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Review Article

Comparative evaluation of Papacarie and Carisolv in effective chemomechanical carious dentin removal in primary teeth: A systematic review

Mahesh Vilasrao Dadpe, Pooja Balaji Shelke, Yogesh Jagannath Kale, Prasanna Trambakrao Dahake, Shrikant Bhujangrao Kendre, Shrawani Mankar

Department of Pediatric and Preventive Dentistry, MIDSR Dental College, Latur, Maharashtra, India

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Address for correspondence:
Dr. Mahesh Vilasrao Dadpe, Department of Pediatric and Preventive Dentistry, MIDSR Dental College, Latur, Maharashtra, India.
E-mail: drmaheshdadpe@gmail.com

ABSTRACT

Background: The goal of this study was to assess the techniques used in earlier conducted clinical investigations on the chemomechanical eradication of dentinal caries, as well as to assess the variances in pain perception, the time required for complete caries excavation, and how microbiological analysis compared before and following caries removal in primary teeth for both Papacarie and Carisolv. **Materials and Methods:** An electronic search was conducted utilizing the databases PubMed, Google Scholar, EBSCOhost, Scopus, and the Cochrane Library. The following categories were included during the assessment process: full text randomized and controlled clinical trials published between January 2000 and December 2021 in the English language only.Adolescent and child patients with open dentinal carious lesion in primary teeth were included.The methodology of the seven clinical studies chosen was evaluated. **Results:** Findings of the study reported that the microbiota in carious dentine was dramatically reduced with the Papacarie therapy, and the pain perception decreased more in the Papacarie group, whereas Carisolv treatment took longer time for complete caries excavation as compared to Papacarie. **Conclusion:** In conclusion, Papacarie had a beneficial impact by decreasing pain and time taken during caries excavation in primary teeth. The tooth surface treated with Papacarie also demonstrated a reduced bacterial count as compared to Carisolv chemomechanical caries removal approach. Overall, Papacarie and Carisolv are viable minimally invasive and painless techniques for effective caries removal in pediatric patients.

Key Words: Caries excavation, dental caries, dentin, lactobacilli colony count, primary teeth, *Streptococcus mutans*

INTRODUCTION

The term "caries excavation" is defined as mechanical treatment of dental caries-induced tooth damage to best fit the remaining parts of the tooth to receive a filling.[1] Ogushi and Fusayama have demonstrated the two zones within a carious lesion. An inner layer of intact collagen (affected dentin) and a second zone with partially destroyed collagen fibrils that cannot be remineralized (infected dentin).[2] Dental researchers worldwide though are

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very interested in the concept of retaining sound dentine.

Caries excavation with the use of air-rotor is frequently associated with patients' discomfort and pain, which subsequently necessitates the administration of local anesthesia.[3] Alternative techniques such as lasers, ultrasonic instrumentation, and air abrasion have been developed for caries removal to decrease the pulpal responses, but they are less often used by the pediatric dentists due to economic concerns of some of these techniques.[4]

Chemomechanical caries removal (CMCR) is a noninvasive procedure that protects healthy tooth structures while eradicating infected tissues without causing pulp irritation or discomfort to the patient.[5] Chemomechanically treated dentin has more surface energy, a stronger affinity for adhesive material, and better bonding than untreated dentin.

Carisolv, the most recent variant of the NaOCl-based chemomechanical agents, was launched in 1998.[6] The gel softens the carious dentine while leaving the healthy tissue unharmed.[7] Because deteriorated collagen has an open structure, it is more susceptible to Carisolv penetration, and this dentin can be simply scraped off with improved Carisolv instruments.[8] The downsides of adopting Carisolv include the substantial training and registration of specialists that is necessary, as well as the need for customized devices, which raises the solution's cost.

Papacarie was made available as a proteolytic gel in 2003.[9] The latex of the Carica papaya is used to make papain. The new medicine contains the collagen degradation features of papain as well as bactericide characteristics of chloramines. By interacting with the exposed collagen and softening the carious dentine, papain dissolves the decaying tissues enabling the removal of the carious dentine without the necessity for drilling or local anesthesia.[10,11] As per Dawkins *et al*., both Gram-positive and Gram-negative organisms replication can be hampered by papain application. With the Papacarie technique of caries removal, dental professionals can remove all of the carious dentine while protecting the unaffected dentine without the use of a special instrument. Papain's enzymatic action is thought to be beneficial in areas with necrotic and purulent tissues.[2,12-15]

There is also a significant lack of systematic research regarding the effectiveness of Papacarie and Carisolv in primary teeth in terms of antibacterial activity. Primary dentition is more prone to lesion progression and development. In addition, there are very few outcome factors in earlier systematic reviews. Therefore, in an effort to compare the effectiveness of Papacarie and Carisolv in primary teeth, we carried out a systematic review.

