

Effect of Papacarie and Alternative Restorative Treatment on Pain Reaction during Caries Removal among Children: A Randomized Controlled Clinical Trial

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Objective: To compare the effect of Papacarie and Atraumatic Restorative Treatment (ART) on pain and discomfort during caries removal among children. **Study Design:** Fifty healthy, 4-8 year-old children were equally and randomly allocated to Papacarie and ART to remove caries from decayed primary teeth. A randomized, controlled, blinded, two parallel-arms clinical trial was conducted in the clinic of the Pediatric Dentistry and Dental Public Health Department, Alexandria University, Egypt in March 2014. Pain and discomfort were assessed blindly by two independent investigators watching videotaped treatment sessions using the Sound, Eye and Motor scale (SEM). Their reliability was assessed using Kappa statistics. The effect of caries removal methods, time spent to remove caries and other confounders on SEM score was assessed using regression analysis. **Results:** Mean time to remove caries using Papacarie and ART was 5.8 and 4.8 minutes, $P = 0.005$. Median Papacarie and ART scores for the S, E and M components were 1, 1, 1 and 3, 2, 3. Adjusted mean SEM score = 3.6 and 7.8, $P < 0.0001$. Method of caries removal was the only factor significantly affecting pain and discomfort. **Conclusion:** Papacarie is associated with minimal pain during caries removal from primary teeth compared to ART, although it has longer working time.

Key Words: Papacarie, Alternative Restorative Treatment, Pain, Caries.

INTRODUCTION

Caries removal using rotary instruments is comparatively quick but has the risk of sound tooth substance destruction¹ and overheating of the pulp/ nerves that may cause intense pain.² Even though pain may be reduced by local anesthesia, fear of needle, the noise and vibration of rotary instruments may increase the anxiety of young children and make them uncooperative during restorative procedures.³

In alternative restorative treatment (ART), soft and demineralized carious tissue is removed with hand instruments followed by conditioning and restoring with an adhesive material that seals pits and fissures.^{4,5} When ART was used to restore carious primary teeth, treatment was well accepted by the majority of young children who reported no pain or discomfort compared to conventional treatment.^{6,7}

Caries can be excavated by the dissolution of necrotic tissues using chemical agents followed by removal of soft infected dentin.⁸ Removal of sound dentin, which is painful, is thus avoided and the need for local anesthesia is minimized^{9,10} Papacarie contains papain which is a proteolytic cleaving enzyme similar to the human pepsin. It breaks partially degraded collagen fibrils, and softens the infected dentin allowing easy removal by blunt hand instruments.¹¹ It is less expensive than other chemo-mechanical caries removal agents such as Carisolv. It does not require the use of specific instruments; therefore it has better chances to be applied on a wide scale.¹²

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ART and Papacarie are useful alternatives to the conventional and more invasive restorative techniques. Both methods do not require sophisticated instruments or costly armamentarium and may thus be used to treat young children in low-resources settings. The aim of the present study was to compare the effect of Papacarie and ART regarding patient comfort during caries removal in young children.

MATERIALS AND METHOD

A randomized, controlled, blinded, two parallel-arms clinical trial was designed and subjects were allocated to each of the two study groups in the ratio 1:1. Approval for the study was obtained from the Research Ethics Committee, Faculty of Dentistry, Alexandria University. The guidelines of the Helsinki declaration were followed in the study where parents/ legal guardians consented to the children's participation in the study and to recording the treatment sessions after full explanation was offered. Participants were ensured of data confidentiality and their right to withdraw from the study at any time if they wanted.

Participants

The study included 50 healthy children. Their ages ranged from 4-8 years. They were recruited from children seeking dental treatment in the outpatient clinic of the Pediatric Dentistry and Dental Public Health Department, Faculty of Dentistry, Alexandria University, Egypt. Male and female children were eligible for the study if they fulfilled the following criteria¹³:

1. No previous experience with dental treatment.
2. Positive/ definitely positive behavior during examination (assessed by Frankl scale¹⁴).
3. Had a primary asymptomatic tooth with open dentinal carious lesion and no pulp involvement.
4. Cavity accessible to hand instruments with medium to soft consistency. Lesion was judged to be medium if the explorer penetrated the dentin with some resistance, and soft if the explorer readily entered the dentin.
5. Normal tooth morphology and structure.
6. No proximal caries seen in bite-wing radiographs.

