REVIEW PAPER

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EFFECTIVENESS OF INTRACANAL CALCIUM HYDROXIDE MEDICAMENT IN TREATING PERIAPICAL LESIONS: A SYSTEMATIC REVIEW

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ABSTRACT

Previous literature has shown that calcium hydroxide (CH) is a useful intracanal medicament for root canals. However, there is no conclusive evidence of its success rate in patients with periapical lesion. This study aimed to investigate the success rate and impact effect of endodontic treatment was done with CH in treating periapical lesions. We searched PubMed, Scopus, Web of Science databases, and Google Scholar as an engine to retrieve relevant interventional studies. Interventional studies were done on the success rate and impact effect of CH for patients with periapical lesion by endodontic treatment/retreatment approaches. Reviews, duplicate, animal studies, and other irrelevant studies were excluded. Two investigators independently following the (PRISMA) guidelines conducted the study selection and data collection process. The outcomes of this review were the status of the periapical lesion at the end of follow-up. We retrieved 8 studies with 481 participants. The success rate of CH in this review was 75.5%. The success rate of CH was 16% in patients with periapical/radicular cysts and 74% in patients with apical periodontitis after intracanal CH medicament. The post-treatment follow-up period showed a high success rate in patients with > 1-year post-treatment follow-up (62%) while the success was 30% in 6 month – 1-year post-treatment follow-ups. CH has a higher healing effect in lesions of ≤ 5 mm diameter than > 5 mm diameter (81.6% vs. 18.4%). Finally, intracanal CH has a clinically significant effect on the healing of periapical lesions. This review suggests orthograde root canal treatment with CH as an alternative to periapical/apical surgery.

Key words: radicular cyst, periapical lesion, root canal therapy, calcium hydroxide, intracanal medicament.

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INTRODUCTION

Periapical lesions are the commonly occurring pathologic lesions that affect the periradicular tissues of the tooth [1]. This lesion can be classified as granuloma, cystic, or abscess [2, 3]. The cystic transformation of periapical lesions was 6-55% in small lesions and 100% in large lesions (> 2 cm) [4], 9.3-87.1% of the lesions develop periapical granuloma, and 28.7-70.7% forms abscess [5]. The pathologic changes seen in some periradicular and periapical cases are due to the presence of microorganisms, and their byproducts. These released toxins have the ability to diffuse through inflamed pulpal tissue and get into the periapical area. In a necrotic pulp, the lack of blood flow in the root prevents host immunity from eliminating the infection [6-8].

Periapical lesions were managed by either surgical or non-surgical methods [9]. It is often reported that root

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canal therapy (RCT) has a success rate of 80-85% [10] with a higher rate in a tooth without periapical radiolucency [11-13]. Furthermore, the success rate of periapical surgery for patients with periapical lesions was 73.9% after a 1-year postoperative follow-up [14]. When strict criteria were used in one study conducted in 2007 by Ng *et al.* [15], found the success rate of therapies completed at least 1 year prior to evaluation was between 68% and 85%. However, a study done by Del Fabbro *et al.* [16] found that at the 1-year postoperative follow-up, there was no clear difference in success rate between surgical and non-surgical approaches (RR 1.15, 95% CI: 0.97-1.35). Even if the surgical intervention has been commonly practiced now, it has its disadvantages such as; affect the vitality of the adjacent tooth, damage vital structures [17-19], and older patients may not tolerate the procedure and feels considerable pain and discomfort [19].

Different studies were used CH as intracanal dressing during RCT of an infected root canal and found significant elimination of pulpal microbes from root canals with periapical lesions after a one-month follow-up [20-22]. The success rate of RCT was 73.8-80.8% after CH intracanal medicament [23, 24]. The characteristic of CH such as: bactericidal effect [25-29], periapical repair and stimulation of hard tissue formation [23, 27, 30], and stimulation of blast cells, aiding in apex genesis and neutralization of endotoxins produced by anaerobic bacteria due to its high pH [31-33] favors the use of CH when managing periapical lesions.

Limited reviews have been conducted on the effect of CH in periapical healing after the end of the treatment [34, 35]. In 2021, one review found that the density of calcium hydroxide, as well as the technique of placement, may have an impact on the healing outcome, particularly in cases of pulp necrosis with apical periodontitis [34]. Some authors have questioned the efficacy of intracanal medicaments or have restricted their use to specific clinical conditions such as "weeping canals," "traumatic injuries," or "large periapical lesions". Others have backed its use in disinfecting infected canals and managing internal resorption [34]. The presence of major patient complaints in surgical intervention urges the researchers to search for non-surgical treatment of periapical lesions [19]. Due to these controversies, the purpose of this systematic review to investigate the success rate and impact effect of endodontic treatment was done with CH as an intracanal medicament in treating periapical lesions.

