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Systematic Review and Meta-Analysis of Randomized Clinical Trials on Chemomechanical Caries Removal

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Clinical Relevance

The sodium hypochlorite–based (Carisolv) chemomechanical caries removal method is more time consuming than the enzyme-based (Papacarie) chemomechanical caries removal method.

SUMMARY

Objectives: The aim of this review was to assess the methodologies used in previously published prospective randomized clinical trials on chemomechanical caries removal and to conduct a meta-analysis to quantify the differences in the excavation time between chemomechanical and conventional caries removal methods.

Methods: An electronic search was performed using Scopus, PubMed, EBSCO host, and Cochrane Library databases. The following categories were excluded during the assessment process: non-English studies published before 2000, animal studies, review articles, laboratory studies, case reports, and nonrandomized or retrospective clinical trials. The methodologies of the selected clinical trials were assessed. Furthermore, the reviewed clinical trials were subjected to meta-analysis for quantifying the differences in excavation time between the chemomechanical and the conventional caries removal techniques.

Results: Only 19 randomized clinical trials fit the inclusion criteria of this systematic review. None of the 19 reviewed trials completely fulfilled Delphi's ideal criteria for quality assessment of randomized clinical trials. The meta-analysis results revealed that the shortest mean excavation time was recorded for rotary caries excavation (2.99±0.001 minutes), followed by the enzyme-based chemomechanical caries removal method (6.36±0.08 minutes) and the the hand excavation method (atraumatic restorative technique; 6.98±0.17 minutes). The longest caries excavation time was

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recorded for the sodium hypochlorite-based chemomechanical caries removal method (8.12±0.02 minutes).

Conclusions: It was found that none of the current reviewed trials fulfilled all the ideal requirements of clinical trials. Furthermore, the current scientific evidence shows that the sodium hypochlorite-based (Carisolv) chemomechanical caries removal method was more time consuming when compared to the enzyme-based (Papacarie) chemomechanical and the conventional caries removal methods. Further prospective randomized controlled clinical trials evaluating the long-term follow-up of papain-treated permanent teeth are needed.

INTRODUCTION

Evidence-based dentistry is "the integration and interpretation of the current research evidence, combined with personal experience, which allows clinicians and academic researchers to make judgments, decisions and improve their clinical practice."[1] Systematic reviews and meta-analytical studies are considered the highest level of evidence that support evidence-based decision making, which is the "formalized process of using a specific set of skills for identifying, searching for and interpreting clinical and scientific evidence, so that it can be used at the point of care."[2]

Chemomechanical caries removal is considered one of the most conservative and convenient caries removal methods.[3] Early studies reported that the sodium hypochlorite–based (NaOCl) chemomechanical caries removal method was a time-consuming process and that its effectiveness was questionable.[4,5] However, this caries removal method has been further developed in the past 10 years by modifying the chemical formula of the original chemomechanical caries removal agents (eg, new Carisolv gel) as well as the introduction of new generations of chemomechanical caries removal agents (eg, enzyme-based agents, such as Papacarie and Biosolv).

Many randomized clinical trials have been performed to evaluate the effect of chemomechanical caries removal agents on excavation time, pain level, and the long-term success rate of restored cavities.[6-12] However, these trials have shown great variability among their objectives, methodologies, and results. In the literature, very few narrative reviews have focused on chemomechanical caries removal methods.[4,5,13] Until now, there appears to be no systematic review or meta-analytical study that has evaluated the clinical trials using chemomechanical caries removal methods. Hence, the evidence supporting the use of the chemomechanical caries excavation method as a useful and efficacious technique remains weak.

The aim of this review was to assess the methodologies used in previously published prospective randomized clinical trials on chemomechanical caries removal and to conduct a meta-analysis for quantifying the difference in the excavation time between the chemomechanical and conventional caries removal methods. The key questions of this systematic review were these: Did the methodologies followed in the previously published studies fulfill the ideal requirements of the prospective randomized clinical trial, and is the chemomechanical caries removal method a time-consuming process compared with the other conventional caries removal methods?

METHODS AND MATERIALS

Protocol Development and Eligibility Criteria

The protocol of this systematic review was designed following the guidelines of the Preferred Reporting Items Systematic Review and Meta-Analysis statement.[14] The clinical trials selected for the current systematic review were at least two-arm prospective randomized clinical trials (RCT) and written in English. For all the selected RCT on NaOCl-based chemomechanical caries removal agents, the modified Carisolv gel (5% NaOCl) has been used. For the selected RCT on the enzyme-based chemomechanical caries removal agents, either papain-based (Papacarie) or trypsin-based (Biosolv) agents have been used. The two chemomechanical caries removal methods were then compared with a conventional hand excavation atraumatic restorative technique [ART] method) or rotary caries removal methods.

Information Source and Search

An electronic search was done by one of the authors (HH) using the following databases: Scopus, PubMed, EBSCO host, and Cochrane Library. The online searching was conducted following this web-search criteria: "Chemomechanical Caries Removal" or "Chemomechanical Caries Excavation" or "Papacarie" or "Papain" or "Carisolv" or "Biosolv." Moreover, a parallel hand search was done through nonelectronic journals (eg, the *American Journal of Dentistry*, the *European Archives of Paediatric Dentistry*, and the *Brazilian Journal of Oral Sciences*).