Intervention

Children were allocated to the two groups according to the method of caries removal. In one group, caries was removed using Papacarie and in the other group, hand excavation was used as ART.

*Papacarie group*¹⁵

Teeth were partially isolated using cotton rolls and saliva ejectors. The tooth was cleaned of debris and plaque using wet cotton pellets. Papacarie gel (Formula & Acao 04106-001 Sao Paulo (sp-Brazil)) was used to remove caries. The 3 ml gel syringe was taken out of the refrigerator 10 minutes before use, applied to the cavity until readily filled and left for 60 seconds. At application, the gel was clear and then it turned turbid due to lesion decomposition. The softened decayed dentin was scraped away with a blunt spoon excavator (71-72 Maillefer, Switzerland). The gel was re-applied if a darkish color was seen without rinsing or drying of the cavity between gel applications. The procedure was repeated until the gel became clear. After caries removal, the remaining gel was removed with sterile cotton pellets soaked in water.

*ART group*¹³

The tip of a dental hatchet (10-6-12 Hu-Friedy, Chicago, USA) was placed at the entrance of the lesion and rotated backwards and forwards to widen the cavity opening and chip off carious enamel if the cavity opening was small. Carious dentin was removed using a small excavator (Spoon excavator 153-154/ 131-132, Hu-Friedy, Chicago, USA) starting at the enamel-dentin junction. Unsupported thin enamel was removed with a hatchet. The cavity was cleaned with wet cotton pellets and dry pellets were used to remove excess moisture.

*Cavity restoration*¹³

Caries was considered removed when leather-like hard texture was reached and the explorer did not stick in dentin or give a "tug-back" sensation.¹⁶ After caries removal, cavities were restored using chemically cured glass ionomer (Fuji IX, GC America Inc. IL, USA). The cavity walls and floor were conditioned by rubbing cotton pellets containing the liquid supplied with the glass-ionomer for 10 seconds, then the cavity was washed and dried with cotton pellets. Fuji IX was mixed for 25-30 seconds using a powder/liquid ratio of 3/1. The mix was applied to the cavity using a carver in small amounts to avoid inclusion of air bubbles and condensed with the round end of a medium sized excavator, and pushed into place. The cavity was slightly over filled and the material was pressed by applying light pressure with a gloved and petroleum jelly-coated finger. Excess material was removed with a carver. In class I restorations, occlusion was checked using a thin articulating paper and any premature contacts were removed with a carver. A protection varnish was applied on the GIC surface to prevent gain or loss of water. The patient was informed not to eat or drink for one hour after restoration placement.

The primary outcome was pain reaction measured by the Sound, Eye, and Motor scale (SEM, Table 1).¹⁷ The SEM assessed child reaction during cavity preparation and caries removal using the two interventions. Assessment was performed by two independent assessors after watching videotapes of caries removal sessions. The assessors were blinded to the nature of intervention and the identity of the child. Their intra-examiner and inter-examiner reliability was assessed using Kappa statistic. The operator recorded the time used to remove caries in minutes using a stop watch.

Sample size calculation was based on results of a previous study¹⁸ after modifications to accommodate differences in type of dentition and age of subjects. The assumptions used were: percent of subjects reporting pain in ART group = 70% and in Papacarie = 30%. Alpha error was set at 5% and beta error at 20%. The minimum required sample size per group was calculated (<http://www.select-statistics.co.uk/sample-size-calculator-two-proportions>) to be 21. This was increased to 25 per group. A total of 50 restorations in 50 children were included in the study.