MATERIAL AND METHODS

This study was conducted by two independent reviewers following the preferred reporting items for systematic review and meta-analysis (PRISMA) guideline [36]. The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO): CRD42021256174.

RESEARCH QUESTION

The following research question was framed according to the population (P), intervention (I), comparison (C), outcome (O), and study design (s) (PICOs) process for this systematic review: "What is the success rate and impact effect of endodontic treatment was done with CH as an intracanal medicament (I) compared with at least one of the other intracanal irrigations/medicaments/materials such as sodium hypochlorite (NaOCl), chlorhexidine (CHX), zinc oxide and eugenol cement (ZOE), or mixture it with CH (C) on partial or total periapical lesion healing (O) in patients that had a periapical lesion (P) among the interventional studies (both randomized and non-randomized)?".

INFORMATION SOURCES

An electronic search was restricted to relevant articles published in English language in the period from 2011 to 2021 due to the lack of updated reviews that were covered in this mentioned period. Also, limited published articles and reviews cover this research area in the dental field.

LITERATURE SEARCH STRATEGY

An intensive electronic search was conducted in March 2021. The literature search was conducted using the following electronic databases: PubMed, Scopus, Web of Science, and Google Scholar digital databases. The search was conducted using the following combination of keywords and Boolean operators ("AND", "OR"): [(periapical cyst) OR (radicular cyst) OR (periapical granuloma) OR (periapical periodontitis) OR (apical periodontitis)] AND [(calcium hydroxide) OR (intracanal medicament) OR (intracanal dressing)]. The electronic search was supplemented by a manual search of the references list of included articles and contacting the authors of some articles for further data or clarification. A detailed description of the search strategy was outlined in Table 1.

ELIGIBILITY CRITERIA

Studies were included if they followed the applied criteria:

1) Published interventional studies were done on the success rate and impact effect of CH for patients with periapical lesion.
2) Published studies that show the effect of CH on periapical lesions and the lesions were confirmed with radiography.
3) Studies were conducted on patients that had a periapical lesion and root canal treatment/retreatment done with CH as an intracanal dressing/medicament.

TABLE 1. Search strategy in the databases for this systematic review

Database	Search strategy	Result
PubMed; from inception up to June 24, 2021; all fields; with no limits	#1 (periapical cyst) OR (radicular cyst) OR (periapical granuloma) OR (periapical periodontitis) OR (apical periodontitis) #2 (calcium hydroxide) OR (intracanal medicament) OR (intracanal dressing) #3, #1 AND #2	#3 = 720
Scopus; from inception up to June 24, 2021; title, abstract, key word; with no limits	#1 "periapical cyst" OR "radicular cyst" OR "periapical granuloma" OR "periapical periodontitis" OR "apical periodontitis" #2 "calcium hydroxide" OR "intracanal medicament" OR "intracanal dressing" #3, #1 AND #2	#3 = 253
Web of Science; from inception up to June 24, 2021; TS – topic; with no limits	#1 TS = ("periapical cyst" OR "radicular cyst" OR "periapical granuloma" OR "periapical periodontitis" OR "apical periodontitis") #2 TS = ("calcium hydroxide" OR "intracanal medicament" OR "intracanal dressing") #3, #1 AND #2	#3 = 146
Google Scholar; from inception up to June 24, 2021; TX – all text; with no limits	"periapical cyst" OR "radicular cyst" OR "periapical granuloma" OR "periapical periodontitis" OR "apical periodontitis"; AND "calcium hydroxide" OR "intracanal medicament" OR "intracanal dressing"	9760

4) Scientific papers were published between 2011 and 2021.
5) Scientific papers that were published in the English language.

Studies were excluded if they met any of the following applied criteria:

1) narrative/critical or systematic reviews;
2) *in vitro* studies, case report/series studies, and *in situ* studies;
3) editorial or personal opinion articles;
4) scientific papers that illustrated different types of intracanal medicament on periapical lesions and excluded the CH used;
5) papers that discussed the effect of CH on periapical lesions by percentages and samples taken from non-human sources.

CRITICAL APPRAISAL

Two independent reviewers screened the titles and abstracts of the studies for the eligibility criteria following PRISMA guidelines. A senior reviewer provided a consult in case of disagreements. Any inconsistencies between the reviewers were solved through discussion until consensus was reached among reviewers.

DATA EXTRACTION

The two reviewers independently read the full articles and considered the following variables: title, abstract, material and methods, and main results. For each included study, two reviewers extracted all relevant information and placed it in a predesigned Microsoft office excel collection form, made specifically for the data.

DATA ITEMS

Data were gathered and organized into columns with the following information: study (author and year), study design, sample (number, type of teeth), gender, age of the patients, the status of endodontic case (primary/previously treated), kinds of endodontic treatments performed, characteristic of the lesion (type of the lesion, size of the lesion), interventions (type/number of intervention), duration of follow-up, number of successful cases using CH, and outcomes of the study.

