

Comparing the efficacies of two chemo-mechanical caries removal agents (2.25% sodium hypochlorite gel and brix 3000), in caries removal and patient cooperation: A randomized controlled clinical trial

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ABSTRACT

Introduction: This study compared and evaluated the effectiveness of Brix 3000 and 2.25 % sodium hypochlorite (NaOCl) gel with conventional rotary instrumentation method in caries excavation of primary molars. The null hypothesis: no difference between the two tested chemo-mechanical caries removal (CMCR) agents used in this trial.

Materials and methods: a randomized controlled clinical trial conducted with 32 children suffering from proximal caries of primary maxillary molars, age ranging between 6 and 9 years old. Subjects were randomly assigned into three groups: Brix 3000, NaOCl gel, and conventional with 10, 12, and 10 teeth in each group, respectively. After isolation of selected teeth, either CMCR agent were applied for two minutes. The application was repeated as needed until a caries-free surface was obtained. The conventional group used low-speed burs to excavate all carious lesions. The time required to obtain a caries-free result for each testing method was recorded. Wong-Baker FACES pain rating scale was used to assess the acceptance of the technique used by the child.

Results: Conventional treatment required significantly less time for caries removal compared to Brix 3000 ($P = .002$) and NaOCl gel ($P = .000$). No significant difference observed between Brix 3000 and NaOCl gel ($P = .679$). Statistically higher pain scores were observed with conventional treatment compared to both Brix 3000 ($P = .000$) and NaOCl gel ($P = .005$). Pain scores were lower with Brix 3000, and NaOCl gel with no significant difference observed between the CMCR agents ($p = .690$).

Conclusions: CMCR agents that are effective in removing the carious dentine of primary teeth without negatively affecting the cooperation of children.

Clinical Significance: The use of a 2.25 % sodium hypochlorite gel can be an effective and well-tolerated method of removing decay from primary teeth and reduce the trauma associated with conventional rotary caries removal.

1. Introduction

The use of rotary instrumentation is the most prevalent technique in caries removal and has been demonstrated to be more rapid in excavating carious tissues than other methods [1]. However, this invasive technique has many negative points: potential for injurious thermal effects on pulpal tissue, the sound that can affect the cooperation of the patient in the dental clinic, and the excessive removal of intact tooth structure. These factors are driving forces in the development of alternative techniques that can overcome these traditional method disadvantages [2].

Chemo-mechanical caries removal (CMCR) agents were introduced in the 1970s and are characterized by chemicals that can dissolve softened tissue in order to aid in manual excavating of carious dental tissues. GK 101 was developed first and is composed of a 5 % sodium hypochlorite (NaOCl) solution [3]. Habib, Goldman, and Kronmann, noticed that a 5 % sodium hypochlorite solution alone could be harmful to intact tissues [3]. A combination of sodium hydroxide, sodium chloride, and glycine was added to GK 101 in order to overcome the undesirable effects of sodium hypochlorite alone. This combination became the product known as Caridex. However, a slow effect on the dissolution of caries affected tooth structure, and the instability of the

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solution limited its usefulness [4].

Another solution called Carisolv, which is composed of 0.95 % sodium hypochlorite solution added to three amino acids (leucine, lysine, and glutamic acid), was subsequently developed. The reaction of NaOCl with amino acids improved the degradation of collagen fibrils in the demineralized areas of carious tissue and improved the process of caries removal [4].

In 2003, a gel that contains papain, a protein extracted from papaya, chloramine, and toluidine blue, was released. It was called Papacarie. The papain protein interacts with the exposed collagen and helps the degradation of that collagen. The gel has further application in the dissolution of minerals from dentin, making the infected dentin more softened, which facilitates its excavation [5].

The most recent modification made on papain-based gels was the introduction of Brix 3000. This product released in Argentina in 2016. It derived from fruits of green papaya [6]. The concentration of papain in Brix 3000 increased to 3000 U/mg in each 10 %, and the papain was bio-encapsulated by EBE technology (Encapsulated Buffer Emulsion). This process gives the gel the ideal pH needed to immobilize enzymes, which leads to enhanced proteolysis of collagen fibrils in decayed tissue, better resistance to unfavorable storage environment, and greater antimicrobial properties [7]. Furthermore, this formulation contains no chloramines, which enhances its toxicological safety feature [8].