Randomization

Each eligible child was allocated a number that was randomized to either one of the two study groups using random allocation software¹⁹ in blocks of 2. Numbers were written on identical sheets of paper that were folded and placed in opaque envelopes and the child's name was written on each envelope. The envelopes were kept in a closed cabinet until the scheduled time of the child's visit when the envelope was opened and the allocated method of

Table 1: Sound, Eye and Motor scale (SEM)

	Score 1 Comfort	Score 2 Mild discomfort	Score 3 Moderately painful	Score 4 Painful
Sound	No sounds indicating pain	Non-specific sounds; possible pain indication	Specific verbal complaints, e.g. "OW", raises voice	Verbal complaints indicates intense pain, e.g. scream, sobbing
Eyes	No eye signs of discomfort	Eye wide, show of concern, no tears	Watery eyes, eye flinching	Crying, tears running down face
Motor	Hands relaxed; no apparent body tenseness	Hands show some distress or tension; grasps chair due to discomfort, muscular tension	Random movement of arms or body without aggressive intension of physical contact grimace, twitch	Movement of hands to make aggressive physical contact e.g. punching, pulling head away

caries removal was used with the child. The random allocation sequence was generated by one of the researchers (MT). Subjects' recruitment, caries removal and cavity restoration was performed by another investigator (AA). The outcome was assessed by two other investigators (MK and WA).

Analysis

The differences in the distribution of gender, arch, tooth and lesion type between the two groups were assessed using chi square. Differences in mean age and time taken to remove caries were assessed using t test. Differences in the distribution of the S, E and M scores between the two groups were assessed using Mann Whitney U test. The effect of the two methods of excavation on mean SEM score was assessed using regression analysis after controlling for, gender, age, arch, tooth, lesion type and time in minutes taken to remove caries. Adjusted mean SEM score for each group was calculated. Statistical analysis was performed using SPSS version 17.0. Significance level was set at 5%.

RESULTS

Males represented 40% of the Papacarie group and 56% of the ART group. The mean age of children was 5.9 and 6.1 years. Most restorations were done in mandibular teeth (60% and 68%), in canines (80% and 72%) and class V (80% and 76% of the Papacarie and ART groups). There were no statistically significant differences between the two groups in relation to gender, child age, arch, tooth or lesion type (P= 0.26, 0.49, 0.56, 0.68 and 0.73, Table 2).

The inter-examiner reliability for assessing the S, E and M scores was 1, 0.78 and 0.85. The intra-examiner reliability for the 1st assessor was 0.9, 1 and 0.78 and for the 2nd assessor was 0.9, 0.78 and 0.7.

The mean (SD) time in minutes taken for caries removal was 5.8 (1.2) and 4.8 (1.0) in the Papacarie and ART groups (P= 0.005, Figure 1).

Figure 1: Mean time in minutes for caries removal in the Papacarie and ART groups

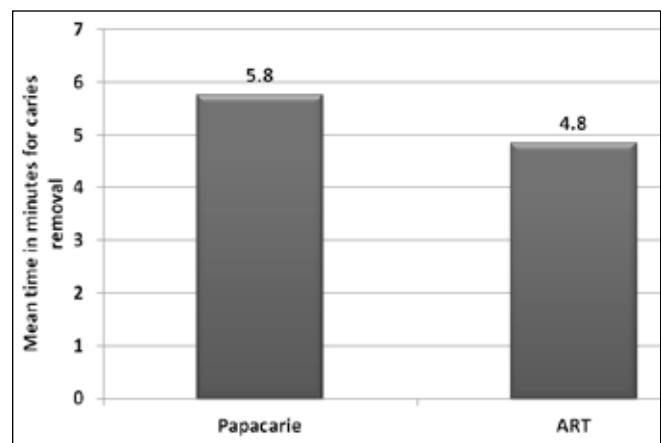


Table 2: Description of children and teeth included the study groups

Variables		Papacarie (n= 25)	ART (n= 25)	P value
Gender	Male: n (%)	10 (40%)	14 (56%)	0.26
	Female: n (%)	15 (60%)	11 (44%)	
Age	Min- max	4.3-7.9	4-8	0.49
	Mean (SD)	5.9 (0.9)	6.1 (1.3)	
Arch	Maxillary: n (%)	10 (40)	8 (32)	0.56
	Mandibular: n (%)	15 (60)	17 (68)	
Tooth	Canine: n (%)	20 (80)	18 (72)	0.68
	First molar: n (%)	2 (8)	4 (16)	
	Second molar: n (%)	3 (12)	3 (12)	
Lesion type	Class I: n (%)	5 (20)	6 (24)	0.73
	Class V: n (%)	20 (80)	19 (76)	