RISK OF BIAS ASSESSMENT OF INCLUDED STUDIES

The quality of the approved studies was evaluated using the risk of bias assessment tool outlined in the Cochrane risk of bias tool (Risk-of-bias VISualization (robvis)) [37]. This assessment was completed and verified by two reviewers independently. The risk of bias assessment tool includes seven specific domains: 1) random sequence generation; 2) allocation concealment; 3) blinding of participants and personnel; 4) blinding of outcomes assessment; 5) incomplete outcome data; 6) selective reporting; and 7) other sources of bias. The domains were determined to be either "low", "unclear", or "high". These assessments were reported for each selected study in the "risk of bias" figures. The review authors' judgment about the risk of bias for each selected study was categorized into "low risk", or "unclear risk", or "high risk" as the following: 1) low risk of bias: all domains were assessed as "low risk"; 2) unclear risk of bias: at least one domain was assessed as "unclear"; 3) high risk of bias: at least one domain was assessed as "high risk".

TYPE OF OUTCOME MEASUREMENTS

Primary outcomes: Studies illustrated the status of the periapical lesion at end of the treatment that would be either partial/total healed or failed after using CH as an intracanal medicament. The success case of CH used in endodontic treatment has been defined in the present systematic review as any case of CH used in endodontic treatment that included significant partial/total healing of periapical

lesion at the end of treatment according to the following periapical healing criteria: a) reduction in size of periapical radiolucency was classified as partial healing; b) absence of the periapical radiolucency and no further treatment required was classified as total healing; and c) no reduction in size of radiolucency or remained the same size of radiolucency was classified as failure healing. The outcomes may present in terms of proportion or number of cases.

Secondary outcomes: 1) studies illustrated the proportion or number of cases where CH successfully treated periapical lesion according to the type/size of lesion and post-treatment follow-up period; 2) studies illustrated the proportion or number of cases has different treatment approaches such as orthograde RCT approach (pulpectomy, non-surgical endodontic treatment (NSRCT), and non-surgical root canal retreatment (NSRCRT)) and periodontal/apical surgery approaches among the CH successfully treated periapical lesion cases.

SYNTHESIS OF RESULTS

The data items were gathered in tables. In one table, data items were prepared as the following: author and year of the study, sample, the status of endodontic case (primary/previously treated), kinds of endodontic treatments performed, the number of cases with CH used as an intracanal medicament, and clinical outcomes when treatment with CH for periapical lesions. The results were synthesized descriptively as complementary data.

STATISTICAL ANALYSIS

No meta-analysis could be conducted due to the heterogeneity between the selected studies. Therefore, only descriptive evaluations of the findings were shown.

RESULTS

STUDY SELECTION

The article search yielded 1797 records from all databases during the initial title and abstract review. After duplicate records were removed, the remaining 819 articles were screened. 678 articles based on abstract and title was excluded. 141 full-text articles passed screening and were then check for eligibility. Only 133 studies were excluded from this review due to different reasons. The reasons for 133 articles' exclusion were mentioned in Figure 1. Only 8 studies ultimately being included in the systematic review. A flow chart summarizing the search for articles in this systematic review is shown in Figure 1.

STUDY CHARACTERISTICS

The 8 human studies chosen for the review were conducted within the past 10 years and met all the inclusion, but none of the exclusion criteria. These studies investigated the success rate and impact effect of using CH as an intracanal medicament at the end of a procedure in treating periapical lesions. After using CH, it was investigated if the treatment either partial/total healed or failed the area. Types of studies included in this systematic review were; one cohort study [38] and seven randomized clinical trials [39-45]. The eight studies in total had a sample size of 481 patients and 500 teeth. The sample size and age range of the studies were 20 to 287 patients and 2-60 years, respectively. The studies were conducted in different countries of the world; Brazil [39, 40, 43, 45], Germany [38], Iran [41], Nigeria [42], and Mexico [44]. A total of five studies were reported the gender of the patients (201 male patients and 214 female patients) [38, 40, 42, 44, 45]. Gender has not been determined in the other three studies (66 patients) [39, 41, 43]. Among the 500 teeth, 127 were anterior teeth, 213 were posterior teeth, and 50 were single-rooted teeth [39-41, 44, 45]. The tooth type was not reported in the other 110 teeth [38, 42, 43]. Only two studies were primary teeth (58 teeth) [40, 45], while six studies were permanent teeth (442 teeth) [38, 39, 41-44]. Seven studies were focused on primary endodontic cases [38, 40-45] and one study was previously treated [39]. The number of cases where CH was mainly used as an intracanal medicament ranged from ten to one hundred thirty-six cases per an included study in this review and the total number of these cases identified was 310. These 310 cases are as follows: ten cases were extracted from a cohort study [38] and three hundred cases were identified from randomized clinical trials [39-45]. A total of 290 cases were focused on primary endodontic cases [38, 40-45] and 20 cases were previously treated case [39]. All the details regarding the characteristics of the eight studies were summarized in Table 2.

