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The effect of sodium hypochlorite and chlorhexidine as irrigant solutions for root canal disinfection: a systematic review of clinical trials

ABSTRACT

Aims: This systematic review aimed to compare the effectiveness of sodium hypochlorite and chlorhexidine for root canal disinfection during root canal therapy.

Methods: A literature search for clinical trials was made on the PUBMED (Medline), Web of Knowledge, SCOPUS, and Science Direct databases and in the reference lists of the identified articles up to January 2015. Quality assessment of the selected studies was carried out according to the CONSORT statement.

Results: One clinical trial and four randomized clinical trials (RCTs) were selected from the 172 papers initially identified. There was heterogeneity in the laboratory methods used to assess the root canal disinfection as well as in the concentrations of the irrigants used. Therefore, meta-analysis was not performed. Two studies reported effective and similar reductions in bacterial levels for both irrigants. Sodium hypochlorite was more effective than chlorhexidine to reduce microorganisms in one study and another reported opposite findings. Both root irrigants were ineffective in eliminating endotoxins from necrotic pulp root canals in one study. Trial design and information regarding randomization procedures were not clearly described in the clinical trials. No study compared laboratory results with clinical outcomes.

Conclusions: The available evidence on this topic is scarce and the findings of studies were not consistent. Additional RCTs using clinical outcomes to compare the use of sodium hypochlorite and chlorhexidine during root canal therapy are needed.

Key words: endodontic, sodium hypochlorite, chlorhexidine, clinical trial

INTRODUCTION

The effectiveness of endodontic therapy involving pulp necrosis depends on the adequate disinfection of the root canal and appropriate seal during canal obturation. In those clinical cases, instrumentation and irrigation procedures using chemomechanical techniques are crucial for root canal disinfection **(1,2).** The cleaning and shaping of the root canal system using irrigant solutions play an essential role in the success of debridement and disinfection **(3,4).**

The failure of root canal treatment has predominantly been associated with an ineffective removal of microorganisms from the root canal system. Therefore, persistent infection in the root canal is related to remaining necrotic tissue and bacteria, which in turn affects tissue healing in the periapical area **(5).**

Distinct chemicals have been suggested as efficient irrigant solutions for root canal disinfection. Among them, sodium hypochlorite is the most widely used in endodontic treatment because of its effective antimicrobial activity and ability to dissolve organic tissues **(4).** Nonetheless, there is a lack of agreement concerning the ideal concentration of sodium hypochlorite. According to one study there was a remarkably reduction in the levels of bacteria in the root canal when sodium hypochlorite at 0.5% and 3% were employed **(6)**. In another study, bacterial diversity of the root canal decreased significantly after chemomechanical endodontic preparation using sodium hypochlorite at 2.5% **(7).** The excellent organic solvent properties of sodium hypochlorite give it its antimicrobial effectiveness as an irrigant agent **(8).** On the other hand, sodium hypochlorite is a potential irritant of periapical tissues, especially at high concentrations **(9-11).** Thus, the search for other root canal irrigants with a lower potential to induce adverse side-effects is desirable.

Chlorhexidine gluconate has been proposed as a promising irrigation agent to replace sodium hypochlorite during root canal disinfection and endodontic instrumentation **(12,13).** The antibacterial properties of chlorhexidine have been extensively demonstrated when used as an adjunct treatment to different oral diseases **(14,15).** Chlorhexidine gluconate has also excellent antiseptic properties and its effectiveness in the chemical control of dental biofilm in patients with periodontal disease has already been proved **(16-18).** The main limitation of chlorhexidine gluconate as an endodontic irrigant is its inability to dissolve pulp tissue **(19).**

The evaluation of endodontic therapy protocols in terms of the chemical irrigant employed during the root canal disinfection is essential to establish evidence based guidelines to improve clinical outcomes in endondontics. Antimicrobial effectiveness is undeniably the foremost chemical property of irrigant solutions used in the treatment of root canals with apical periodontitis **(20).** Previous studies have pointed out the antimicrobial effectiveness of sodium hypochlorite and chlorhexidine during root canal treatment. However, no systematic review comparing the effectiveness of these irrigant agents during endodontic treatment has been conducted. The aim of this study was to conduct a systematic review of clinical studies on the effectiveness of sodium hypochlorite and chlorhexidine for root canal disinfection during root canal therapy.