Study Selection, Exclusion Criteria, and Article Assessment Process

Assessment of the clinical trial depended on title, abstract, and full text (if needed). All articles found by both electronic and hand searching were collected onto one sheet and printed as three copies that were distributed among the three authors. Each author, individually, checked the eligibility criteria for each study, and the agreement of at least two authors was essential for exclusion/inclusion of the clinical trial for the systematic review. The selected trials were discussed and selections matched in face-to-face meetings. The following categories were excluded during the assessment process: non-English studies published before 2000, animal studies, review articles, laboratory studies, case reports, and nonrandomized or retrospective clinical trials (RCT; Figure 1). Moreover, all the RCT, which were performed using either the Caridex or the old version of the Carisolv (2.5% NaOCl) chemomechanical caries removal agent, were excluded.

The objectives, results, and conclusions of each clinical trial were summarized and evaluated. Furthermore, the methodology of each RCT was assessed, based on the Delphi's ideal criteria for quality assessment of randomized clinical trials, from different aspects, namely, randomization, sample size, type of subjects, rubber dam application, study design, ethical- related issues, degree of blindness of the evaluation process, performance of an intraexaminer calibration test, methodology of clinical examination and long-term clinical follow-up.

Meta-Analysis of Mean Caries Excavation Time

The majority of the RCT evaluated the time taken for caries excavation by chemomechanical (test group) and conventional (control group) caries removal methods. For each caries excavation method, the sample size and the mean caries excavation time (minutes) were extracted from the studies and subjected to a meta-analysis using Comprehensive Meta-Analysis software, version 2 (Biostat, Englewood, NJ, USA), at the 95% confidence interval. The meta-analysis of this systematic review followed the statistical model of Borenstein[15], which has been designed for comparing the meta-analysis outcomes of different groups within the same study. Thus, the results of the meta-analysis were subjected to a further one-way analysis of variance, followed by the Tukey *post hoc* multiple comparison test using GraphPad Instat software, version 3.10 (GraphPad Software, Inc, San Diego, CA, USA). This additional step was performed to quantify the difference in the excavation time between the conventional and the chemomechanical caries removal methods.

RESULTS

The initial search through the Science Direct database resulted in 157 articles being identified and was then followed by a subsequent search of the three other databases in addition to the manual searching. This added a further article; hence, the total number of originals screened was 158. Twelve articles were excluded because they were not written in English. Moreover, another 45 studies were excluded because they utilized either Caridex or the old version of the Carisolv gel. From the remaining 101 articles, nine were animal based, three were reviews, and 52 were laboratory studies, all of which were excluded. Another six studies were excluded because they utilized chemomechanical caries removal agents for other purposes not related to caries excavation, such as treatment of oral ulcers,[16] periodontal therapy,[17,18] cleaning of organic debris prior to application of pit and fissure sealants,[19] plaque removal,[20] and root canal irrigation.[21] From the remaining 31 clinical studies, three were case reports, and seven were nonrandomized clinical trials and were therefore excluded. Two clinical trials were further excluded, because they were conducted on special needs patients.[22,23] Finally, 19 randomized clinical trials fit the inclusion criteria of this systematic review. The detailed study selection procedure is illustrated in Figure 1.

The selected clinical trials had the following geographic distribution; nine were performed in Europe (47%), four in India (21%), three in South America (17%), and one each in Pakistan (5%), the United States (5%), and Egypt (5%). Fourteen clinical trials were performed using the NaOCl-based (Carisolv) agent (74%), while three RCT used papain-based (Papacarie; 15.5%). Moreover, two clinical trials by Bohari and others[12] and Kochhar and others[24] compared NaOCl-based (Carisolv) and papain-based (Papacarie) chemomechanical caries removal agents (10.5%). Fourteen of the 19 clinical trials were conducted on deciduous teeth (74%), while the remaining five were conducted on permanent teeth (26%). Only the study by Peric and others[25] compared the effect of chemomechanical caries removal agents on both dentitions (5%). Long-term clinical follow-up was performed in only seven of the clinical trials (37%) fulfilling the search criteria, while the remaining 12 clinical trials