Although Brix 3000 has an improved mechanism of action, it comes at a very high cost [7]. Interest in finding a more cost-effective agent has developed over time. Thus, a new formulation of sodium hypochlorite combined with carboxymethyl cellulose has been developed. This sodium hypochlorite gel is now available for studies. It is reported to make NaOCl more controllable by modifying its viscosity while maintaining comparable properties to the solution [9].

1.1. Objectives

The purpose of this random clinical trial is to evaluate the effectiveness of a 2.25 % sodium hypochlorite gel and Brix 3000 as a CMCR agent compared to each other based on the time needed and patient acceptance of caries removal from primary teeth clinically, compared to the conventional methodology of rotary instrumentation. The null hypothesis: no difference between the two tested chemo-mechanical caries removal (CMCR) agents used in this trial.

2. Materials and methods

2.1. Study design

A Randomized controlled single-blinded clinical trial with samples composed of one tooth of each participant. Forty cooperative children aged between 6–9 years participated in the trial, and each participant was evaluated for one tooth only. Forty primary maxillary molars with dentine cavitated carious lesions were selected. Digital x-rays were utilized in the standardizing depth of caries in the selected teeth. The selection was based on the extent of the carious lesion and required caries to extend into the middle third of dentine. Eight teeth were

excluded due to extensive depth of caries into the pulpal third of dentine or due to clinical or radiographic signs of pulpal involvement

After obtaining the approval of the Ethics scientific committee at the study institution, the trial was registered in the Australian New Zealand Clinical Trials Registry (ANZCTR) (trial id: ACTRN12619000440123).

2.2. Study groups

Randomization of each group participant was developed by using <https://www.random.org/> into three groups as follows:

Group A: 10 carious teeth excavated using Brix 3000® (Brix S.R.L., Argentina).

Group B: 12 carious teeth excavated using 2.25 % sodium hypochlorite gel.

Group C: 10 carious teeth excavated using conventional rotary instrumentation method with low-speed conventional tungsten carbide burs (H1 SE, Komet, Lemgo, Germany).

2.3. Intervention

Digital X-ray periapical radiographs were taken for each tooth before enrolling it into the trial determined the carious lesion depth. Once accepted into the trial, the areas treated were isolated with cotton rolls and salivary ejectors. The application of either Brix 3000 or 2.5 % NaOCl gel for two minutes using hand excavators (EXC 19W4 Brasseler, USA) to remove all carious dentin and then checked with a sharp tip explorer (dental probe DA 410R; Aesculap, Tuttlingen, Germany). When dentine demonstrated slight resistance with no tug-back while pressing an explorer into dentin, the application of the chemo-mechanical agents was stopped. CMCR agent application continued and timed until the whole carious lesion was tactilely determined to be removed, as previously described.

Two blinded investigators were involved with the detection of cavities and to make decisions to stop or repeat the application of the CMCR agents. Cavities were thoroughly washed and dried before investigator determination. In the conventional group, rotatory instrumentation with low-speed burs (800 rpm) was used to excavate all carious lesions. All burs were new and had the same ISO size (H1 SE 204).

The timing of each procedure was set immediately upon the first application by using an iPhone 7plus stopwatch and turned off when there is no carious dentine left in the cavity — the time needed for complete caries removal recorded. After complete removal of decay, as determined by the blinded investigators, the teeth were restored with glass ionomer cement filling (Medifil IX AC™, Promedica, Germany).

Wong-Baker FACES pain rating scale was used in this trial to determine the level of pain after excavating caries with each testing mechanism. The subjects choose one of the scale's faces that best described how they felt through the procedure that they underwent. (Fig. 1)

2.4. Data analysis

Data were analyzed using IBM SPSS version 23 (IBM Corp., Armonk, USA). Descriptive results, including minimum, maximum, mean, and

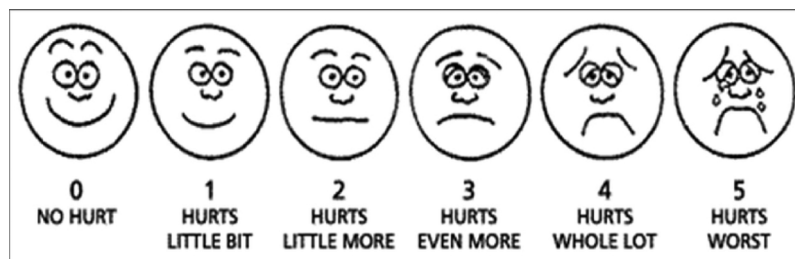


Fig. 1. Wong-Baker FACES pain rating scale.