MATERIALS AND METHODS

The methodology used in this systematic review includes 1) a literature search strategy, 2) selection criteria, 3) screening and data extraction and 4) a quality assessment.

Literature search strategy

The search strategy covered electronic databases and the reference lists of such papers identified published through to January 2015. The electronic databases searched were: PUBMED (Medline), Web of Knowledge, SCOPUS, and Science Direct. The following combination of key words and medical subject heading (MeSH) terms through the Boolean operator used were: “sodium hypochlorite”, “chlorhexidine”, “endodontic treatment” and “clinical trials”.

Selection Criteria

Clinical trials and randomized controlled trials were selected; however only papers comparing chlorhexidine and sodium hypochlorite as irrigant agents during root canal treatment were included. Other inclusion criteria were studies published in English, root canal treatment involving permanent teeth with pulp necrosis and the use of laboratory outcome measures to assess root canal disinfection. Observational studies, previous reviews, case studies, case series, in vitro studies and those that did not quantify the antimicrobial effect of irrigants were excluded.

Screening and data extraction

Initially, potential relevant publications involving endodontic irrigants were retrieved independently by two reviewers (C.V.A. Jr. and R.C.V.R). All papers were submitted to selection criteria and those that fulfilled all criteria were read in full. Disagreements were resolved by consensus after discussion with a third reviewer (L.S.G.). The extraction of information from studies was conducted by the same reviewers.

Quality Assessment

The quality of the selected studies was assessed according to the Consolidated Standards of Reporting Trials (CONSORT) statement (21). All sections of articles were analyzed using the CONSORT 2010 checklist: title and abstract, introduction, methods, results and discussion. Each section was subdivided into items, as described in the CONSORT statement (21).

The methodological parameters related to the validity of the studies were:

Description of trial design (including allocation ratio): was the trial design clearly defined? Yes/No

Intervention: were the interventions clearly defined? Yes/No

Concentration of endodontic irrigants: was the concentration of the endodontic irrigants clearly defined? Yes/No

Calibration: were the examiners calibrated for endodontic clinical procedures? Yes/No

Outcomes: were the outcomes clearly defined? Yes/No

Outcomes assessment: was the outcome assessed in the same manner between groups? Adequate: when the effectiveness of irrigant solution was assessed in the same manner between groups. Inadequate: when the effectiveness of irrigant solution was not assessed in the same manner between groups.

Laboratory method to evaluate root canal disinfection: was the laboratory method employed to evaluate root canal disinfection clearly informed: Yes/No

Sample size calculation: did the paper explain the rationale for the study sample size? Yes/No

Randomization: were the irrigant agents randomized among participants? Yes/No

Randomization / Sequence: was the method used to generate the random allocation sequence reported? Yes/No

Randomization / Generation: was the type of randomization reported? Yes/No

Randomization / Allocation concealment: concealment/mechanism: was the mechanism used to implement the random allocation sequence reported? Yes/No

Randomization / Implementation: was the information concerning who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions reported? Yes/No

Blinding: were the examiners blinded regarding the endodontic irrigants? Yes/No

Statistical procedures: was adjusted analysis carried out? Yes/No

Intention-to-treat analysis: was intention-to-treat analysis conducted? Yes/No

When the information was not available, the article was classified as unclear.

RESULTS

Figure 1 summarizes the search strategy process. The initial search identified 172 potential papers. However, 152 were in vitro studies and therefore were excluded. Twenty of the remaining 15 clinical trials were also excluded because no comparisons between NaOCl and CHX were made (14 papers) and the effectiveness of root disinfection was not tested (1 paper). In the end, four randomized clinical trials and one non-randomized clinical trial were included in this systematic review.