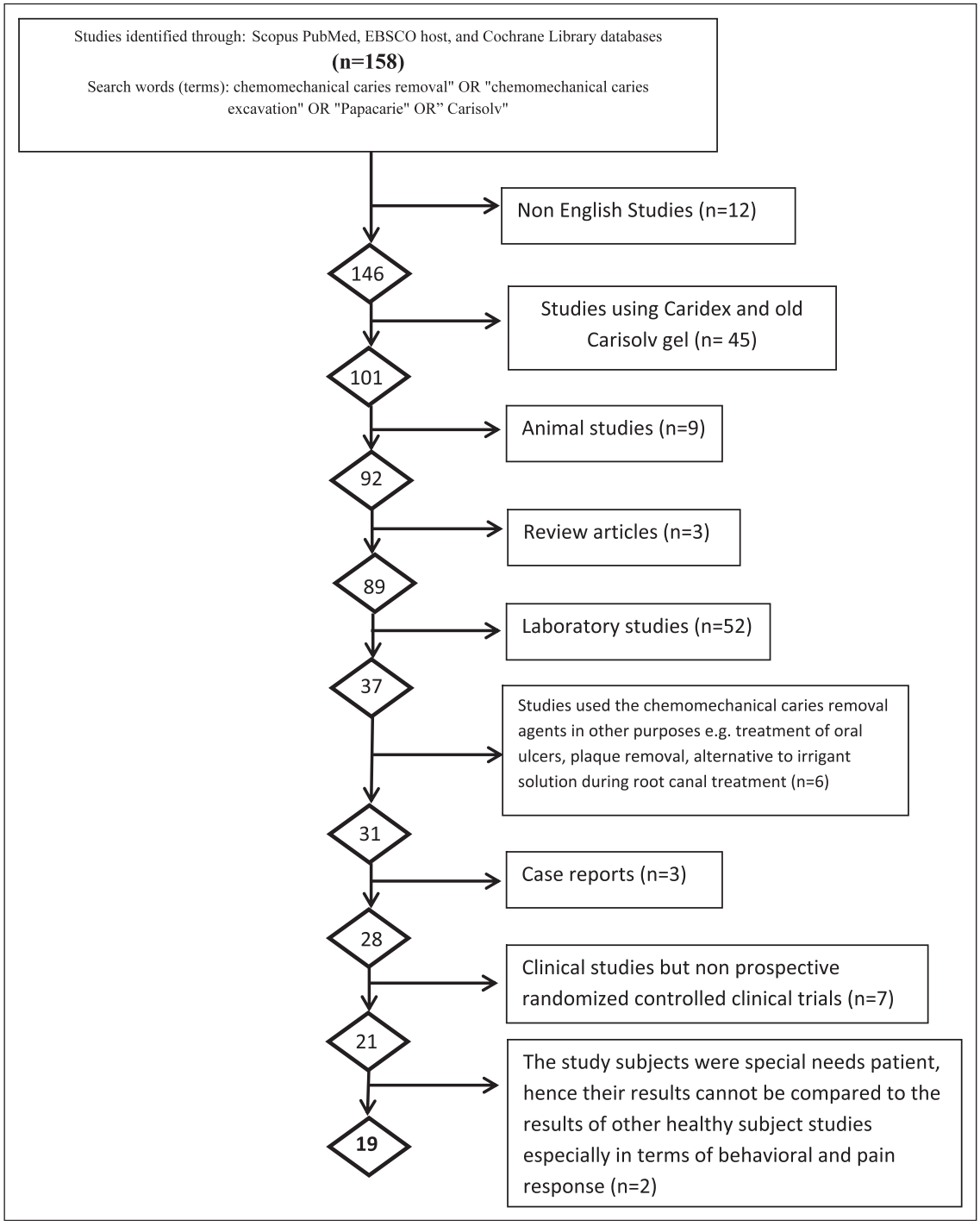

Figure 1. *Flow chart of the study selection procedure.*

published only the immediate short-term outcomes (Table 1).

The assessment of the methodologies used in the reviewed clinical trials is summarized in Table 2. Thirteen of the 19 clinical trials (68%) clearly mentioned the randomization protocols of their study population, while the remaining six did not. Two clinical trials[12,26] out of the 19 did not mention the total number of the study population, and only one clinical trial, by Topaloglu-Ak and others,[10] showed that a sample size calculation method had been used. Furthermore, two clinical trials out of the 19 did not equalize the number of subjects in both

Table 1: *Summary of the Search Characteristic Findings of the Clinical Trials*

Geographic Distribution	Europe 9 (47%)	India 4 (21%)	South America 3 (17%)	Egypt 1 (5%)	Pakistan 1 (5%)	United States 1 (5%)
Chemomechanical caries removal agent	Carisolv 14 (74%)		Papacarie 3 (15.5%)		Carisolv and Papacarie 2 (10.5%)	
Tooth subject	Deciduous 14 (74%)		Permanent 5 (26%)		Deciduous and permanent 1 (5%)	
Follow-up	Performed 7 (37%)			Not performed 12 (63%)		
Study design	Split-mouth 10 (53%)		Parallel 5 (26%)		Not clearly mentioned 4 (21%)	

the test and the control groups.[8,27] The majority (15 RCT [79%]) of the clinical trials mentioned the inclusion/exclusion criteria; however, the remaining four (21%) did not clearly present the eligibility criteria for subject selection. Among the selected clinical trials, seven (37%) used a rubber dam during the restorative procedures, and nine (47%) did not, while the remaining three (16%) failed to clearly mention the isolation method used.

Among the reviewed clinical trials, 10 (53%) used a split-mouth design, five (26%) used a parallel design, and four (21%) did not clearly mention the design. Eleven (58%) of the 19 clinical trials indicated that ethical approval was obtained from an appropriate institute, while the remaining eight studies did not clearly indicate the ethical-related issues. Three trials did state, however, that signed informed consents from the child's parents or guardians were obtained.[6,9,28]