The purpose of this systematic review is to assess the methodology used in earlier published medical studies on Papacarie and Carisolv, as well as to investigate the difference in pain perception, time required, and microbiological analysis before and after caries removal in primary teeth.[16,17]

MATERIALS AND METHODS

Protocol development and eligibility criteria

The systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database (CRD42022298034) and reported using the Preferred Reporting Items for Systematic Reviews (PRISMA) statement's recommendation.

Focused question

"Is the caries removal efficiency of Papacarie better than Carisolv in primary teeth?"

The PICO pattern was employed in the search technique for Medical Subject Headings terms and free words.

Population: Adolescent and child patients with open caries lesion with dentin involvement in primary teeth. Human studies were included without gender restriction.

Intervention: Papacarie-based CMCR.

Comparison: Carisolv-based CMCR.

Outcome: Pain perception, length of time needed, and microbiological colony-forming units before and after the caries removal were recorded separately for both the methods.

Trial design-randomized controlled trials and prospective CCT were included and reviewed.

Information source and search

An electronic search was done by one of the authors using the following databases: Scopus, PubMed, EBSCO, and Google Scholar to search the articles from January 2000 to December 2021. English was the only language selected for the literature. To combine the terms according to the PICOS format Boolean

terms such as OR and AND were used. The internet search was carried out using the following web search criteria: Papacarie OR "Papain gel" AND Carisolv AND "Primary Teeth" OR "Deciduous teeth." Titles and abstracts were reviewed for the study selection following the strategy. Duplicate studies from different database were identified and removed.

Eligibility criteria

Inclusion criteria

Full-text English randomized controlled clinical trials and controlled clinical trials were chosen from the beginning of 2000 to the end of 2021. The study population included adolescent and child patients with open dentinal carious lesion in primary teeth. Studies evaluating both Papacarie and Carisolv; studies in English language; and studies evaluating either pain perception, time taken for caries removal; and microbiological colony-forming units before and after caries removal.

Exclusion criteria

The following studies were excluded: studies in non-English languages, systematic review, rapid review, literature review, narrative review, scoping review, *in vitro* studies, and animal studies. Teeth showing clinical or radiographic evidence of pulp, furcation, or periapical pathosis were not included.

Data extraction

The eligibility of the studies was assessed separately by two reviewers. Discussion was used to settle any disagreements. A third author was contacted when needed. The inclusion and exclusion criteria were used to choose the publications. Data were extracted and tabulated as follows: (i) author and publication year; (ii) study design; (iii) characteristics of participants: sample size, age; (iv) pain assessment scale; (v) time taken for caries removal (vi) microbiological assessment; and (vii) authors' conclusion.

Quality assessment

A pair of reviewers independently assessed the quality of the papers that were considered using the Revised Cochrane Risks of Bias Assessment for Randomized Trials (ROB2). For each study, the following biases were documented: Selection bias, attrition bias, performing bias, detecting bias, and reporting bias, and other bias. Each domain was judged using Yes, No, Possibly Yes, Possibly No, and Unclear responses. After a thorough assessment of all the domains, those having low risk bias were scored as "low risk," however, a research having a "moderate risk of bias" or a "high risk of bias" was the one which were rated as "unclear risk" or "high risk of bias," respectively. All of these data were evaluated by two reviewers, and any disputes were addressed through discussion or contact with a third author. Choices on research documentation were made notably.

RESULTS

Selection results of studies

A total of 2106 articles were identified during the first phase of the study selection using the databases and manual searches. After removing the repeated/duplicate results, 526 studies remained for the analysis of study population and type of the study. After the analysis of population and type of the study, only 43 studies remained for the analysis of titles and abstracts. After the detailed analysis, only 20 studies were eligible for the full-text analysis. After reading the full texts, the qualitative synthesis comprised seven well-designed papers with distinct treatment techniques. Figure 1 depicts the flow chart of the study selection.