PRIMARY OUTCOMES

All 8 studies described the status of the periapical lesion at end of the treatment after using the CH as intracanal medicament that which partial or total healed by (75.5%) 234 successful cases and (24.5%) 76 failed healed cases among the 310 of CH cases from all the eight included studies [38-45]. Among the 310 CH cases, 234 (75.5%) of the cases had a high success rate in treating periapical lesions as defined by partial or total healing. Only 76 (24.5%) CH cases were classified as a failure because the periapical lesion was unhealed and had a continuation of inflammation. A majority of these studies showed a high success rate of CH in treating periapical lesions, which were partial/total healed in the following studies: 95.0% (19 cases) in Barbosa-Ribeiro *et al.* study [39], 96.4% (13 cases) in Cassol *et al.* study [40], 95.5% (10 cases) in Al Khasawnah *et al.* study [38], 86.7% (13 cases) in Donyavi *et al.* study [41], 97.1% (34 cases) in Menakaya *et al.* study [42], 95.5% (10 cases) in Ferreira *et al.*

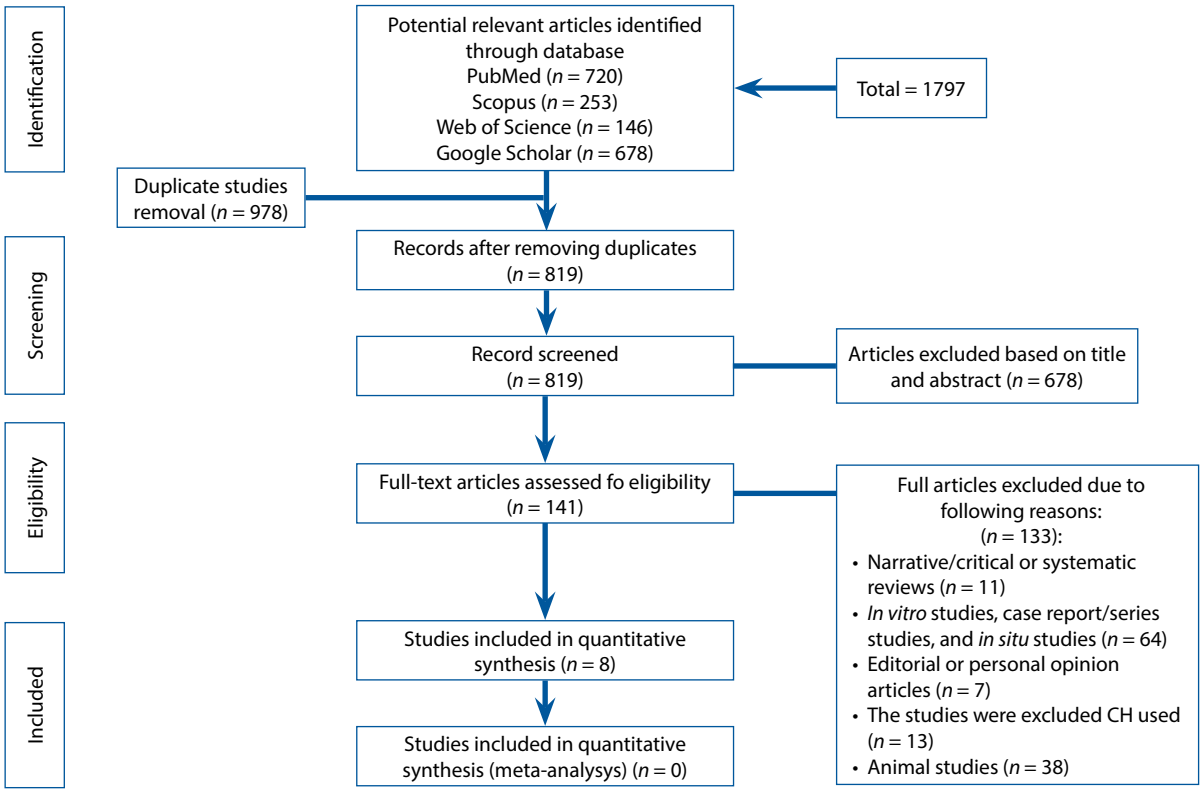

FIGURE 1. Flowchart of studies selection in this systematic review

study [43], 88.9% (121 cases) in Paredes-Vieyra and Enrique study [44], and 87.5% (14 cases) in Pinto *et al.* study [45] as shown in Table 2.