As shown in Table 2, the final evaluation was performed by one investigator in six (32%) clinical trials and by two investigators in 5=five (26%) clinical trials. Furthermore, the remaining eight studies (42%) did not clearly mention the number of investigators who participated in the study. An intraexaminer calibration test was performed in all of the two-investigator clinical trials, except the study by Bergmann and others.[29] The blinding of the evaluators to the treatment method was reported in only four trials (21%), while the remaining trials did not clearly describe the methods of keeping the principal investigator(s) blinded to the groups tested. Eighteen (94%) of the 19 clinical trials used conventional visual and tactile methods for evaluation of the excavated surfaces. In addition to the tactile and visual methods, caries detector dyes were used in two (11%) trials,[24,30] microbial analysis was used in another two (11%) trials,[7,11] and the DIAGNOdent (KaVo Dental, Biberach, Germany) was used in one (5%) trial.[12] Among the 13 clinical trials that recorded the behavioral responses of the patients before, during, and after treatment, six (46%) trials[11,12,24,30-32] used standardized scales (eg, Face-Leg-Activity-Cry-Consolability [FLACC] scale, Sound, Eyes and Motor [SEM] scale, Visual Analogue and Verbal scale, Frankl scale,[33] and Wong Baker Faces Pain scale). Conversely, the remaining seven trials used questionnaires and subjective methods to record the behavioral and pain responses of the study subjects.[6,8,9,25,27,29,34]

The results of the meta-analysis of the mean caries excavation time for rotary, ART, NaOCl-based (Carisolv), and papain-based (Papacarie) gels are shown in Figures 2 through 5, respectively. According to statistical model by Borenstein and others,[15] results of one-way analysis of variance and the Tukey *post hoc* test revealed that the shortest estimated mean excavation time was recorded during rotary caries excavation (2.99±0.001 minutes), followed by the papain-based (Papacarie) chemomechanical caries removal method (6.36±0.08 minutes) and the hand excavation method (ART; 6.98±0.17 minutes). The longest caries excavation time (8.12±0.02 minutes) was recorded for the NaOCl-based (Carisolv) chemomechanical caries removal method (Table 3).

DISCUSSION

Those clinical trials that used Caridex and the old version of Carisolv (0.25% NaOCl) were excluded due to limited clinical usage of these chemomechanical caries removal agents as well as their non-availability in the dental market.[5] Furthermore, their relative long excavation time may have affected the meta-analysis results.

Initially, it was decided to restrict the search to the long-term follow-up trials. However, after screening all long-term follow-up trials, it was found that most of them reported no significant difference between the immediate and the long-term follow-up outcomes; thus, all the immediate follow-up trials were

Table 2: *Evaluation of the Methodologies Used in the Clinical Trials Reviewed*[a]

Study	Sample Size	Inclusion and Exclusion Criteria	Application of Rubber Dam	Study Design
Bohari and others[12]	120 primary molars	✓	✓	Parallel
Kochhar and others[24]	120 primary molars	?	✓	Parallel
Singh and others[11]	80 primary molars	✓	✓	Split-mouth
Bussadori and others[26]	14 permanent molars	✓	X	?
Kotb and others[32]	74 primary molar	✓	X	Split-mouth
Peric and others[25]	120 primary and permanent molars	✓	X	Parallel
Topaloglu-Ak and others[10]	327 primary molars	✓	X	Parallel
Subramaniam and others[41]	40 primary molars	?	✓	Split-mouth
Barata and others[35]	100 permanent molars	✓	X	Split-mouth
Hosein and Hasan[28]	60 permanent molars	✓	?	Split-mouth
Pandit and others[30]	150 primary molars	?	X	?
Kirzioglu and others[34]	56 primary teeth	✓	X	Split-mouth
Peters and others[27]	50 primary teeth	✓	X	Parallel
Lozano-Chourio and others[31]	80 primary teeth	✓	✓	Split-mouth
Bergmann and others[29]	92 primary molars	?	X	Split-mouth
Fure and Lingstrom[8]	202 permanent molars	✓	✓	?
Azrak and others[7]	42 primary molars	✓	?	Split-mouth
Kavvadia and others[9]	92 primary molars	✓	Not in all the cases	?
Kakaboura and others[6]	90 permanent molars	✓	?	Split-mouth

[a] ✓ *yes; X, no; ?, not clearly stated.*
Abbreviations: A, rotary caries removal; B, hand excavation (atraumatic restorative technique [ART]); C, sodium hypochlorite (NaOCl)-based (Carisolv) chemomechanical caries removal; D: papain-based (Papacarie) chemomechanical caries removal; E, laser caries removal; FLACC, Face-Leg-Activity-Cry-Consolability scale; MH, Mount and Hume classification of the contact area; SEM, Sound, Eyes and Motor scale; USPHS, US Public Health Service; VAV, Visual Analogue and Verbal scale; WBFP, Wong Baker Faces Pain scale.

included in the current review.[8,10,25,26,29,34,35] The two clinical trials by Carrillo and others[22] and Guare Rde and others,[23] which were conducted on special needs subjects, were excluded because their results should not be compared with the healthy subjects, particularly in terms of analyzing behavioral and pain responses.

It was noticed that around 50% of the clinical trials were performed in Europe, which could be attributed to the early availability of Carisolv in this region. Most of the trials (~85%) utilized the NaOCl-based (Carisolv) chemomechanical agent due to its popularity and knowledge of its existence. Conversely, only a few clinical trials used the papain-based (Papacarie) chemomechanical caries removal agent due to its recent introduction to the market.[11,12,24,26,32]

None of the 19 reviewed trials completely fulfilled Delphi's ideal criteria for quality assessment of randomized clinical trials, which was published in

Table 2: Extended.