The median score for the sound (S) component was significantly lower in the Papacarie than in the ART group (1 and 3, $P < 0.0001$). Similarly, the median eye (E) and motor (M) scores in the Papacarie group were lower than in the ART group (1 compared to 2, $P = 0.003$ and 1 compared to 3, $P = 0.001$, Table 3).

Table 3: Comparison between Papacarie and ART groups in sound, eye and motor scores

	SEM score	Papacarie N (%)	ART N (%)	P value
S	Score 1: (comfort)	21 (84)	6 (24)	
	Score 2: (mild discomfort)	4 (16)	4 (16)	
	Score 3: (moderately painful)	0	8 (32)	<0.0001*
	Score 4: (painful)	0	7 (28)	
	Median score	1 (comfort)	3 (moderately painful)	
E	Score 1: (comfort)	19 (76)	7 (28)	
	Score 2: (mild discomfort)	6 (24)	11 (44)	
	Score 3: (moderately painful)	0	3 (12)	0.003*
	Score 4: (painful)	0	4 (16)	
	Median score	1 (comfort)	2 (mild discomfort)	
M	Score 1: (comfort)	14 (56)	4 (16)	
	Score 2: (mild discomfort)	10 (40)	7 (28)	
	Score 3: (moderately painful)	0	6 (24)	0.001*
	Score 4: (painful)	1(4)	8 (32)	
	Median	1 (comfort)	3 (moderately painful)	

S: sound, E: eye, M: motor, *: P of Mann Whitney U test statistically significant at $P \leq 0.05$

Table 4 shows the effect of caries removal method (Papacarie and ART) on SEM score adjusted for gender, age in years, arch, tooth, lesion type and time to remove caries in minutes. The method of caries removal was the only variable with a significant effect ($P < 0.0001$). The regression model explained 45% of the variation in SEM score (adjusted $R^2 = 0.45$). After adjusting for the effect of various factors, the mean (95% confidence interval) SEM scores in the Papacarie and ART groups was 3.6 (1.9, 5.2) and 7.8 (6.6, 9.1) (Figure 2).

DISCUSSION

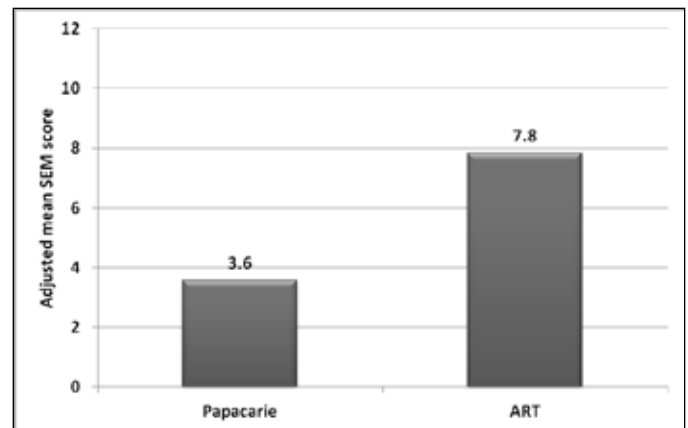
Our primary study outcome was pain and discomfort during excavation. This was objectively assessed using SEM scale which is useful with young children who may have difficulty expressing their feelings due to verbal-cognitive developmental problems.¹⁷ The scale was applied by two independent assessors who were blinded to the type of intervention so that assessor bias was reduced. Their agreement with each other and over time was assessed and ensured, thus increasing the reliability of our findings. Because the outcome occurred at the time of the intervention and was recorded for

Table 4: Effect of caries removal method and other factors on mean SEM score in regression analysis

