas 1 RCT used the numeric rating scale (NRS) to assess post-operative pain. Three RCTs had a moderate Risk of Bias (RoB), whereas 1 had a low and 1 had a high RoB.

Conclusion: Based on the current evidence the concentration of NaOCl used during irrigation did not have any effect on the post-operative pain developed regardless of the use of a gel or solution forms. Future randomized studies with standardized protocols are needed to further investigate the efficacy of NaOCl concentration on postoperative pain in endodontic treatment.

Keywords: Root canal, irrigation, Sodium hypochlorite, postoperative pain, endodontic.

1. Introduction

Postoperative pain can be experienced following root canal treatment, which can be short or long-lasting, with an overall incidence reported as 39% - 65% within the first 24 hours [1, 2]. Several factors can affect postoperative endodontic pain, such as preoperative pain level [3, 4], the number of appointments [3, 5], the method of determination of the working length [3, 6], type of tooth [3, 7], type of the instrument [3, 8], movement kinematic of the device [3, 9], extrusion of root canal filling material and sealer [3, 10], apically extruded debris [3, 11], occlusal reduction [12], and method of irrigation [3, 13]. Despite the type and form of irrigation used, the challenge of eliminating residual microorganisms still exists and can significantly affect the treatment outcome [3, 14]. Sodium hypochlorite is the most common type of irrigation used in root canal treatment. One of the main reasons for its use is its physicochemical and antibacterial properties and its capability to dissolve organic tissue remnants [3, 15, 16]. Different concentrations of NaOCl have been used, ranging from 0.5% to 8.25%. A survey showed that American Association of Endodontists (AAE) members used NaOCl at concentrations higher than 5% [17, 18]. Another cross-sectional survey done in dental schools in the United Kingdom and Ireland reported that the most frequently used concentration of NaOCl in schools was 2-3%, where no institute supported the use of NaOCl concentrations higher than 3% [19]. A survey done among endodontic postgraduate students in dental schools in India, assessing irrigation protocols, has demonstrated that the most frequently used concentration of NaOCl was between 2.6% and 4% [20]. However, there is no consensus regarding the optimal concentration of NaOCl during root canal preparation [17]. Higher concentrations of NaOCl are more cytotoxic while producing increased tissue-dissolving effects [17, 21]. Previous studies on postoperative pain have utilized 2.5–5.25% or higher concentrations of NaOCl [17, 22-24]. AAE members and dentists have documented them in the USA, which limits the generalization of the results globally [18, 25]. A study by Kleier et al. reported that 42% of endodontists reported experiencing NaOCl accidents resulting from its extrusion from the foramen [26]. A spontaneous injection of NaOCl solution into the periapical

tissue may result in ulceration, hemolysis, tissue necrosis, allergic reaction, and postoperative pain [3, 27, 28].

Studies have shown that the gel form of NaOCl may be advantageous in reducing postoperative pain. However, the effectiveness of gel form in disinfection and smear removal is inconclusive [1]. Previous studies have evaluated the impact of several NaOCl forms on root canal dentin's microhardness. They have reported that the NaOCl gel and solution forms have similar results on dentinal microhardness, smear removal, and antibacterial properties [29, 30]. However, the tissue dissolution ability of the NaOCl solution has been reported to be higher than that of the gel form [31]. A study by Mostafa *et al.* reported that 1.3% compared to 5.25% of NaOCl solution resulted in less post-endodontic pain in mandibular molars [32]. In contrast, Farzaneh *et al.* reported that the 5.25% NaOCl led to significantly reduced postoperative pain compared to 2.5% NaOCl during the first 72 hours following root canal treatment of mandibular molars [17]. Moreover, a study by Karatas *et al.* concluded that the NaOCl gel results in less postoperative pain than the NaOCl solution on day 1 of endodontic treatment [3]. Another survey by Ozlek *et al.* showed that using the NaOCI gel form during root canal irrigation resulted in postoperative pain similar to that of the solution form [1]. Nonetheless, the comparison between different concentrations and formulations of NaOCl in root canal treatment has not been systematically assessed. Therefore, the objective of the present review was to compare self-perceived post-operative pain levels in patients undergoing root canal treatment with various concentrations of NaOCl used as an irrigation medium in solution or gel formulation.