Study	Study Groups		Obtaining Ethical Approval and Signed Informed Consent	No. of Investigators	Blindness of the Investigator
	Control	Test			
Bohari and others[12]	A	C, D, and E	✓&✓	?	?
Kochhar and others[24]	A	B, C, and D	✓&?	?	?
Singh and others[11]	A	D	✓&✓	1	?
Bussadori and others[26]	X	D	✓&✓	?	?
Kotb and others[32]	A	D	?&?	1	?
Peric and others[25]	A	C	✓&✓	1	✓
Topaloglu-Ak and others[10]	B	(B+C)	✓&✓	2	✓
Subramaniam and others[41]	A	C	?&?	?	?
Barata and others[35]	B	C	✓&✓	2	✓
Hosein and Hasan[28]	A	C	?&✓	1	?
Pandit and others[30]	A	B and C	?&?	?	?
Kirzioglu and others[34]	B	C	✓&✓	1	?
Peters and others[27]	A	C	✓&✓	1	?
Lozano-Chourio and others[31]	A	C	✓&✓	1 for assessment of caries removal 2 for assessment of cavity entrance size	✓
Bergmann and others[29]	A	C	✓&✓	1 investigator per center	?
Fure and Lingstrom[8]	C (0.25% NaOCl) Carisolv gel	C (0.5% NaOCl) Carisolv gel	✓&✓	?	?
Azrak and others[7]	A	C	?&?	?	?
Kavvadia and others[9]	A	C	?&✓	?	?
Kakaboura and others[6]	A	C	?&✓	?	?

[a] ✓ *yes; X, no; ?, not clearly stated.*
Abbreviations: A, rotary caries removal; B, hand excavation (atraumatic restorative technique [ART]); C, sodium hypochlorite (NaOCl)-based (Carisolv) chemomechanical caries removal; D: papain-based (Papacarie) chemomechanical caries removal; E, laser caries removal; FLACC, Face-Leg-Activity-Cry-Consolability scale; MH, Mount and Hume classification of the contact area; SEM, Sound, Eyes and Motor scale; USPHS, US Public Health Service; VAV, Visual Analogue and Verbal scale; WBFP, Wong Baker Faces Pain scale.

1998.[36] The trial by Topaloglu-Ak and others[10] is the only clinical trial that fulfilled most of Delphi's criteria: the sample size calculation method, the number of operators and investigators, and blindness of the investigators to the treatment was clearly stated. However, the detailed randomization and teeth isolation methods were not clearly reported, which may have affected the follow-up results of the resin composite restorations. The trial by Barata and others[35] was the only clinical trial that clearly described the detailed randomization method. All the reviewed trials were at least two-arm clinical trials, except the study by Bussadori and others,[26] which was a one-arm trial. This trial was included in the current review because it was the only clinical study that has been conducted on permanent teeth using enzyme-based (Papacarie) with a long-term follow-up of 24 months. However, this trial was not included in the meta-analysis because it is a one-arm trial and the caries excavation time was not evaluated.

Table 2: Extended.

Study	Intraexaminer Calibration Test	Clinical Examination Criteria	Use of Standardized Scales to Record Patient Response	Follow-Up
Bohari and others[12]	?	Tactile and DIAGNOdent	✓ FLACC	X
Kochhar and others[24]	?	Ericson scale and caries detector dye	✓ VAV	X
Singh and others[11]	NA	Erickson's criteria and microbial evaluation	✓ WBFP	X
Bussadori and others[26]	?	Visual and tactile methods	NA	6, 12, and 24 mo
Kotb and others[32]	NA	Tactile	✓ SEM	X
Peric and others[25]	NA	Tactile	X Questionnaire	1 wk, 6 mo, and 12 mo
Topaloglu-Ak and others[10]	✓	MH[42]	NA	6, 12, and 24 mo
Subramaniam and others[41]	?	Tactile	NA	X
Barata and others[35]	✓	?	NA	12 mo
Hosein and Hasan[28]	NA	Tactile	NA	X
Pandit and others[30]	?	Ericson scale and caries detector dye	✓ VAV	X
Kirzioglu and others[34]	NA	Tactile	X Questionnaire	3, 6, 9, and 12 mo using USPHS Ryge[43] criteria
Peters and others[27]	NA	Tactile	?	X
Lozano-Chourio and others[31]	NA ✓	Tactile	✓ Frankl and others[33] scale	X
Bergmann and others[29]	?	Tactile	X Questionnaire	6 mo
Fure and Lingstrom[8]	?	Tactile	X Questionnaire	1 yr
Azrak and others[7]	?	Tactile and microbial evaluation	NA	X
Kavvadia and others[9]	?	Tactile	Subjective scale	X
Kakaboura and others[6]	?	Tactile	X Questionnaire	X

[a] ✓ *yes; X, no; ?, not clearly stated.*
Abbreviations: A, rotary caries removal; B, hand excavation (atraumatic restorative technique [ART]); C, sodium hypochlorite (NaOCl)-based (Carisolv) chemomechanical caries removal; D: papain-based (Papacarie) chemomechanical caries removal; E, laser caries removal; FLACC, Face-Leg-Activity-Cry-Consolability scale; MH, Mount and Hume classification of the contact area; SEM, Sound, Eyes and Motor scale; USPHS, US Public Health Service; VAV, Visual Analogue and Verbal scale; WBFP, Wong Baker Faces Pain scale.