Because of the heterogeneity of the laboratory methods employed to evaluate the effectiveness of endodontic irrigants, meta-analysis could not be performed.

Of the five selected studies, four reported the eligibility criteria **(20,22-24).** These studies only included single rooted teeth and teeth with pulpal necrosis. Patients who had received antibiotic treatment had been excluded from these four studies.

All studies reported the concentration and amount of the irrigants used in the trials as well as the microbiological techniques to assess the effectiveness of the irrigant. Distinct protocols of endodontic treatment were assessed since different concentrations of irrigant solutions were compared. NaOCl concentrations were tested at 2.5% **(20,22-24)** and 5.25% (**25)**, while CHX was evaluated using 0.12% **(20)**, 0.2% **(22)** and 2%

(23-25). Calibration of the examiners for the endodontic clinical procedures was not conducted in any study. Outcomes were clearly reported in four studies **(20,22-24).** The effectiveness of the irrigant solution was assessed in the same manner between groups in all studies.

The laboratory methods employed to evaluated root canal disinfection were heterogeneous among studies; the main ones were: culture techniques **(22-25)** and molecular methods **(20,23).**

The five studies **(20,22-25)** investigated the effectiveness of root canal disinfection comparing NaOCl and CHX by collecting samples from the root canal before and after the protocol treatments. Periapical radiographs were used to confirm the presence of radiolucency whereas pulpal necrosis and apical periodontitis were assessed through clinical examination in all studies. No study reported sample size calculation or justified the final sample size.

Randomization was conducted in four of the five studies **(22-25)**. However, the procedures used to assure adequate randomization were not reported in any study. There was a lack of information regarding randomization sequence, generation, allocation and concealment in all studies. No study informed whether the examiners were blinded regarding the endodontic irrigant. Adjusted analysis and intention-to-treat analysis were carried out in all studies. The number of participants for each group was informed in all studies; however, no study provided recruitment and follow-up dates as well as baseline data.

The sample sizes varied from 20 to 54 patients. The mean age of patients was described in three of the five studies **(23,24,25)**, ranging from 18 to 63 years old. All studies addressed potential limitations; however, generalizability was not presented in any study.

There was a lack of agreement between the findings of the selected studies. **Vianna et al. (23)** concluded that sodium hypochlorite at 2.5% was more effective than CHX at 2%. NaOCl displayed not only a higher capacity to eliminate endodontic pathogens but was also more capable of removing cells from the root canal. Ercan et al. (25) concluded that chlorhexidine at 2% was more effective than NaOCl at 5.25%. Kuruvilla and Kamath (22), and Rôças and Siqueira (20) reported that NaOCl at 2.5% and CHX at 0.2% and 0.12% were effective in reducing the levels of bacterial in infected root canals. Gomes et al. (24) reported that NaOCl at 2.5% and CHX gel at 2% were not effective in eliminating endotoxin from the primarily infected root canals.

DISCUSSION

The success of endodontic therapy depends on the substantial removal of vital and necrotic tissues, microorganisms and their products from the root canal system **(26).** In some cases, the complexity of the root canal system causes some difficulties to adequately shape and clean the root canal. Chemomechanical debridement combining mechanical instrumentation with chemical irrigants can promote an adequate disinfection of the root canal systems during the endodontic treatment. This is probably due to the significant reduction of intracanal microorganisms and necrotic tissues **(22,25,27).**

NaOCl is the most widely solution employed to irrigate root canals during endodontic therapy and it has been used in different concentrations (0.5% to 5.25%). Of the five studies included in this review, four trials have used NaOCl at 2.5% (20, 22-24) whereas one study

(25) has used NaOCl at 5.25%. CHX showed better results against both NaOCL concentrations. The variations in the NaOCl concentration among the included studies probably did not influence the results, because it has been reported that the concentration of NaOCl does not influence the antibacterial efficacy (28,29,30). Nevertheless, although the efficacy of NaOCl is strongly related to the volume and frequency of irrigation, this information was not recorded in the trials (29). In addition, the duration of NaOCl irrigation, representing the time that the canal has been exposed to NaOCl, may influence its antibacterial effectiveness. In fact, a higher concentration will not necessarily result in a deeper penetration of the solution in the intricacies of the root canal (30).