2. Materials and methods

2.1 Protocol and registry

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [33]. The protocol of this study was registered with PROSPERO (CRD42023395599). The study duration was 7 months from November 2022 to June 2023. An electronic search was conducted of indexed databases PubMed, EMBASE, Scopus, ISI Web of Knowledge, and Cochrane Library without time restriction up to and including November 2023, based on the "Preferred Reporting Items for Systematic Review and Meta-analysis" (PRISMA) guidelines [33]. The following keywords were used: (1) Root canal treatment; (2) Root canal therapy; (3) endodontic therapy; (4) Irrigation solution (5) Sodium hypochlorite (NaOCl); (6) Sodium hypochlorite (NaOCl) solution; (7) Sodium hypochlorite (NaOCl) gel; (8) post-operative endodontic treatment pain. These keywords were combined using Boolean operators (OR, AND) to expand the search results (Supplementary Table A). Two authors (MA and GA) screened the titles and abstracts of studies identified with the above-mentioned protocol, and full texts of relevant studies were read independently. Hand-searching the reference lists of relevant original studies and review articles was also performed to identify studies that might have been missed in the previous step. Disagreements were solved through mutual discussion between authors, and in case of a lack of consensus through discussion, a third author (JK) and a fourth author (ZZ) were involved if needed. A meta-analysis was not performed due to high heterogeneity in the included studies.

2.2 Eligibility criteria

The present systematic review included randomized controlled clinical trials comparing self-perceived pain levels in patients undergoing root canal treatment with a 5.25% solution of NaOCl irrigation compared with other concentrations or gel forms. The focused question was, "Does a 5.25% solution of NaOCl irrigation induce less postoperative pain levels than other concentrations of NaOCl solution or 5.25% NaOCl of the gel in patients undergoing root canal treatment? Based on the following Participants-Interventions-Comparisons-Outcome-Study design (PICOS) approach: (P): Patients undergoing root canal treatment, (I): 5.25% solution or gel of NaOCl irrigation, (C): Other concentrations of NaOCl, (O): self-perceived postoperative levels, (S): randomized controlled clinical trials. Case reports, case series, letters to the editor, commentaries, reviews, and retrospective, experimental, non-randomized, and cross-sectional studies were excluded.

2.3 Study selection, data collection, and risk of bias

All the information from the included studies was synthesized by tabulating the data according to (a) study design, (b) the characteristics of NaOCl, (c) the relevance of study characteristics of participants undergoing root canal treatment, (d) duration of the follow-up treatments, (e) study outcomes of NaOCl on patients with root canal treatment. In addition, a quality assessment was performed. Two authors (MA and LJ) assessed the risk of bias (RoB) of included studies using the Cochrane Collaboration's RoB tool for RCTs [34].

3. Results

3.1 Search strategy

An electronic search that was performed without time restrictions up to and including April 2023, using the search engines PubMed, Embase, Scopus, Web of Science, and Cochrane revealed a total of 1005 manuscripts. After removing duplicates, 379 studies remained. Three manuscripts were added for screening after a hand search of the references in relevant manuscripts. After reading the titles and abstracts, 11 manuscripts underwent full-text assessment for eligibility, and six articles were excluded (Appendix A). Five RCTs [1, 3, 17, 32, 35] were included in the present systematic review for qualitative analysis and processed for data extraction (Figure 1).

3.2 General Characteristics of Included Studies

All RCTs included in the present systematic review had a parallel group design. The number of participants in the included RCTs ranged between 60 and 308, and the mean±standard deviation (SD) of the ages of the included participants ranged between 28.34±7.61 years and 43.3±19.0 years. All RCTs included both male and female subjects. Four RCTs [1, 3, 17, 35] reported patient dropouts. The reason for the dropout was either the patient was lost to follow-up or was not reachable by phone. In contrast, Mostafa *et al.* [32] reported no patient dropouts. A variability was noted amongst the included RCTs regarding the preoperative pain medication. The study duration ranged between 3 and 4 months, reported in 3 RCTs [17, 32,

35], and two RCTs [1, 3] did not report the study duration (Table 1).