The sizes of the test and control groups in the clinical trials by Fure and Lingstrom[8] and Peters and others[27] were not equal in size, which may have affected the accuracy of the statistical analysis. Also, the results of the multi-comparison analysis of the study by Bohari and others[12] were not well presented in the manuscript. All reviewed trials used conventional visual and tactile sensation for the evaluation of the excavated surfaces. In addition to conventional diagnostic means, Bohari and others[12] used the DIAGNOdent for quantifying the results. Furthermore, the calibration method of the DIAGNOdent was clearly described in the study. Pandit and others[30] and Kochhar and others[24] used caries detector dyes for verifying complete caries removal; however, the use of caries detector dyes may give false-positive results.[37-39] These false results were attributed to the nonspecificity of the dye to damaged collagen fibers of the infected dentin and resulted in staining of demineralized caries-affected

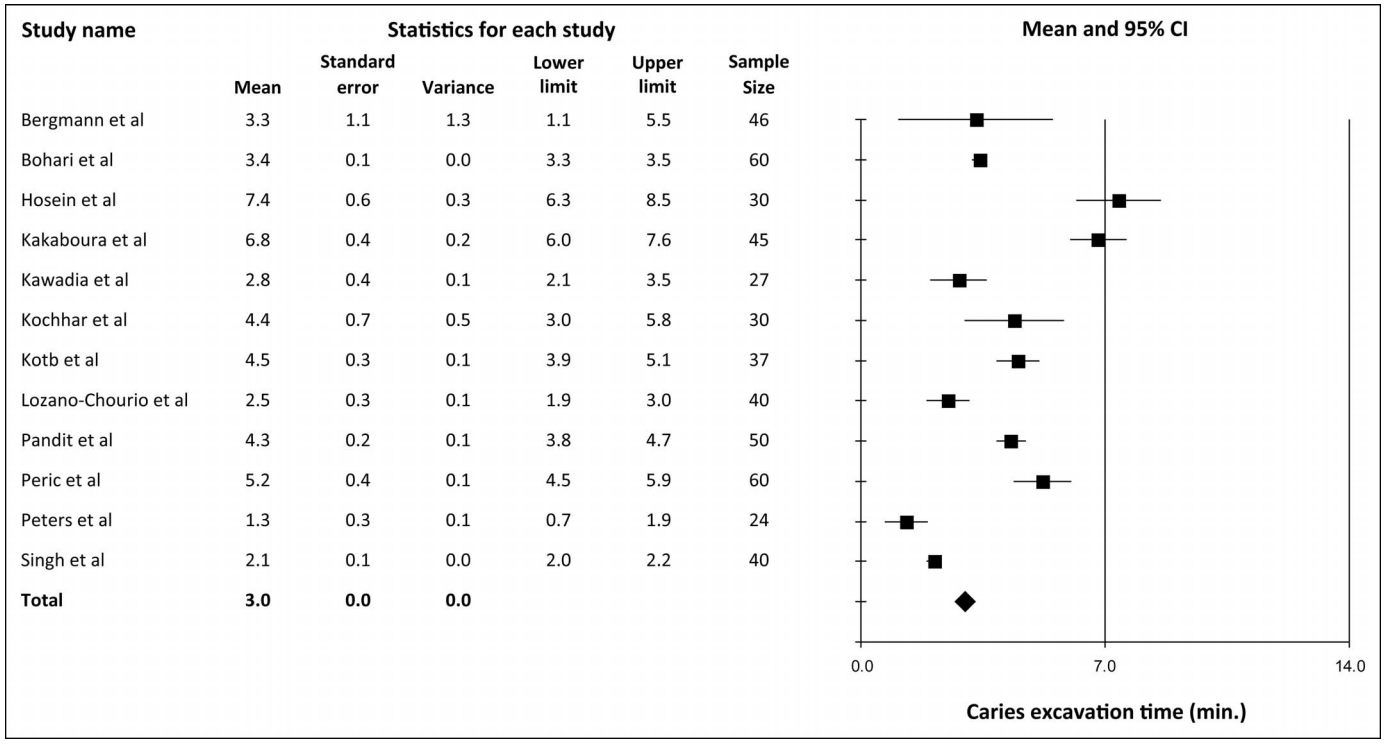

Figure 2. *Meta-analysis results of the mean excavation time for the conventional rotary caries removal method.*

dentin.[37,38,40] Also, microbial analysis of pre- and postexcavation samples were used in two trials for assessment of the efficacy of the caries removal process.[7,11]

Some trials used subjective patient behavioral and pain response assessment methods (questionnaires).[6,8,9,29,34] Conversely, the other trials[11,12,24,30-32] used standardized scales (eg, FLACC, SEM, Visual Analogue and Verbal scale, Frankl scale,[33] and Wong Baker Faces Pain scale), increasing the reliability of their results due to their unbiased outcomes. The majority of trials[8,10-12,24,25,27,29,31,34,35] obtained ethical approval from their respective institutes or at least signed informed consent by the child's parent or guardian.[6,9,28] However, four trials[7,30,32,41] did not clearly mention any ethical related issues, which may have affected the confidence toward their methodologies and results.