SECONDARY OUTCOMES

The secondary outcomes reported were variable and included three studies were on apical periodontitis (AP) [39, 42, 44], three on periapical/radicular cyst [38, 40, 45], and two studies that were not reported the type of periapical lesions [41, 43]. Five studies showed lesions with small size (≤ 5 mm in diameter) [40-44] and three studies showed a lesion with large size (> 5 mm in diameter) [38, 39, 45]. The lesions with small size (≤ 5 mm in diameter) had a higher success rate by (81.6%) 191 cases than large lesions by (18.4%) 43 cases (Table 2). Regarding the post-treatment follow-up period, four studies were 6 months to 1-year follow-up [40-43], three studies were more than 1-year follow-up [38, 44, 45], and one study was less than 6 months [39]. All eight studies favored the use of a specific treatment approach to treat different periapical lesions which is the orthograde RCT approach (pulpectomy, NSRCT, and NSRCRT) compared with different surgical treatment approaches among the 310 CH cases [38-45]. Only two studies were pulpectomy for primary teeth [40, 45], while six studies were NSRCT/NSRCRT for permanent teeth [38, 39, 41-44]. No one study was used periodontal/apical surgery as a treatment approach in their cases [38-45].

RISK OF BIAS ASSESSMENT

The quality of the included studies was assessed using the risk of bias assessment tool outlined in the Cochrane risk of bias tool (Risk-of-bias VISualization – robvis) [37]. The majority of studies mentioned in this review had a low risk of bias regarding the following domains: random sequence generation (87.5%); allocation concealment (87.5%); incomplete outcome data (75%), selective reporting (75%), and all studies presented a low risk of bias (100%) with regard to blinding of participants and personnel; blinding of outcomes assessment, and other sources of bias domains (Figure 2). When analyzing the overall risk of bias among the 8 studies, none were classified as a high risk of bias, 4 studies (50%) were considered as a low risk of bias [40, 42, 44, 45], and four studies (50%) had an unclear risk of bias [38, 39, 41, 43] as shown in Figure 3. Three studies had an unclear risk of bias because there was not enough information to make a clear judgment concerning the following domains: incomplete outcome data and selective reporting (Figure 3). The authors' judgment about each risk of bias domain is illustrated in Figure 2. The authors' judgment of the risk of bias items for their respective studies is summarized in Figure 3.

DISCUSSION

This systematic review illustrated the success rate and impact effect of CH in treating periapical lesions were

TABLE 2. Details of the included studies

Author/Year	Study design	Sample		Gender	Age of the patients (Mean ± SD)	Status of endodontic case (primary/ previously treated)	Kinds of endodontic treatments performed	Type and number of Interventions	Number of successful cases with CH	Type and size of lesion	Follow-up period	Main outcomes
		Number	Type of teeth									
Barbosa-Ribeiro *et al.* [39] 2019	RCTs	20	(20) Single rooted teeth	NR	NR	Previously treated	NSRCRT	(20) Intracanal medicament of CH was used for 30 days	(19) cases	Apical periodontitis and size more than 5 mm	30 days	CH-based intracanal medications had a positive effect on microbial reduction and showed partial or total remission of the periodontitis.
Cassol *et al.* [40] 2019	RCTs	23 with 27 teeth	(20) Anterior + (7) Posterior	Male: 14 Female: 13	2-7 years old (3.68 ± 1.67)	New cases (primary treatment cases)	Pulpectomy (partial root canal: up to 3 sizes of k-files for instrumentation in primary teeth)	(27) primary teeth I: CH C: Iodoform I: 13 C: 14	(13) cases	Cyst and size (2-4 mm)	6 months – 1 year	The level of the root canal filling was better in the CH group with partial or total remission of the cyst.
Al Khasawnah *et al.* [38] 2018	Cohort	20	NR	Male: 10 Female: 10	NR	New cases (primary treatment cases)	NSRCT	(20) I: CH (10 teeth) C: Calcium Hydroxide-Iodoform-Silicon-Oil Paste (CHISP) (10 teeth)	(10) cases	Cyst and size (5-8 mm)	2 years	Complete healing at the end of the 120th day.
Donyavi *et al.* [41] 2016	RCTs	30	(30) Single rooted teeth	NR	NR	New cases (primary treatment cases)	NSRCT	(30) I: CH + CHX for two weeks C: NaOCl I: 15 C:15	(13) cases	Not reported the type of periapical lesions but the size average (3.8 mm)	6 months	It showed partial or total remission of the periapical lesions with the CH + CHX group more than the NaOCl group.
Menakaya *et al.* [42] 2015	RCTs	55 with 70 teeth	NR	Male: 27 Female: 28	17-60 years old (34.8 ± 9.91)	New cases (primary treatment cases)	NSRCT	(70) teeth I: CH (35 teeth) C: CH + CHX (0.2%) (35 teeth)	(34) cases	Apical periodontitis and size (2.0 × 2.0 mm)	6 months	A post-treatment favorable outcome of 97.1% in the intervention group and 94.3% in the control group.