Characteristics of eligible studies

The trials were published between January 2000 and December 2021. Four studies evaluated the pain perception prior to and following different caries eradication strategies; the scales used in these investigations, however, differ substantially. Four investigations evaluated the period required for full caries eradication in seconds. Antimicrobial efficacy was assessed by three studies in terms of colony-forming units of *Streptococcus mutans* and *Lactobacillus*. The features that were present in the studies are shown in Table 1.

Pain perception

The perception of pain during the treatment of primary tooth caries was covered in four studies.[18-20] Although the Wong-Baker face pain rating scale score is a subjective rating, it is a very straightforward and practical tool for documenting how young children felt following treatment. In both the Papacarie and Carisolv methods, pain scores were shown to be lower before and after caries eradication.[21-25] When comparing the two groups, Papacarie group experienced less pain perception. Since the Carisolv and Papacarie gel works only on denuded fibers in demineralized dentin, painful removal and harm to healthy dentin are prevented. It has also been

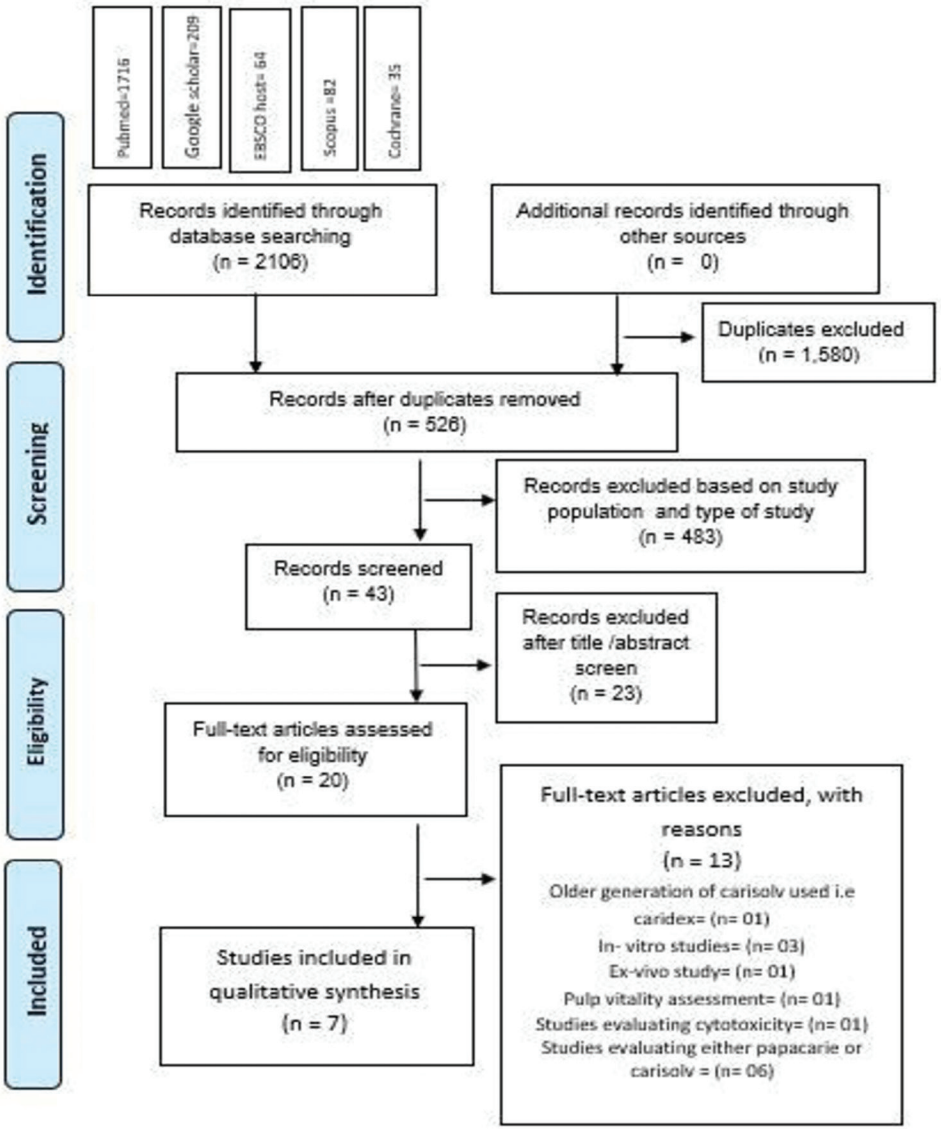

Figure 1: PRISMA flow chart to show the study selection process.