Nonetheless, CHX is a potential chemical irrigant indicated for root canal treatment. NaOCl has some advantages over CHX when used as an endodontic irrigant including its tissue-dissolving capacity and broad-spectrum of antimicrobial activity (4,31). However, NaOCl is highly cytotoxic to the periapical tissues representing a clear disadvantage (32).

CHX has been described as a potential substitute for NaOCl during chemomechanical debridement in endodontic treatment. CHX is less cytotoxic to the periapical tissues than NaOCL; however as an antimicrobial it is highly effective against a range of Gram-positive and Gram-negative oral bacterial species (33). The substantivity of CHX in dentin seems to be an advantage over NaOCl (34). Thus, different studies have been conducted to compare the effectiveness between NaOCl and CHX for the disinfection of the root canal.

In the present systematic review, only five studies met the inclusion criteria (20,22-25). However, two of them did not report significant differences when comparing NaOCl and CHX (20,25). One study showed that NaOCl was more effective than CHX during chemomechanical preparation in endodontic therapy (23). While Ercan et al., (25) concluded that CHX was more effective. Another study described that both irrigants were ineffective in eliminating endotoxin from the primarily infected root canals (24).

Three of the five studies analyzed the antibacterial effects of these two irrigants using culture-dependent methods (22,24,25) that has been traditionally used for the identification of endodontic bacteria (35). However, this method has significant limitations due to its low sensitivity and inability to detect viable and as yet-uncultivable phylotypes. These limitations may underestimate the resistance rates of bacteria and/or inaccessible location to the treatment procedures (7,36). Recently, molecular biological methods have greatly expanded the knowledge about the bacterial diversity in endodontic infections. Two of the selected studies in this systematic review used molecular methods to investigate the antibacterial efficacy of the irrigants during endodontic therapy. NaOCl was more effective than CHX in one study (23) whereas another did not show significant differences between the irrigants (20).

The different laboratory methods employed in the included studies is also an important factor to help understand the variability of their findings. Nevertheless, the two studies that have used molecular methods also did not find similar results (20,23).

In the current systematic review, all studies evaluated the effectiveness of the irrigant substances in single-rooted teeth and through microbiological analysis (20,22-25). The use of only single-rooted teeth imposes an important limitation of their findings as the results cannot be applied to multi-rooted teeth. The anatomical complexity of root canals found in molars is a challenge for root disinfection since microorganisms can be hidden in the canal niches. The anatomical and morphological complexities of root canal systems represented by isthmus, lateral canals and curvatures are significant challenges for effective root canal disinfection (37, 38).

Future clinical trials on this topic should address some flaws and limitations identified in this systematic review. Although most studies informed the allocation of the irrigant solutions was randomized between intervention groups (22-25), the procedures to assure an adequate randomization of the irrigant agents was not clearly reported. All selected studies evaluated the effectiveness of the root canal disinfection using chemical substances immediately after the chemical mechanical preparation, but did not correlate the microbiological and laboratory results with clinical outcomes, which restricts the translation of the findings into clinical practice. Ideally, forthcoming clinical trials should correlate the microbiological characteristics of the root canals before and after the use of the two irrigant agents with the clinical conditions after the treatment. The latter could be assessed through the absence of clinical signal and symptoms relief or by the healing of periapical tissues confirmed by image exams such radiograph or cone beam computed tomography. The available in vivo microbiological studies present limitations because they have collected samples using absorbent paper points. This technique may reveal bacteriological conditions only in the main root canal as absorbent paper points do not reach microorganisms located in isthmuses, dentinal tubules, lateral canals and apical ramifications. Bacteria can pass unnoticed by the paper point sampling approach (39). The sampling collection method using paper points might not able to obtain samples that can really represent the bacterial population of the root canal system of infected teeth, which is crucial for the improvement of the treatment protocols (40-44).