Only seven of the 19 trials performed long-term follow-up of the treated cases.[8,10,25,26,29,34,35] The trial by Topaloglu-Ak and others[10] was the only one that described the long-term follow-up (6, 12, and 24 months), which was performed under standard illumination conditions (battery-powered headlight).

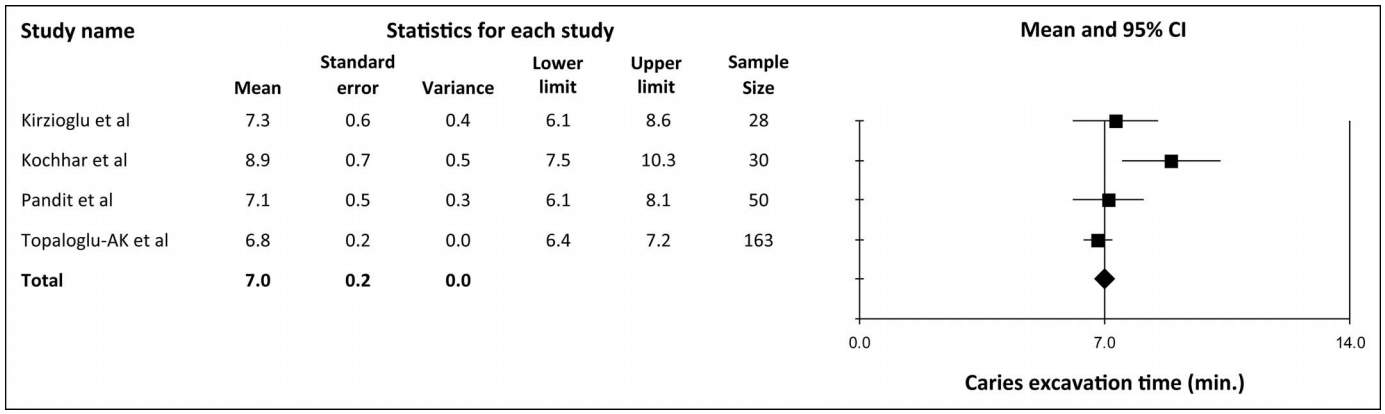

Figure 3. *Meta-analysis results of the mean excavation time for the hand excavation (ART) caries removal method.*

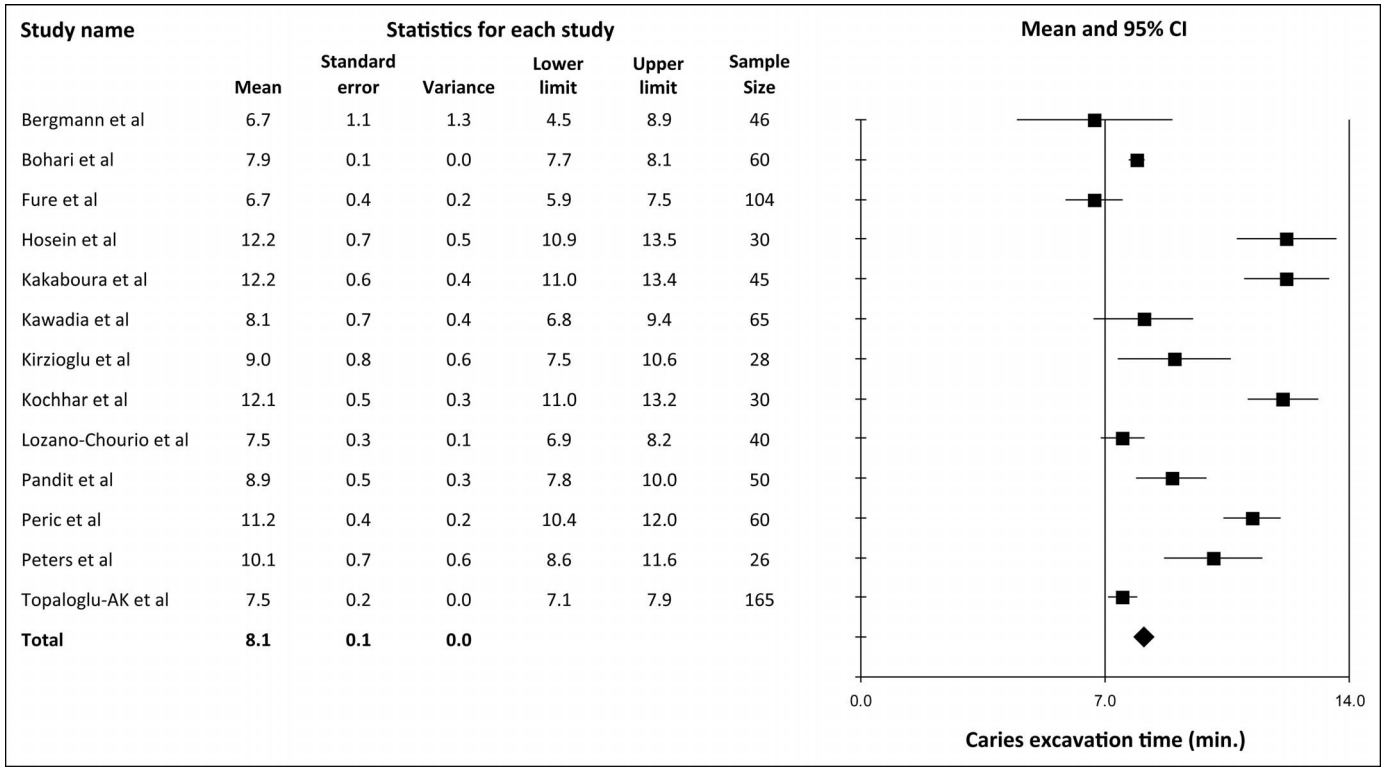

Figure 4. *Meta-analysis results of the mean excavation time for NaOCl-based (Carisolv) chemomechanical caries removal method.*