noted that the Papacarie gel has a slight anesthetic effect.[19,20]

Time taken for caries removal

Four studies investigated the implications of treatment duration. The time elapsed from the start of gel application until the appearance of clear gel and hardening of the cavity surface was calculated. In all four investigations, the time needed for Carisolv was longer than the time taken for Papacarie technique.[17-20,26] According to Kochhar *et al*., the need for numerous applications to eradicate caries may be the cause of Carisolv's longer processing time.[20]

Effectiveness of Papacarie and Carisolv in reducing the cariogenic microbiota

The results of three experiments on the reduction of microorganisms were reported.[16,19-21] Dentin samples were serially diluted and anaerobically cultivated on several agar plates, including blood agar, Mitis salivarius agar, and Rogosa agar plates. For total bacterial, mutans streptococci, and lactobacilli counts, colony-forming units were calculated. The microbiota in caries dentin was shown to be greatly reduced when Papacarie treatment was used.

Quality assessment

The risk of bias for each article was rated independently based on the answers given to each domain in the tool (ROB2). Answers were recorded using color coding. Green color suggests low risk, yellow shows some concerns while red color is for high risk of bias [Figure 2].

The research conducted by El-Tekeya *et al*., Chowdhry *et al*., Hegde *et al*., and Moimaz *et al*.

Table 1: Summary of characteristics of the included studies (*n*=7)

Author, year, country	Study design	Sample size (patients/number and distribution of teeth)	Age (years)	PAS (mean values)	Treatment time mean (s)	Microbiological assessment (CFU)	Authors' conclusion
Kochhar *et al.*[20] India	RCT	80/120 Hand instrumentation (*n*=30) Papacarie (*n*=30) Carisolv (*n*=30) Airotor (*n*=30)	5–9	VAS Papacarie - 7.33 Carisolv - 19.33 VPS Papacarie - 0.73 Carisolv - 1.93	Papacarie - 590.8 Carisolv - 723.73	*Streptococcus* Papacarie - 0.86±1.38 Carisolv - 2.03±0.76 *Lactobacillus* Papacarie - 0.17±0.67 Carisolv - 1.58±0.45	Papacarie was clinically more efficient than carisolv with respect to amount of time required and pain perception for complete caries removal
El-Tekeya *et al.*[16] Egypt	RCT	NR/45 Papacarie (*n*=15) Carisolv (*n*=15) Conventional hand excavation (*n*=15)	4–8	NR	NR	*Streptococcus* Papacarie - 0.86±1.38 Carisolv - 2.03±0.76 *Lactobacillus* Papacarie - 0.17±0.67 Carisolv - 1.58±0.45	Papacarie exhibited better antimicrobial efficacy than carisolv
Bohari *et al.*[26] India	CCT	NR/120 Airotor (*n*=30) Carisolv (*n*=30) Papacarie (*n*=30) Er: YAG laser (*n*=30)	5–9	FLACC Carisolv - 1.13 Papacarie - 1.37	Papacarie - 471.3 Carisolv - 474.7	NR	Papacarie and carisolv exhibited comparable pain perception and took equal length of time for caries excavation
Ammari *et al.*[21] Brazil	RCT	46/74 Papacarie (*n*=25) Carisolv (*n*=27) Manual (*n*=22)	5–9	NR	NR	*Streptococcus* Papacarie - 3.4×10^2 Carisolv - 3.4×10^4 *Lactobacillus* Papacarie - 3.4×10^2 Carisolv - 3.4×10^4	Papacarie and Carisolv exhibited equal antimicrobial efficacy
Chowdhry *et al.*[17] India	RCT	30/90 Papacarie (*n*=30) Carisolv (*n*=30) Conventional method (*n*=30)	6–9	NR	Papacarie - 387.83 Carisolv - 375.33	NR	Papacarie and carisolv took equal length of time for caries excavation
Hegde *et al.*[18] India	RCT	60/183 Papacarie (*n*=50) Carisolv (*n*=50) Rotary (*n*=50)	5–12	WBF Papacarie - 2.14 Carisolv - 2.22	Papacarie - 322.49 Carisolv - 341.21	NR	Papacarie was clinically more efficient than carisolv with respect to amount of time required and pain perception for complete caries removal
Moimaz *et al.*[19] Brazil	RCT	32/64 ART (*n*=32) Papacarie (*n*=16) Carisolv (*n*=16)	6–9	Questionnaire pain was reported by 25% of the patients with papacarie, whereas 31% of the patients reported pain with carisolv	Papacarie - 442.2 Carisolv - 465	*Streptococcus* Papacarie - 6.50×10^3 Carisolv - 7.06×10^3 *Lactobacillus* Papacarie - 7.79×10^2 Carisolv - 10.44×10^3	Papacarie and carisolv exhibited comparable pain perception and took equal length of time for caries excavation as well as exhibited comparable antimicrobial efficacy