The use of CONSORT criteria in the quality assessment revealed that essential information to evaluate the methodological aspects of the selected studies was missing or unclear. Based on the available scientific literature, there is no evidence to suggest whether NaOCl or CHX should be the irrigant agent of choice during endodontic therapy of single-rooted teeth with pulp necrosis.

Additional well-designed randomized clinical trials comparing the effectiveness between NaOCl and CHX for root canal disinfection during root canal therapy using clinical outcomes and analyzing single and multi-rooted teeth are needed. They should consider an appropriate report of the research design protocol, including the randomization process, as well as a clear description regarding the implementation of the intervention. The use of CONSORT when reporting clinical trials is a powerful tool and the adherence to CONSORT guidelines is imperative in future studies (45).

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The authors deny any conflicts of interest related to this study.

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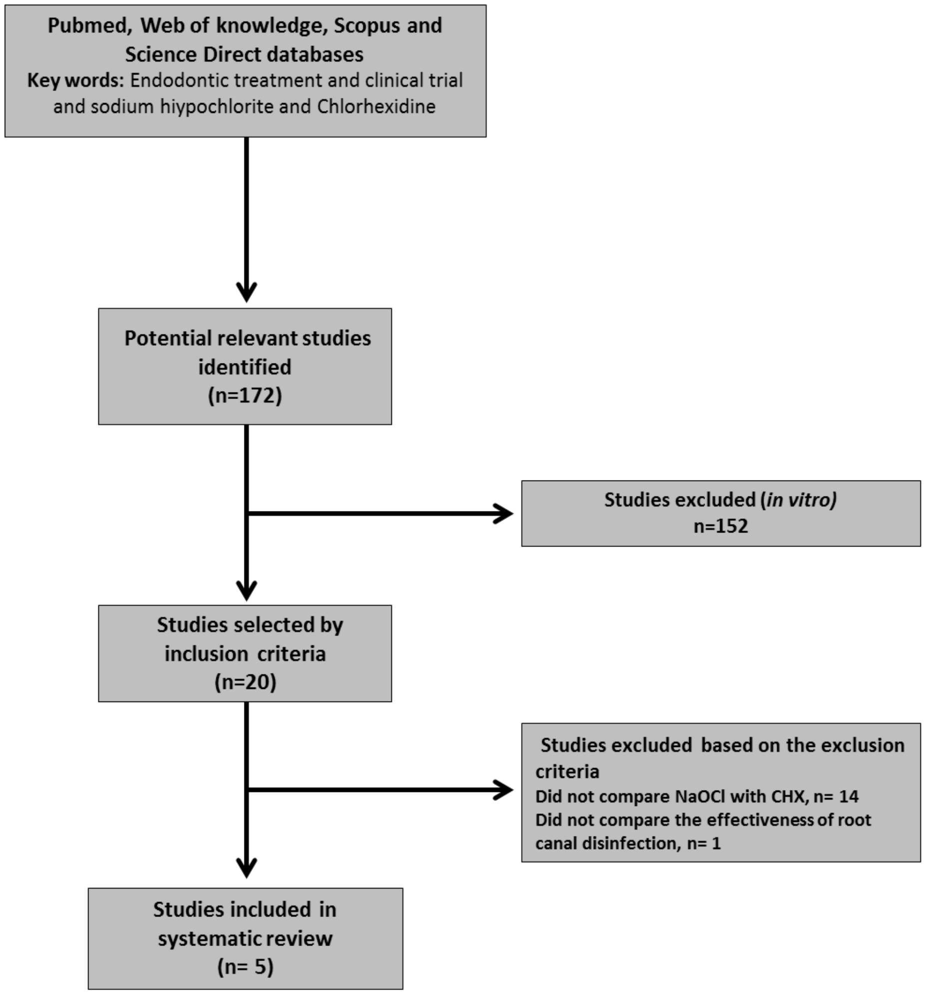