Bergmann and others[29]and Peric and others[25] did not restore the treated cavities with the same restorative material (amalgam, glass ionomer, or resin composite were used), which may have impacted the follow-up results. Bussadori and others[26] followed up the restored cavities radiographically using periapical radiograph films. However, the method of standardizing the radiographic procedures during the different follow-up sessions was not clearly stated.

The majority of trials reported that NaOCl-based (Carisolv) chemomechanical caries removal is an effective method for caries removal and is more comfortable for patients compared with conventional hand or rotary caries excavation methods. However, most studies also reported that it is a time-consuming method, which is supported by the meta-analysis results. Moreover, trials conducted on papain-based chemomechanical agent (Papacarie) concluded that the enzyme-based chemomechanical caries removal method is considered a viable alternative to the conventional caries removal method and is less time consuming than the NaOCl-based method.

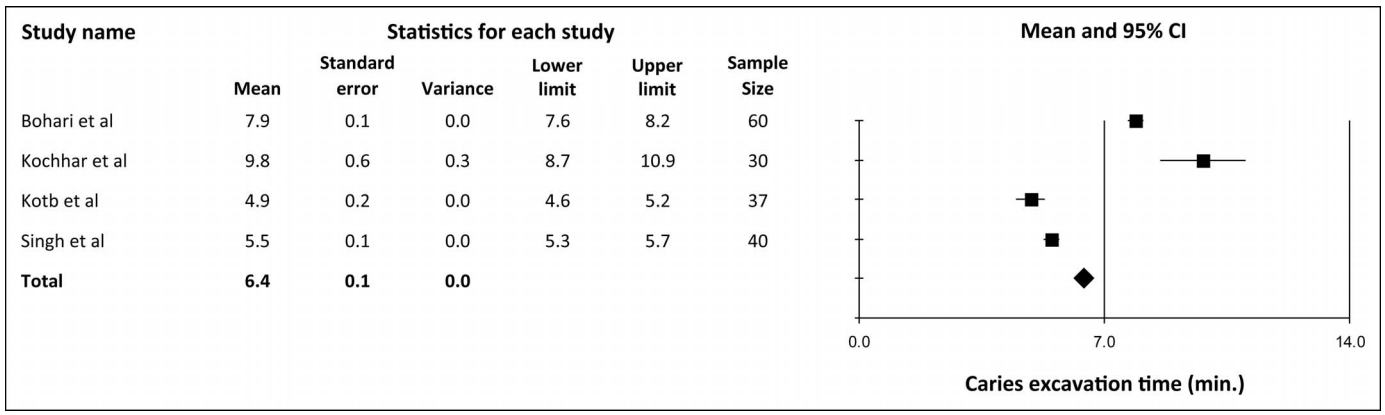

Figure 5. *Meta-analysis results of the mean excavation time for enzyme-based (Papacarie) chemomechanical caries removal method.*

Table 3: *Analyses of Caries Excavation Time*

Caries Removal Method	N (Study)	ET Mean ± SD (min)*
Rotary	12	2.99 ± 0.001 A**
Hand excavation (ART)	4	6.98 ± 0.17 C
NaOCl-based (Carisolv) chemomechanical caries removal	13	8.12 ± 0.02 D
Papain-based (Papacarie) chemomechanical caries removal	4	6.36 ± 0.08 B

** Results are based on a one-way analysis of variance and the Tukey* post hoc *test of the meta-analysis data following the statistical model of Borenstein and others.*[15]
*** Groups identified by different superscripts were significantly different at* $p<0.05$.
Abbreviations: ART, atraumatic restorative technique; ET, excavation time; NaOCl, sodium hypochlorite; SD, standard deviation.

The results of the current review revealed that the number of long-term follow-up clinical trials using Papacarie and conducted on permanent teeth was few in the literature. Therefore, further trials are needed to strengthen the scientific evidence.

Limitations of the Study

The currently available NaOCl-based (Carisolv) and enzyme-based (Papacarie) chemomechanical caries removal agents originate from non–English-speaking countries, Sweden and Brazil, respectively. Thus, the excluded non-English articles, particularly those written in Swedish and Portuguese, may contain useful information about the clinical usage of both chemomechanical caries removal agents.

CONCLUSIONS

It was found that none of the current reviewed trials fulfilled all the ideal requirements of clinical trials. Furthermore, the current scientific evidence shows that the NaOCl-based (Carisolv) chemomechanical caries removal method was more time consuming when compared to enzyme-based (Papacarie) chemomechanical and conventional caries removal methods. Further prospective randomized controlled clinical trials evaluating the long-term follow-up of papain-treated permanent teeth are needed.

Conflict of Interest

The authors have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

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