NR: Not reported; RCT: Randomized control trial; CFU: Colony-forming unit; WBF: Wong-Baker faces; FLACC: Face, legs, activity, cry, consolability scale; VAS: Visual Analog Pain Scale; VPS: Verbal Pain Scale; PAS: Pain Assessment Scale; CCT: Controlled clinical trial; ART: Atraumatic restorative treatment

Figure 2: Risk of bias assessment.

revealed a low risk of evaluation bias.[16-19] Kochhar *et al*. and Ammari *et al*. discovered a moderate risk of bias due to the certain issues about outcome data blinding.[20,21] High risk of bias was shown by only one study of Bohari *et al*. due to some concerns in random sequence generation and allocation concealment.[26]

DISCUSSION

CMCR involves chemically softening carious dentine and then gently excavating it. It has gained importance due to its property of selective removal of carious lesion with avoidance of pain.[8] One of the justifications for the specialty of pediatric dentistry is the instillation of a good attitude toward oral health care as well as comfort, peace, and alleviation. The patients' dental health for the rest of their lives may be impacted by a mild and painless treatment experience.[27-30] A mild and comfortable treatment experience may have a long-term impact on the patients' oral health.

Ansari *et al*. favored the CMCR method over the conventional method because it is less distressing, requires less local anesthesia, has a high patient preference, has a lower probability of exposure in deep carious cavities, is helpful in immunocompromised patients and patients with bleeding disorders, and has better bonding to restorative materials.[22,31,32] Papacarie is a CMCR procedure that consists of papain, chloramine, toluidine blue, deionized water, preservatives, stabilizers, and salts that aid in the removal of damaged tissues. Infectious tissues lack anti-trypsin, a plasmatic anti protease found only within healthy dentine which is responsible for preventing tooth structure destruction. Flindt showed that papain's action was restricted in these bacterial tissues.[11,23] After the first application of Papacarie gel for 30–60 s, dental caries is excavated using hand instruments. The procedure is repeated until the lesion surface feels firm and the gel is clear. The cavity is then sprayed with water and cleaned with a cotton pellet. Papacarie works by dissolving the collagen molecules that have partially disintegrated. Collagen fibril crosslinks are hydrolyzed by it. During the clinical procedure, the development of bubbles

on the surface and blearing of the gel show that the degradation is happening and oxygen is being released, proving that the elimination process has started.[24]

Carisolv is a NaOCl-based CMCR product that is commercially marketed. The three amino acids, namely glutamic acid, leucine, and lysine are differently charged. Each of Carisolv's three chloro-amino acids electrotatically attracts one of the hydrophilic and hydrophobic patches present in protein peptide chains such as collagen.[4] It promotes reactive power along the entire length of the collagen fiber while decreasing the unfavorable adverse effects of hypochlorite. The chemical outcome of these activities is collagen breakdown, which is common in the demineralized section of a carious lesion. This softened dentine with deteriorated collagen can be easily scrapped off with Carisolv instruments.[5] Consequently, the goal of this systematic review was to compare the Papacarie technique of caries removal to the Carisolv strategy in terms of pain perception in a clinical setting, time taken, and microbiological assessment before and after carious removal in primary teeth.