Figure 1. **Search strategy flow chart**

Table 1. Characteristics of studies comparing the effectiveness of sodium hypochlorite and chlorhexidine in the root canal disinfection during root canal therapy

Authors/Year	Title and abstract	Introduction		Methods						
		Explanation the rationale	Justify need for a new trial	Trial design	Elegibility (exclusion) criteria	Settings and locations	Biological condition of the root canal	Intervention	Concentration of endodontic irrigants	Calibration
Kuruvilla & Kamath, 1988	Title: No Abstract: No	Yes	Yes	No	Yes: Antibiotic therapy, multirooted teeth	No	Yes: pulpal necrosis	Yes	Yes: 2.5 % NaOCl 0.2% CHX	No
Ercan et al., 2004	Title: No Abstract: No	Yes	Yes	No	No	No	Yes: pulpal necrosis	Yes	Yes: 5.25% NaOCl 2% CHX	No
Vianna et al., 2006	Title: No Abstract: No	Yes	Yes	No	Yes: vital teeth, antibiotic therapy, systemic disease, multirooted teeth	Yes: University dental clinic, Brasil	Yes: pulpal necrosis	Yes	Yes: 2.5% NaOCl 2% CHX	No
Gomes et al., 2009	Title: No Abstract: No	Yes	Yes	No	Yes: Periodontal disease, antibiotic therapy, systemic disease, multirooted teeth	Yes: University dental clinic, Brasil	Yes: pulpal necrosis	Yes	Yes: 2.5% NaOCl 2% CHX	No
Rôças & Siqueira Jr., 2011	Title: No Abstract: No	Yes	Yes	No	Yes: Antibiotic therapy in the last 3 months, teeth with gross carious lesions, root or crown fracture, periodontal pockets > 4mm, multirooted teeth	Yes: University dental clinic, Brasil	Yes: pulpal necrosis	Yes	Yes: 2.5% NaOCl 0.12% CHX	No

Author/Year	Methods								
	Outcomes	Outcomes assessments	Laboratory method	Sample size	Randomization Sequence	Randomization Generation	Randomization Allocation concealment	Implementation	Blinding
Kuruvilla & Kamath, 1988	Yes	Adequate	Yes: Cultura technique	No	No	No	No	No	No
Ercan et al., 2004	No	Adequate	Yes: Culture technique	No	No	No	No	No	No
Vianna et al., 2006	Yes	Adequate	Yes: Culture and molecular method	Yes	No	No	No	No	No
Gomes et al., 2009	Yes	Adequate	Yes: Culture technique	Yes	No	No	No	No	No
Rôças & Siqueira Jr., 2011	Yes	Adequate	Yes: Molecular method	Yes	Not RCT	Not RCT	Not RCT	Not RCT	No

Author/Year	Methods		Results					Discussion	
	Statistical procedures	Intention-to-treat analysis	Participant flow	Recruitment	Baseline data	Numbers analysed	Outcomes and Estimation	Limitations	Generalisability
Kuruvilla & Kamath, 1988	Yes	Yes	Yes	No	No	N=40 Age group: NI	Adequate	Yes	No
Ercan et al., 2004	Yes	Yes	Yes	No	No	N=20 Age group: 20-52	Adequate	Yes	No
Vianna et al., 2006	Yes	Yes	Yes	No	No	N=32 Age group: 19-63	Adequate	Yes	No
Gomes et al., 2009	Yes	Yes	Yes	No	No	N=45 Age group: 18-62	Adequate	Yes	No
Rôças & Siqueira Jr., 2011	Yes	Yes	Yes	No	No	N=50 Age group: NI	Adequate	Yes	No

NI: not informed