3.3 General Characteristics of NaOCl

All RCTs reported that the diagnosis of the teeth was either necrotic pulp or irreversible pulpitis. Two RCTs [17, 35] reported no preoperative pain, and 3 RCTs [1, 4, 33] reported preoperative pain. Three RCTs [1, 17, 32] reported the type of tooth was mandibular molars, Karatas *et al.* [3] reported that the teeth treated included both mandibular and maxillary molars, and Demenech *et al.* [35] did not report the type of teeth treated. Two RCTs [17, 35] reported that the root canal treatment provider was an endodontist. At the same time, 2 RCTs [1, 32] reported that the endodontic treatment provider was a postgraduate student. Karatas *et al.* [3] did not report the provider. A variability was noted amongst the included RCTs in the instrumentation technique using rotary vs. manual, irrigation needle, irrigation technique, and final flush. Three RCTs [1, 17, 35] reported that the root canal treatment was completed in one session, and 1 study reported that the root canal treatment was completed in two sessions [32]. One study did not report the number of sessions required for root canal treatment [3] (Table 2).

3.4 General Characteristics of Outcome Variables

All RCTs reported that the person who assessed the pain was the patient. Four RCTs [1, 3, 17, 35] used the visual analog scale (VAS) to assess post-operative pain, whereas 1 study used a numeric rating scale (NRS) to evaluate postoperative pain [32]. A variability was noted amongst the included RCTs regarding the post-operative medication and interval of pain evaluation.

Domenech *et al.* [35] reported no statistical significance when comparing post-operative pain at different post-treatment intervals using different NaOCl concentrations. Farzaneh *et al.* [17] reported that the 5.25% NaOCl group was associated with significantly lower post-operative pain than 2.5% NaOCl during the first 72 hours. Mostafa *et al.* [32] reported that 1.3% NaOCl was associated with statistically significantly less intense and less frequent post-endodontic pain. Karatas *et al.* [3] reported that NaOCl gel during root canal preparation resulted in statistically less post-operative pain on day 1 following endodontic treatment. Ozlek *et al.* [1] reported that the gel and solution forms of NaOCl resulted in similar post-operative pain with no statistical significance (Table 3).

3.5 Risk of bias within studies

Three RCTs [1, 17, 35] had a moderate, one had a high [3], and one RCT had a low RoB [32] (Table 4, Figure 2). Power analysis for sample size estimation was performed in the included RCTs.