Author/Year	Study design	Sample		Gender	Age of the patients (Mean ± SD)	Status of endodontic case (primary/ previously treated)	Kinds of endodontic treatments performed	Type and number of Interventions	Number of successful cases with CH	Type and size of lesion	Follow-up period	Main Outcomes
		Number	Type of teeth									
Ferreira *et al*. [43] 2015	RCTs	20	NR	NR	NR	New cases (primary treatment cases)	NSRCT	(20) I: CH C: CH + CHX I: 10 C: 10	(10) cases	Not reported the type of periapical lesions but the size was (2.0 × 2.0 mm)	6 months – 1 year	The CH group showed partial or total remission of the periapical lesions.
Paredes-Vieyra and Enrique [44] 2012	RCTs	287 with 300 teeth then, the authors reduced the number of teeth to 282 teeth (18 teeth were excluded due to lost to follow up)	(76) Anterior + (206) Posterior	Male: 138 Female: 149	18-60 years (mean = 55 years)	New cases (primary treatment cases)	NSRCT	(282 teeth) I: CH in two visits (136 teeth) C: NaOCl in a single visit (146 teeth)	(121) cases	Apical periodontitis and size (≥ 2.0 × 2.0 mm)	2 years	At end of the study, 141 of the 146 teeth (96.57%) in the 1-visit group and 121 (88.97%) of the 136 teeth in the 2-visit group were classified as healed.
Pinto *et al*. [45] 2011	RCTs	26 with 31 teeth	(31) Anterior teeth only	Male: 12 Female: 14	2.6 years - 5.10 years (mean = 3.4 years)	New cases (primary treatment cases)	Pulpectomy (partial root canal: up to 3 sizes of k-files for instrumentation in primary teeth)	(31) Traumatized primary teeth I: CH (16 teeth) C: ZOE (15 teeth)	(14) cases	Periapical or radicular cyst and size ≥ 5 mm	1.5 years	In the CH group, the success rate was 87.5% among the deciduous teeth with partial or total remission of the periapical or radicular cysts.

SD – standard deviation, NR – not reported, RCTs – randomized clinical trials, NSRCRT – non-surgical root canal retreatment, f – non-surgical root canal treatment, CH – calcium hydroxide, NaOCl – sodium hypochlorite, CHX – chlorhexidine, ZOE – zinc oxide and eugenol cement, I – intervention, C – control.

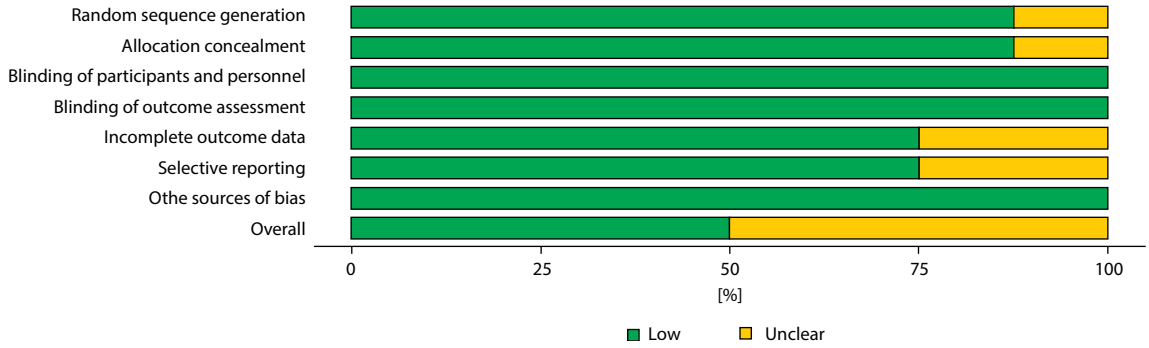

FIGURE 2. Risk of bias graph: review authors' judgment about each risk of bias item presented as percentages across all included studies. Green and yellow refer to low risk of bias, and unclear risk of bias, respectively