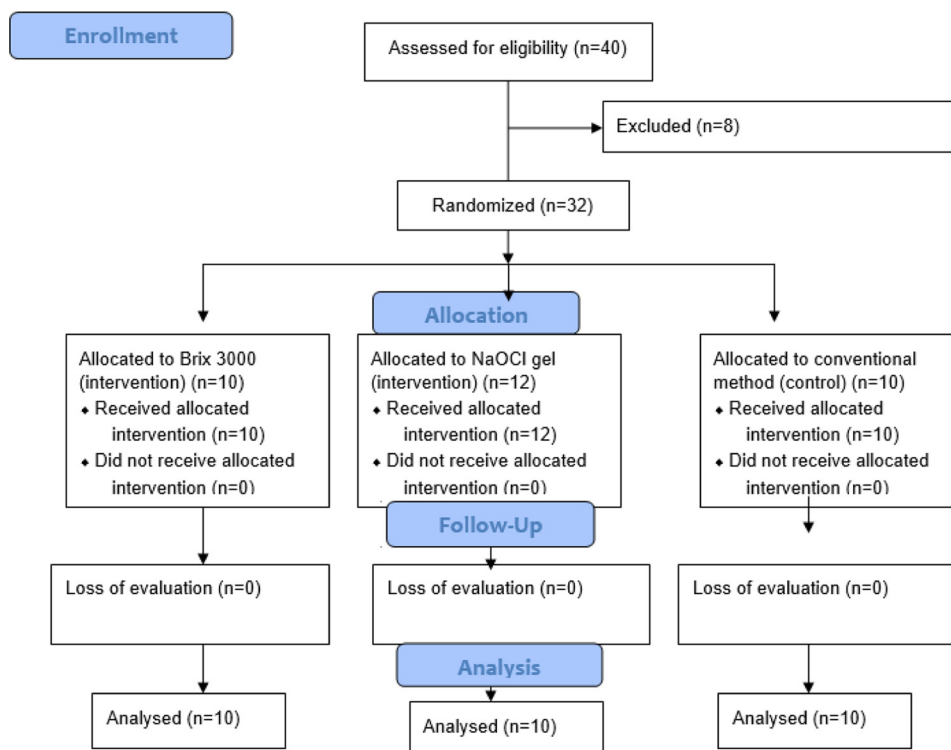


Fig. 2. Consort flowchart of the trial.

standard deviation, were calculated for the evaluated groups.

The normality of distribution was determined using the Kolmogorov-Smirnov test. Kruskal-Wallis testing determined significant differences in the duration of caries removal between the three groups.

Kruskal-Wallis H testing determined the significant difference among the ordinal data of the Wong-Baker scale between the three groups.

P-value of 0.05 was considered the level of significance.

3. Results

Thirty-two participants were enrolled in this study (12 Female and 20 Male) with a mean age of 5.94 ± 1.29 . Fig. 2 shows the CONSORT flow diagram of the progress through this randomized trial.

Descriptive results of the time required for caries removal showed that NaOCl gel required the longest time to remove all carious tissues as tested, followed by Brix 3000, and then conventional rotary instrumentation method (6.40, 5, and 1,60 min respectively) (Table 1).

Kruskal-Wallis test showed significant differences concerning the time required for caries removal between all three groups ($P = .000$) (Table 1).

Pairwise comparison using Mann-Whitney *U* test showed that the conventional rotary instrumentation method required significantly less time for caries removal as compared to Brix 3000 ($P = .002$) and NaOCl gel ($P = .000$), with no significant difference observed between Brix 3000 and NaOCl gel ($P = .679$) (Table 2).

The frequency and descriptive results, including the mean rank of the Wong-Baker scale for the evaluated groups, are reported in

Table 1
Characteristics of enrolled patients.

Female		Male		Age
N	%	N	%	Mean±SD
12	37.5 %	20	62.5 %	5.94±1.294

SD_ Standard Deviation.

Table 2

Demonstrates the descriptive results of Kruskal-Wallis test regarding the time required for caries removal (min).

	Minimum	Maximum	Mean±SD	P Value
Conventional	1	3	1.60±0.843	.000 ^a
Brix 3000	2	8	5±1.595	
NaOCl	4	10	6.40±1.838	

SD_ Standard Deviation.

^a Statistically significant.

Table 3

Pairwise Comparison of Mann Whitney *U* test (Min).

Comparison	Difference of means	SE	P-Value
Conventional-brix	-13.408	3.918	.002 ^a
Conventional-NaOCl	-18.150	4.092	.000 ^a
Brix-NaOCl	-4.742	3.918	.679 ^a

SE- Standard Error.