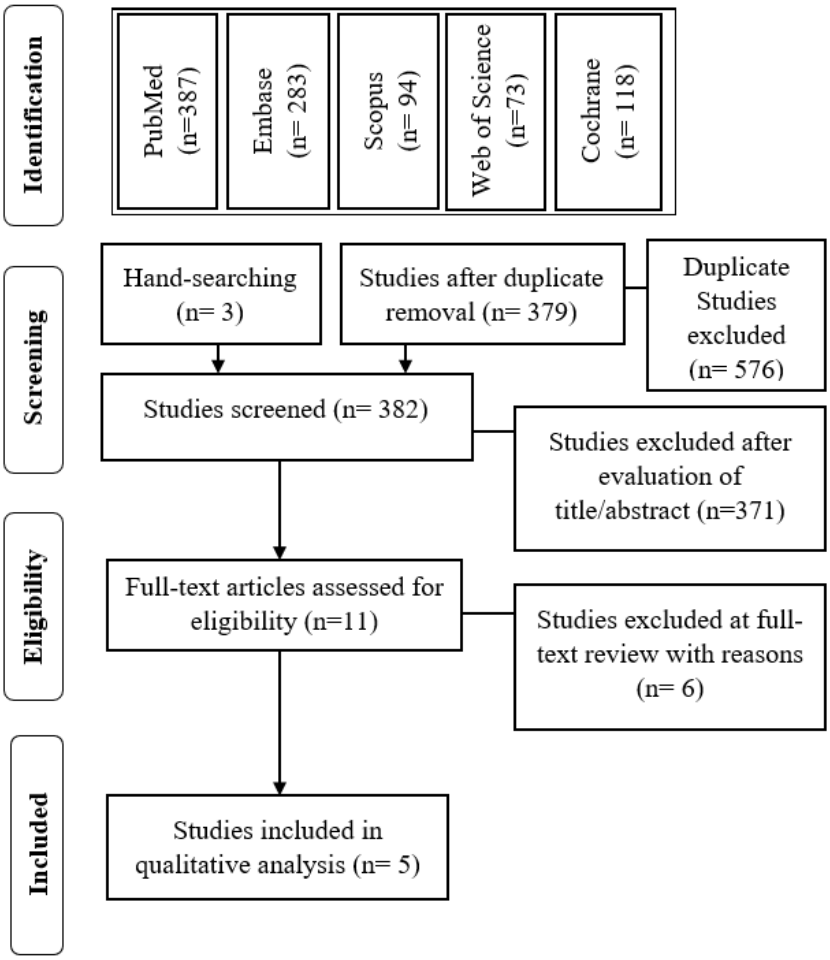

Figure. 1 Study flowchart based on the PRISMA guidelines.

Table 1: Characteristics of included studies

Author	Study design	Country	Initial subject included (Actual subjects included)	Groups	Mean age (±SD, yrs.)	Male/Female	Preoperative pain medication	Study duration
Demenech *et al.* 2021 (35)	Double Blind RCT	Brazil	Total n= 180 (169) 2.5% NaOCl n= 45 (43) 5.25% NaOCl n= 45 (42) 8.25% NaOCl n= 45 (41)	Four parallel groups in a 1:1:1:1 ratio. (2.5% NaOCl, 5.25% NaOCl, 8.25% NaOCl, 2% CHX)	2.5% NaOCl: 34.7 (±12.1) 5.25% NaOCl: 37.8 (±12.0) 8.25% NaOCl: 43.3 (±19.0)	2.5% NaOCl: 16/27 5.25% NaOCl: 16/26 8.25% NaOCl: 15/26	Analgesics and NSAIDs Not allowed	4 months
Farzaneh *et al.* 2018 (17)	Triple Blind RCT	Iran	Total n= 122 (110) 2.5% NaOCl n= 62 (55) 5.25% NaOCl n= 60 (55)	Two parallel groups in a 1:1 ratio. (2.5% NaOCl, 5.25% NaOCl)	2.5% NaOCl: 28.56 (±8.68) 5.25% NaOCl: 28.34 (±7.61)	2.5% NaOCl: 20/35 5.25% NaOCl: 19/36	Analgesic intake 6 hr. before Tx was not allowed	4 months
Karatas *et al.* 2020 (3)	Single Blind RCT	Turkey	Total n= 60 (51) 5.25% NaOCl Solution n= 30 (25) 5.25% NaOCl Gel n= 30 (26)	Two parallel groups in a 1:1 ratio (5.25% NaOCl Solution, 5.25% NaOCl Gel)	5.25% NaOCl Solution: 34.36 (±15.1) 5.25% NaOCl Gel: 39.62 (±16.5)	5.25% NaOCl Solution: 13/12 5.25% NaOCl Gel: 15/11	Analgesic intake 12 hr. before Tx was not allowed	NR
Mostafa *et al.* 2020 (32)	Double Blind RCT	Egypt	Total n= 308 (308) 1.3% NaOCl n= 154 (154) 5.25% NaOCl n= 154 (154)	Two parallel groups in a 1:1 ratio. (1.3% NaOCl, 5.25% NaOCl)	1.3% NaOCl: 32.14 (±5.79) 5.25% NaOCl: 31.60 (±5.87)	1.3% NaOCl: 62/92 5.25% NaOCl: 68/86	Analgesics and antibiotics 1 month before Tx were not allowed	3 months
Ozlek *et al.* 2021 (1)	RCT	Turkey	Total n= 114 (104) 5.25% NaOCl Solution n= 57 (52) 5.25% NaOCl Gel n= 57 (52)	Two parallel groups in a 1:1 ratio (5.25% NaOCl Solution, 5.25% NaOCl Gel)	5.25% NaOCl Solution: 31.25 (±8.76) 5.25% NaOCl Gel: 29.27 (±10.32)	5.25% NaOCl Solution: 24/28 5.25% NaOCl Gel: 25/27	Analgesics 12 hr. before Tx not allowed	NR