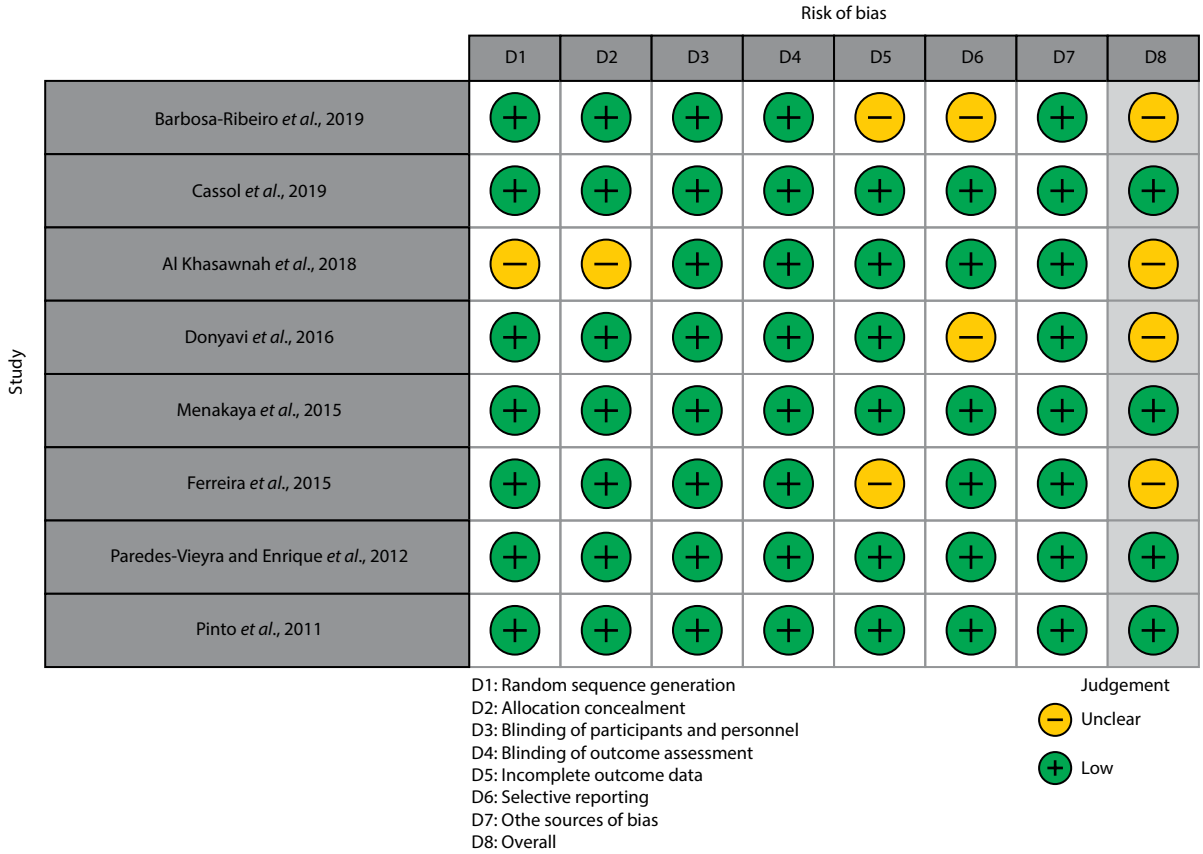

FIGURE 3. Risk of bias summary: review authors' judgment about each risk of bias item for each included study. Green and yellow refer to low risk of bias, and unclear risk of bias, respectively

radiographically confirmed across 8 studies. The present review found CH had a success rate of 75.5% in a patient with a periapical lesion which is in line with a study done by Mandhotra *et al.* [46], and a meta-analysis done by Jia *et al.* [47]. Moreover, a study done by Fernandes and de Ataide [8] revealed intracanal CH had a positive effect after thorough irrigation. However, these results are not similar to a previous systematic review looking at the antibacterial efficacy of CH in intracanal dressing [35]. There was no statistically significant change between pre- and post-medication ($p = 0.12$) [35]. Also, CH has limited efficiency in eradicating germs from human root canals when evaluated by culture methods [35].

Intracanal CH dressing can completely restore the periapical tissue in patients with a periapical/radicular cyst of large size (10 mm × 15 mm) after a 2-year follow-up [48] which supports the present review where (18.4%) 43 of the participants with large lesions (> 5 mm diameter) were partial/total healed from the lesion at end of the NSRCT or pulpectomy after different follow-

up periods [38, 39, 45]. Nonsurgical healing of a radicular cyst has been reported following extra-radicular calcium hydroxide placement [49]. However, a similar study in Turkey showed that CH aided in the substantial healing of large periapical lesions and confirms that they can respond successfully to NSRCT [50].

Kusgoz *et al.* in their study revealed that pulpal necrosis and large periapical lesions showed a significant bone healing at the end of the 2nd year follow-up after intracanal CH was applied [51]. This result is similar to the present review where the success rate of CH intracanal medicament was 62% in 145 patients with more than 1-year post-treatment follow-up [38, 44, 45]. The success rate decreased to 30% and 8% for those from 6 months to 1-year follow-up periods [40-43] and less than 6 months period [39], respectively which disagreement with a previous finding that, the administration of intracanal CH for a longer duration doesn't have justifiable antibacterial efficacy [52] rather it might increase the fracture tendency of a tooth [53].