Variables	F of ANOVA	P value
Method of caries removal	30.76	<0.0001*
Gender	3.665	0.06
Age in years	0.08	0.78
Arch	0.06	0.81
Tooth	1.78	0.18
Lesion type	3.09	0.09
Time in minutes	1.99	0.17

Model F= 6.06, $P < 0.0001$, Adjusted $R^2 = 0.45$, *: Statistically significant at $P \leq 0.05$

Figure 2: Adjusted mean SEM scores in the Papacarie and ART groups



subsequent evaluation, no cases were lost to follow up, thus eliminating concerns for drop out bias. Randomization and allocation concealment helped in reducing allocation and examiner biases. The effect of potential confounders was also controlled using regression analysis in order to rule their effect on the study outcome.

In the current study, the time taken for caries removal in the Papacarie group was longer than that in the ART group. This may be attributed to the accessibility of the lesions included in the study which were open for hand instruments using ART, whereas Papacarie was applied several times to remove caries chemo-mechanically. In addition, the Papacarie syringe made the children somewhat apprehensive and long time was needed to explain that it is used for gel application and not for anesthesia. The present findings are consistent with other studies assessing working time of Papacarie compared to conventional caries removal.²⁰⁻²² On the other hand, a 2015 systematic review, based on 19 studies concluded that Papacarie had longer excavation time than rotary instruments but slightly less than ART (mean = 6.36, 2.99 and 6.98 min). Our estimate falls within the confidence limit of the review for Papacarie but is lower than the confidence limit for ART. This might be attributed to the difference between our study and the studies included in the review in type of lesions and their accessibility as well as subjects' age.²³

The mean SEM score in the Papacarie group was significantly lower than that in the ART group. This might be due to the less pressure required to remove the softened carious dentin as well as the thermal insulating property of Papacarie, as it covers the cavity during the procedure.²⁴ In addition, cutting sound or affected dentin using ART results in some level of pain.²⁵ Our results are similar to several studies comparing discomfort of young children during caries excavation between Papacarie and conventional methods. In these studies, using Papacarie was associated with less pain and discomfort and less or no need for local anesthesia.^{20-22,26,27} In one study by Matsumoto *et al*,²⁸ no significant difference was reported in pain sensation between two groups of 5-8 year-old children; one using Papacarie and the other using the conventional method. In that study, however, pain assessment was performed by a dental assistant and there was no evidence that she was blinded to the intervention and no reliability statistics were reported.

The current study adds to the existing and rather limited body of knowledge by comparing Papacarie and ART as opposed to conventional caries removal methods. In a previous similar study, Papacarie was associated with less pain during caries removal compared to hand instruments in 5-9 year-old children (7.33 and 65.67 on the visual analogue scale from 0 to 100 and 0.73 compared to 3.00 on the verbal pain scale from 0 to 4).²⁹

One limitation of the present study was the use of tactile criteria to assess the end point of caries removal. Tactile criteria are not 100% accurate in assessing carious dentin and using additional

methods might have increased this accuracy.³⁰ However, tactile and / or visual criteria are among the most widely used methods for clinically assessing the caries-free status of the lesion.³¹ Our study aimed at comparing pain and discomfort during routine restorative procedures rather than assessing the efficacy of the two methods in removing carious dentin. In that latter case, the use of additional caries diagnosis methods might have been important.

Future research is needed to assess the effectiveness of these two minimally invasive restorative techniques in field conditions, especially those where resources are limited, as well as among special care needs children, children with behavior management problems and those with negative previous dental treatment experience.

CONCLUSIONS

Papacarie and ART appeared to be comfortable and simple techniques for treating open dental lesions that required neither the use of local anesthesia nor drilling. Although Papacarie took one minute longer in average than ART, it caused significantly less pain and discomfort. It would thus be particularly useful with children requiring several restorations, those who are very young or who might be difficult to manage. The present findings are generalizable to healthy children with open, accessible cavities with no proximal caries. Applying the interventions in more extensive lesions or caries in non-healthy or special needs children may produce different outcomes hence; further studies are needed before a recommendation of using Papacarie in these groups is made.

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