NR: Not reported, Tx: Treatment, RCT: Randomized control trial, hr: hours

4. Discussion

The present study aimed to evaluate postoperative pain in patients undergoing endodontic treatment with NaOCl as an irrigation medium at various concentrations and formulations. Pain management during and following endodontic treatment is a standard objective of a dentist [32, 36]. One of the reasons for postoperative pain can be the type and volume of irrigant used during the endodontic procedure [32, 37, 38]. Pre-treatment factors affecting the outcome include gender, age, tooth type, and preoperative pain [39]. Intra-treatment aspects include canal instrumentation technique, the number of visits, irrigant, an intracanal medication used, and the kind of sealer [7, 40, 41]. Moreover, Pamboo *et al.* reported no difference in age and postoperative pain [42]. Ali *et al.* [43] reported higher pain levels in the mandibular compared to the maxillary arch post-operatively. In contrast, Arias *et al.* [43] reported a higher incidence of postoperative pain, specifically in the mandibular molar teeth. Other studies show that the level of preoperative pain significantly affects the levels of postoperative pain [43-46]. Mie Hou *et al.* have reported that using reciprocating instrumentation in endodontic treatment leads to a higher incidence of postoperative pain compared to rotary systems [47].

Table 2: Characteristics of Sodium hypochlorite (NaOCl)

Author	Diagnosis	Preoperative pain	Tooth Type	Operator	Technique (Rotary vs. Manual)	NaOCl (Intervention group concentration)	NaOCl (Control group concentration)	Irrigation needle features	Irrigation technique	Final flush	Number of sessions
NaOCl solution form											
Demenech et al. 2021 (35)	Necrotic Pulp, Vital pulp with or without lesion	No	NR	Endodontist	Rotary (Continuous and Reciprocating)	5.25%	2.5% 8.25%	6 mL Endo - Eze tip needle/ NR	Not Reported	0.9% saline solution	1
Farzaneh et al. 2018 (17)	Irreversible Pulpitis with normal periapical radiographic appearance	No	Mandibular molars	Endodontist	Hand instruments and RaCe rotary instruments	5.25%	2.5%	2 mL irrigant w/ 30 -Gauge, side- Perforated needle	Needle penetration depth 2 mm short of the working length	3 mL 17% EDTA followed by 5 mL Saline solution	1
Mostafa et al. 2020 (32)	Symptomatic / Asymptomatic necrotic molars with or without radiographic evidence of apical periodontitis	Yes	Mandibular molars	Postgraduate students evaluated by endodontic faculty	Rotary NiTi files	5.25%	1.3%	3 mL irrigant w/ a 27- Gauge, notched-tip needle	Needle penetration depth 3 mm shorter than the working length	5 mL Saline solution	2
NaOCl gel form											
Karatas et al. 2020 (3)	Symptomatic apical periodontitis and a pulpal diagnosis of symptomatic irreversible pulpitis without radiolucency	Yes	Mandibular and maxillary molars	NR	Reciproc R25 files Rotary files	5.25% NaOCl solution	5.25% NaOCl Gel	2 mL irrigant / NR	Not Reported	6 mL of 17% EDTA	NR
Ozlek et al. 2021 (1)	Symptomatic Irreversible Pulpitis	Yes	Mandibular molars	Postgraduate students	Hand instruments and Rotary Pro Taper files	5.25% NaOCl solution	5.25% NaOCl Gel	5 mL irrigant w/ 30 Gauge, NaviTip irrigation needle	Needle penetration depth 2 mm short of the working length	5 mL of 17% EDTA, 5 mL of 5.25% NaCl solution and 5 mL of Saline solution	1