Intracanal CH had a favorable outcome in participants with apical periodontitis [39, 42, 44]. In addition, most of these three studies with apical periodontitis showed a high success rate (74%) (174 cases) of healing after using CH in NSRCT [42, 44] for primary endodontic cases and NSRCRT [39] for previously treated cases without the need for surgical intervention such as surgical RCT or periodontal/apical surgery.

A microbiological analysis on root canals showed that extensive apical reaming and dressing with CH significantly reduces bacterial growth in the root canal and periapical repair with partial or total healing at different post-treatment follow-up periods [39, 41]. However, one study done by Ferreira *et al.* [43] found that when comparing CH to CH + CHX, there were no significant differences in median percentage values for the reduction of cultivable bacteria. Both treatment groups did and have a significantly less amount of bacterial species and periapical repair with partial or total healing among the successful CH cases [43].

In our review, two studies were discussed the endodontic treatment with CH in primary teeth. The first study was a randomized controlled trial done in Brazil on the effect of CH against iodoform in periapical lesion found more than 90% of the participants had partial/total healing in their primary teeth at the end of the 6-month follow-up and participants on CH group partial or total remission of the periapical/radicular cysts after a one-year follow-up [40]. The second study was focused on traumatized primary teeth [45]. They found the success rate was 87.5% with partial or total remission of the periapical or radicular cysts [45]. Thus, the primary teeth with periapical/radicular cysts can respond successfully to pulpectomy with CH as intracanal medicament without the need to tooth extraction.

A study done in Iran revealed that 89.7% of periapical lesions completely healed with initial treatment and 85.7% healed after retreatment [54]. This finding corresponds to the present review where the success rate was relatively higher in the primary endodontic cases by (92%) 215 successful CH cases were pulpectomy for primary teeth and NSRCT for permanent teeth. While NSRCRT for previously treated was (8%) 19 successful CH cases. Furthermore, none of the eight studies included in this review had a case of failed endodontic treatment requiring surgical intervention (Table 2).

The fact remains that, as long as the debate over single-visit versus multi-visit endodontic treatment continues, intracanal medicaments will be useful, particularly in the endodontic treatment of apical periodontitis [55-58]. When used for the successful management of teeth with periapical lesions, calcium hydroxide has been shown to have a success rate of more than 80% [59]. In another study, the authors stated that endodontic treatment with intracanal dressing has a high success rate of over 94% [60]. On the other hand, the authors of one study discovered direct contact between calcium hydroxide and periapical tissues improve the material's inductive activity [24]. In this review, however, 75.5% of cases that utilized CH showed a high success rate in treating periapical lesions. The success rate of CH with partial/total healing outcomes in orthograde RCT was high in apical periodontitis, small size of lesions, and more than 1-year post-treatment follow-up patients by 74%, 81.6%, and 62%, respectively [38-45].

The included studies in this review showed large heterogeneity in the type and number of Interventions, number of successful cases with CH, type/size of the periapical lesion, post-operative follow-up periods, and type of evaluated teeth. However, further studies related to the outcomes of our aim are needed, to help clinicians that are facing similar dilemmas in their daily practice. In order to set a standardized treatment approach can provide by evidence-based practice.

STUDY STRENGTHS AND LIMITATIONS

The strength of our systematic review includes a thorough comparison of all peer-reviewed studies published within the 10 years in line with our inclusion and exclusion criteria. This systematic review presents comprehensive knowledge on the effect of CH on periapical lesions and the success rate of this intracanal medicament in periapical healing. A clinician needs to detect the proper intracanal medicament during root canal treatment to enhance periapical lesion healing. To our knowledge, this is the only systematic review that has done an in-depth investigation about the use of CH as an intracanal medicament influencing periapical lesion healing after the end of the treatment. To complete this review, we used Public Medline [PubMed], Web of Science, and Scopus as databases, and also Google Scholar as a search engine. One advantage of using Google Scholar was to prevent

missing any appreciated research published in journals that are not cited in PubMed, Web of Science, and Scopus databases. Although the studies were selected randomized in this review, the included studies compared different types of interventions and showed different types/sizes of periapical lesions and this is the main reason why meta-analysis cannot be done. Moreover, an assessment of the impact of publication bias in the results of this review was not possible.

CONCLUSIONS

Intracanal CH has a clinically significant effect on the healing of periapical lesions. Regardless of the lesion size, lesion type, or previous status of the tooth, NSRCT/NSRCRT approaches are a favored treatment option. Larger lesions and endodontic treatments with a long-term prognosis can necessitate longer follow-ups. As a result of the favorable properties of CH in treating periapical lesions, this review suggests that for patients with periapical lesion, orthograde RCT with CH can be performed as an alternative to periapical/apical surgery.

CONFLICT OF INTEREST

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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