Various scales have been used to capture patients' feelings following caries eradication, as pain perception is a subjective measure. Wong-Baker Faces Pain Rating Scale (WBFPS) is more sensitive as compared to other pain assessment scales. The WBFPS depicts six faces. Kids are asked to choose the expression that best represents their own personal suffering. Faces 0 and 2 do not hurt at all, whereas Faces 4 and 6 do hurt somewhat more, Face 8 significantly more, and Faces 10 as severely as you can conceive. Kochhar *et al*. used Visual Analogue Scale as well as VPS, Hegde *et al*. used WBF and Moimaz *et al*. used a mere questionnaire for recording pain perception.[18-20] Pain perception was almost similar for both Papacarie and Carisolv in all the three trials with Papacarie technique proving to be less painful as compared to Carisolv. Pain associated with Carisolv might probably be because of the prolonged time taken to remove the caries. Bohari *et al*. used FLACC scale and found Carisolv to be less painful.[26] Subjective nature of pain as well as variability of the pain threshold among individuals may be responsible for difference in results. The CMCR agents cover the entire cavity during treatment; they may serve as a heat insulator. In addition, the technique anticipates opening less dentinal tubules than drilling. Chemomechanical techniques, which are almost painless, are effective for treating special health care needs children because any stimulation, whether aural, sensory, or emotional, might cause adverse reactions.[27] Individuals' terror of the dentist increased in the CMCR group while it decreased marginally in the normal rotary procedure, according to Inglehart *et al*. This finding has been attributed to the CMCR technique's lengthy treatment time.[28]

In the present systematic review, treatment time was chosen as outcome to evaluate the efficiency of Papacarie and Carisolv in caries removal. Kochhar *et al*., Bohari *et al*., Chowdhry *et al*., Hegde *et al*., and Moimaz *et al*. made a conclusion that Carisolv method is more time consuming than Papacarie.[17-20,26] However, because there is no agreed-upon standard for measuring treatment duration, the variability of treatment time is substantial. Time was registered with a stopwatch by Chowdhry *et al*., Hegde *et al*., and Moimaz *et al*.[17-19] Less time was required for Papacarie as compared to Carisolv as fewer number of applications are required with the Papacarie method. The use of customized Carisolv hand instruments all the more increases the treatment time.[29] Papacarie's work time acceptance in pediatric dentistry was demonstrated by Carrillo *et al*. in 2008 as 4–8 min.[27]

Bacteriological investigation was selected as a means of evaluation to determine the efficacy of both procedures (Papacarie and Carisolv) for caries eradication. El-Tekeya *et al*., Ammari *et al*., and Moimaz *et al*. examined antibacterial efficiency by giving particular results of CFU decrease.[16,19,21] Papacarie could significantly reduce the colony-forming units of both *S. mutans* and *Lactobacillus* as compared to Carisolv.[30] A proteolytic enzyme called papain possesses anti-inflammatory, antibacterial, and bacteriostatic properties. The chloramine chlorinates the deteriorated dentine collagen, which is then simple to remove using an excavator. Toluidine blue is a photosensitive pigment present in Papacarie that binds to the bacterial membrane and has been discovered to be quite efficient against *S. mutans*.[24]

Two studies in the present systematic review showed risk of bias due to problems in random sequence generation, allocation concealment, and blinding of outcome assessment. The study of Kochhar *et al*. showed moderate risk of bias as the outcome assessors

were aware of the interventions received by the study participants. The study of Bohari *et al*.[20,26] showed high risk of bias as there was some concern arising from the randomization process as the allocation sequence was not randomized. There was also moderate risk arising due to deviation from intended intervention in this study. However, the remaining five studies demonstrated low risk of bias which improved the quality of the review.

Advantages and limitations of the review

In this review, a comparison of reductions in cariogenic microbiota prior to and following caries eradication using Papacarie and Carisolv was performed. There has been no comprehensive comparison of Papacarie with Carisolv in primary teeth. All the researches in this concerned area with the inclusion of chemomechanical caries eradication in primary teeth was investigated in the current systematic review. The research strategy was carefully considered to reduce the danger of bias, which enhanced the review's quality.

It is vital to highlight the major limitations in the current review. Primarily, the study was undertaken in a number of nations, including India, Egypt, and Brazil, limiting the findings' generalization. The outcomes may have been impacted by variations in caries eradication between nations. Greater variability of institutional settings and other economic, social and cultural influences have been reported in different countries. There are variations in how nations focus and advance their understanding of novel approaches. To evaluate the efficacy of Papacarie and Carisolv, the subsequent caries rate must also be considered as an objective. The lack of information in the included research on the location of caries may have an effect on how successfully it is eliminated. Further studies are needed to find out if these CMCR procedures alter the restorative rate of survival.[33]

CONCLUSION

Papacarie reduced pain perception during caries excavation in primary teeth and had a quicker treatment time.[34,35] Papacarie is also far more effective than Carisolv at reducing cariogenic bacteria in the dentin of primary teeth as assessed by the included studies with low risk of bias.

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Conflicts of interest

The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or non-financial in this article.

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