Table 3: Study outcomes

Author	Post Operative Medication	Who assessed the pain	The interval of pain evaluation	Pain scale	Statistical group comparisons		Outcome
					Time intervals	p-value	
NaOCl solution form							
Demenech et al. 2021 (35)	Nimesulide 100 mg every 12 hrs. for 3 days	The Patient	24hr, 48hr and 72hr	Visual analog scale	24hr 48hr 72hr	p>0.05 p>0.05 p>0.05	No significant difference in the postoperative pain with various conc of NaOCl irrigation solutions
Farzaneh et al. 2018 (17)	Gelofen 400mg on-demand use	The Patient	6hr, 12hr, 24hr, 48hr, 72hr, 4d, 5d, 6d and 7d	Visual analog scale	6hr 1hr 24hr 48hr 72hr 4d 5d 6d 7d	p<0.05 p<0.05 p<0.05 p<0.05 p<0.05 p>0.05 p>0.05 p>0.05 p>0.05	5.25% NaOCl was associated with significantly lower postoperative pain compared to 2.5% NaOCl during the first 72hrs.
Mostafa et al. 2020 (32)	Sham analgesic, to be taken in case of pain. If pain persisted, Ibuprofen 600 mg	The Patient	Immediately after instrumentation, 3hr, 24hr, 48hr, and 7 d after the first visit and, on the second visit, immediately after root filling	Numeric rating scale	Preoperative Immediately 3hr 24hr 48hr 7d Post obturation	p>0.05 p<0.05 p<0.05 p<0.05 p<0.05 p<0.05 p<0.05	1.3% NaOCl was associated with less intense and less frequent post-endodontic pain than 5.25% NaOCl.
NaOCl gel form							
Karatas et al. 2020 (3)	Not Reported	The Patient	24hr, 48hr, 72hr and 1 week	Visual analog scale	Preoperative 1d 2d 3d 7d	p>0.05 p<0.05 p>0.05 p>0.05 p>0.05	NaOCl gel form during root canal preparation resulted in less postoperative pain on day 1 compared to the NaOCl solution.
Ozlek et al. 2021 (1)	400 mg of Ibuprofen prescribed for severe pain only	The Patient	6hr, 24hr, 48hr, 72hr and 1 week	Visual analog scale	Preoperative 6hr 24hr 48hr 72 7d	p>0.05 p>0.05 p>0.05 p>0.05 p>0.05 p>0.05	The gel and solution forms of NaOCl resulted in similar postoperative pain.

Table 4: Table Risk of bias

Domain	Demenech *et al.*, 2021 (35)	Farzaneh *et al.*, 2018 (17)	Karatas *et al.*, 2020 (3)	Mostafa *et al.* 2020 (32)	Ozlek *et al.* 2021 (1)
Random sequence generation	Low	Low	Low	Low	Low
Allocation concealment	Low	Low	Low	Low	Low
Blinding of participants and researchers	High	High	High	Low	High
Blinding of outcome assessment	High	High	High	Low	High
Incomplete outcome data	Low	Low	High	Low	Low
Selective outcome reporting	Low	Low	Low	Low	Low
Other bias	Low	Low	Low	Low	Low
Overall	**Moderate**	**Moderate**	**High**	**Low**	**Moderate**