^a Statistically significant.

(Table 3).

Kruskal-Wallis H test demonstrated a statistically significant difference in the Wong-Baker scale between the three groups ($P = .001$) (Table 3). However, the Mann Whitney *U* test showed statistically higher pain score differences in the conventional rotary instrumentation method compared to both Brix 3000 ($P = .000$) and NaOCl gel ($P = .005$). In contrast, there was no significant difference in pain score observed between Brix 3000 and NaOCl gel ($p = .690$) (Tables 4, 5).

4. Discussion

The intention of Minimally invasive dentistry (MID) is to make dental procedures more conservative in biological direction [10]. However, the most common technique is the use of conventional methods: rotary instrumentation and low-speed burs. However, this

Table 4
Frequency of Wong Baker scale among the three groups and the results of Kruskal-wallis H test.

Scale	Conventional		Brix		NaOCl		P Value
	N	%	N	%	N	%	
Grade 0	0	0	5	16.6	6	18.8	.001
Grade 2	2	6.3	6	18.8	2	6.3	
Grade 4	1	3.1	1	3.1	1	3.1	
Grade 6	1	3.1	0	0	0	0	
Grade 8	4	12.5	0	0	0	0	
Grade 10	2	6.3	0	0	1	3.1	
Mean Rank	25.30		12.67		12.30		

Table 5
Mann Whitney U test to analyze the differences in Wong Baker scale between the evaluated groups.

Comparisons	Mean Rank	P Value
Conventional	16.65	.000 ^a
Brix 3000	7.21	
Conventional	14.15	.005 ^a
NaOCl	6.85	
Brix 3000	11.96	.690
NaOCl	10.95	

^a Statistically significant.

method has many disadvantages, such as 1) being invasive, 2) patient dislike for the sound and feel of rotary instrumentation, and 3) being potentially harmful to pulpal tissue [11]. As a result, there have been several recent studies concentrating on chemo-mechanical caries removal agents (CMCR) as an MID method for excavating carious dental tissues [12].

In this trial, two types of CMCR agents (Brix 3000 and 2.25 % NaOCl gel) are compared to each other and the use of the conventional rotary instrumentation methods for 1) the time needed to create a caries-free surface in primary molars and 2) the acceptance of the technique by children enrolled in the study.

Each patient enrolled in this study was evaluated after excavating only one maxillary primary molar. Therefore, the study was not able to be designed as a cross-over study.

Primary molars with proximal caries that are not pulpally involved were selected for this study. Radiographs were taken to standardize the selected teeth, and only teeth that have two-thirds of dentin cariously involved with an intact inner third were selected for inclusion.

CMCR agents were applied for two minutes in each application needed. The duration (two minutes) of the application of Brix 3000 was determined according to the manufacturer's instructions. A two minute application time was also used for the NaOCl gel group in order to standardize procedural steps of intervention and to compare the speed of caries removal effectively.

Tactile assessment of remaining caries was employed in the assessment of the effectiveness of caries removal in this study. According to Sadasiva et al., the tactile method of detecting caries is as efficient as caries dye use or laser fluorescence in evaluating remaining dental caries [13,14].

Visual and tactile detection of caries is a verified method according to many systematic reviews and studies [15–17].

Moreover, one of the most important aims of using CMCR in dentistry is to conserve as much dental tissues as possible. We know that some methods of caries detection, such as caries detection dyes [18] may cause unnecessary removal of sound tooth structure. These detectors can stain the organic matrix of less mineralized dentin, including normal circum-pulpal dentin and sound dentin in the area of dentin-enamel junction (DEJ) [19]. Banerjee et al. reported that the use of dyes is not routinely advocated in lesions extending into the middle

third of dentin or deeper due to the increased risk of unnecessary and often avoidable pulpal involvement during cavity preparation [20]. Consequently, tactile method of detection can be considered more conservative than others.

Furthermore, many factors can affect caries removal. The operator, the excavator and softness of carious dentin are some critical factors that can affect the results in the excavation of caries. In order to standardize those factors between all enrolled teeth of the study, a single practitioner performed excavation of caries for all teeth so that caries removal and excavation were identical for all groups with more than half an hour break after excavating each cavitated tooth.

The same type of hand excavator was used to excavate all teeth with taking its sharpness into consideration. For that reason, the sharpness of excavators was examined before each excavation by using the fingernail test [21]. To standardize the softness of the carious dentin radiographs were taken and cavitated teeth were selected in which the carries extended into the middle third of dentin.