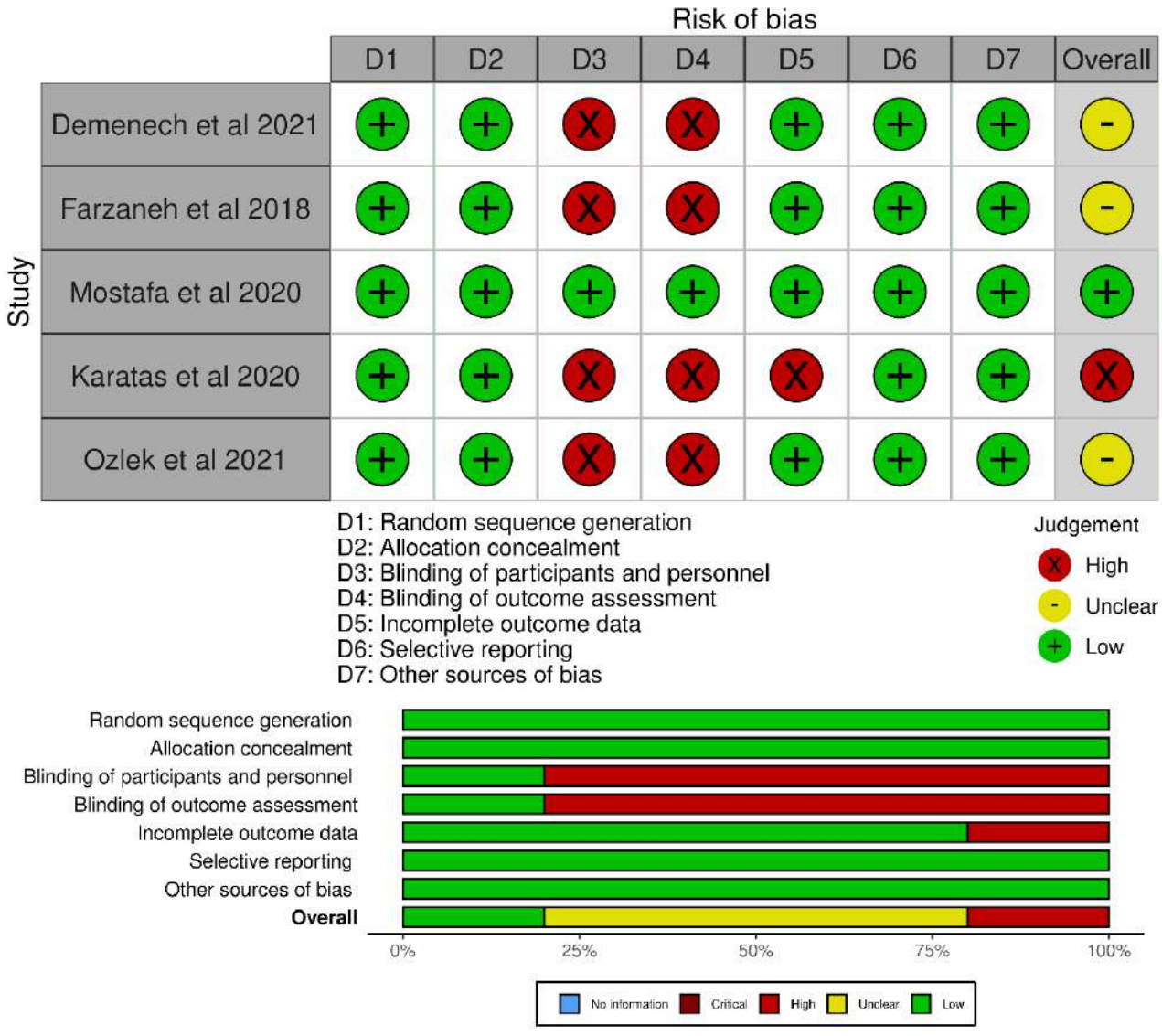

Figure 2. Quality assessment of the randomized clinical trials according to Cochrane Collaboration for risk of bias (RoB) tool.

Furthermore, a systematic review by Manfredi *et al*. shows that a one-visit root canal treatment can likely lead to higher pain levels post-operatively within the first week [48]. When comparing different concentrations of NaOCl, Farzaneh *et al*. reported that 5.25% NaOCl was associated with significantly less postoperative pain compared to a lower concentration of 2.5% NaOCl during the first 72 hours [17]. On the contrary, Mostafa *et al*. reported that the lower concentration of NaOCl, 1.3%, was associated with significantly less postoperative pain than 5.25% NaOCl [32]. Finally, Demenech *et al*. reported no significant difference between different concentrations of NaOCl regarding postoperative pain [35]. In addition, the RCTs that were comparing different forms of NaOCl also had some variability in their reported results. Karatas *et al*. concluded that using NaOCl in the gel form resulted in significantly less postoperative pain when compared to using NaOCl in the solution form [3]. However, this significant reduction in post-operative pain was limited to day one following treatment. Ozlek *et al*. reported no significant difference in postoperative pain when comparing the solution and the gel forms of NaOCl [1]. Many studies have shown that the gel form of NaOCl might reduce postoperative pain. However, the effectiveness of gel form in disinfection and smear removal is inconclusive [1]. Several studies have reported that the gel and solution forms of NaOCl have similar results on dentinal microhardness, smear removal, and antibacterial properties [29, 30]. Additionally, the tissue dissolution ability of the NaOCl solution has been reported to be higher than that of the gel form [31]. A study was done by Faria *et al*. to evaluate the penetration of sodium hypochlorite (NaOCl) gel or NaOCl solutions with surfactants and the effect of passive ultrasonic irrigation (PUI) on penetration into dentinal tubules. The study showed that the 3% NaOCl gel had less penetration depth into dentine than the solution form, which its viscosity could explain. The lower penetration depth of 3% NaOCl gel may impair the disinfection of dentinal tubules[49]. However, further studies are needed in this regard. Nonetheless, based on the currently available evidence, it is challenging to identify the ideal NaOCl concentration following endodontic treatment and finalize the long-term success of a concentration of 5.25% NaOCl in postoperative pain outcomes.

The strength of the present systematic review is the inclusion of solely RCTs, which included both genders. In addition, all the included RCTs performed a power analysis for sample size estimation, thus reducing the probability of type II error during statistical analysis of the results. However, a limitation of this review was the methodological inconsistencies observed in the included RCTs regarding the interval of pain evaluation, control groups heterogenicity, NaOCl concentration, irrigation needle size and technique, materials used for final flush, number of sessions needed to finish the endodontic treatment and the post-operative analgesic medication used. Patients in the included RCTs were asked not to take pain medications at least 12 hrs. before endodontic treatment to control the preemptive effect on post-endodontic pain. This resulted in high variability in the results when comparing different concentrations of NaOCl as well as different forms of NaOCl. It is worth mentioning that three RCTs [1, 17, 35] had a moderate RoB, one RCT [3] had a high RoB, and one RCT [32] had a low RoB. The main reasons that introduced potential biases in the RCTs included the lack of blinding of participants, researchers, and outcome assessment. Based on these limitations, caution is recommended when interpreting individual study results. In three RCTs [1, 32, 35], adjustments were made for multiple testing when comparing intervention with control groups, such as using the Bonferroni correction. The authors of the present systematic review perceive that all RCTs' p-values should have been adjusted using multiplicity correction to account for the multiple group comparisons among several time points. Therefore, the warning is recommended when interpreting individual study results based on these restrictions. Due to the limited number of RCTs, it was not possible to perform sensitivity analysis and subgroup analyses for the patient and intervention-related characteristics and assess the risk of publication bias across studies.

In the present review, the authors recognize that the VAS was a practical instrument in evaluating postoperative pain in patients undergoing endodontic treatment. However, potential biases such as mood bias and false reporting bias cannot be overlooked. The VAS scale was used because it is a simple, valid, and reliable method for assessing self-reported pain levels. In addition, it is a measurement tool that is more accessible for patients to interpret and record their pain perceptions [1, 50]. From a clinical perspective, additional characteristics should be considered before recommending a 5.25% NaOCl solution as the best concentration for postoperative pain outcomes. It is a common practice to use a concentration of 5.25% NaOCl in the solution form for irrigation during endodontic procedures. However, NaOCl solution is antimicrobial, can dissolute the pulp, and has low biological compatibility, which may induce postoperative pain [16, 51]. Moreover, the nature of the pulp and periapical status may modify post-endodontic pain response [7, 32, 40]. Post-endodontic pain is associated with pulp necrosis, symptomatic apical periodontitis, and preoperative periapical radiolucency [32, 40]. Preoperative periapical radiolucency was also associated with pain lasting more than two days [7, 32]. Hence, future standardized studies are needed to measure the potential role of the concentration of 5.25% NaOCl on postoperative pain in patients undergoing root canal treatment.

6. Conclusion

Overall, the NaOCl solution concentration did not have a significant effect on the post-operative pain. One study showed that the gel form was more effective in reducing pain 1-day post-operative when compared to the 5.25% solution form. Preoperative periapical radiolucency was associated with pain lasting more than two days. The authors suggest that further well-designed RCTs are needed to identify the potential role of the concentration and formulations of NaOCl on postoperative pain outcomes in patients undergoing root canal treatment.

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