Face scales have become a prevalent instrument for pain measurement since the 1980s, especially in children [22]. Many studies have evaluated different scales to assess the validity and reproducibility of the scale that makes it applicable in researches [22–24]. Wong-Baker FACES pain rating scale is composed of six faces of pain rated 0–10, in which the child is instructed to point to the face that represents his/her level of discomfort during treatment [25]. Its reliability, reproducibility, low cost, and attractiveness to children prompted us to use it in our study.

Two blinded examiners helped in deciding the health of remaining dentine within each cavity after rinsing the cavity vigorously to remove any remnants of the material that may interfere with blinding.

Cohen's kappa test calculated Intra-examiner reproducibility and inter-examiner reliability for diagnosis. The kappa for intra-examiner agreement and inter-examiner reliability was 0.90.

In this study, the mean time of caries removal with the conventional method was 1.60 min, while the CMCR groups of Brix 3000 and NaOCl were 5 and 6.40 min, respectively. Chemo-mechanical caries removal was significantly slower compared to the conventional method, regardless of the material used. This finding was consistent with the in-vitro study done by Kitsahawong et al., which showed that the mean-time for caries removal using Papacarie (3.5 min) was significantly higher than the conventional method (1.70 min) [26]. However, the difference in the meantime of CMCR efficacy in this study compared to the study of Kitsahawong et al. could be attributed to the clinical design of the followed, and the increased amount of carious tissues included (which was two-thirds of the dentin) within selected teeth of this study.

Our findings were also in accordance with Singh et al. study, which revealed that Papacarie required (328.5 s ~ 5.4 min) compared to (124.6 s ~ 2 min) rotary instruments. (27)

Sodium hypochlorite is a proteolytic agent able to dissolve collagen fibers within demineralized dentin [26,28]. Furthermore, it can potentially be used in caries removal procedures [28]. Availability and low cost also make it more practical to use NaOCl rather than other CMCR agents.

Many studies selected Carisolv as root canal irrigant due to the sodium hypochlorite content of its formula [29,30]. NaOCl's efficacy in smear layer removal, its antimicrobial effect, and its slight irritation to healthy tissues makes it a desirable solution [31].

The concentration of sodium hypochlorite in Carisolv is 0.95 %, compared to the 2.25 % concentration in NaOCl gel used in this trial. The hypothesis was that this concentration of NaOCl would be as effective as Brix 3000, which does not contain any sodium hypochlorite. Moreover, the sodium hypochlorite gel selected for this trial makes it more controllable in application and use than a typical NaOCl solution.

In contrast, Dammaschke et al. [32] reported that NaOCl gel is not as effective as Carisolv in caries removal. This observation may have been influenced by the method that NaOCl gel was prepared. The gel in that study involved preparation by mixing a NaOCl solution with

Carmellose to convert it into a gel. In contrast, the NaOCl gel used in this study, was supplied by a local chemical distributor. The mechanism of preparation may be of a higher quality in this study as compared to the aforementioned study.

The mean pain score, obtained by this study, was significantly higher in the use of conventional method as compared to CMCR, while no significant difference was noted in CMCR groups regardless of the material used. These findings are in accordance and comparable with Singh et al., who demonstrated less pain sensation than conventional methods using Papacarie [27] which has a mode of action that involves the removal of dead infected dentin through the degradation of proteoglycan matrix [33].

The elimination of vibration and sounds and the use of local anesthesia administration can justify the positive behavior of children in the CMCR group. Kleinknecht et al. [34] reported that dental anxiety mainly results from invasive dental procedures such as "injections" and "drilling", while these are not needed with the use of CMCR agents. Limitations of this study are the dependence on manual detection of caries only and the small sample size.

5. Conclusions

Within limitations of this study, the null hypothesis is accepted: Brix 3000 and 2.25 % sodium hypochlorite gel are CMCR agents that are effective in removing of carious dentine of primary teeth without affecting children's cooperation. However, conventional drilling technique is much faster in the excavation of caries.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee of the study institution and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards." Informed consent was obtained from all individual participants included in the study.

Disclosure statement

The authors declare that they have no conflict of interest.

CRediT authorship contribution statement

Muazz M. Alkhouli: Investigation, Writing - original draft. **Salma F. Al Nesser:** Formal analysis, Data curation. **Nada G. Bshara:** Conceptualization, Methodology, Supervision, Writing - review & editing. **Awab N. AlMidani:** Investigation, Resources. **John C. Comisi:** Writing - review & editing.

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