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ORGINAL ARTICLE

Effects of pre-emptive analgesia on efficacy of buccal infiltration during pulpotomy of mandibular primary molars: a double-blinded randomized controlled trial

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ABSTRACT

Objective: To assess the effect of preoperative administration of ibuprofen and acetaminophen on the efficacy of buccal infiltration for pulp therapy in mandibular primary molars.

Materials and methods: A randomized controlled trial with an ID no. NCT03423329 in *ClinicalTrials.gov* was conducted in the outpatient clinic of Paediatric Dentistry Department at Ain Shams University. The study was designed with two test arms where either ibuprofen or acetaminophen was administered to children whereas in the control arm a multivitamin placebo was used. Children's self–reported pain responses were recorded using Wong–Baker FACES pain scale. For statistical analysis, Chi-square test or Fisher's exact test was used to compare between the three groups whereas Friedman's test was used to study changes within each group.

Results: In a sample of 60 children, a significant decrease in the mean pain rating scores was detected in all groups where success rates ranged from 40% with ibuprofen to 55% and 65% with acetaminophen and placebo, respectively. However, there was no statistically significant difference between the three groups regarding severity of pain during access cavity preparation.

Conclusions: Both analgesics have no clinical advantage over the placebo in increasing the efficacy of buccal infiltration during pulp therapy in mandibular primary molars.

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Local anaesthesia; pain; primary molars; pulpotomy; acetaminophen; ibuprofen

Introduction

Pain is an unpleasant sensory experience with emotional and cognitive components which occurs due to actual or potential damage to tissues [1]. Dental pain per se is one of the most obnoxious sensations that human beings may experience throughout their lives. Pain control during dental treatment is considered the cornerstone of behaviour management among children as it helps in building up trust and facilitates child's cooperation in future appointments [2].

Regional blockade of the inferior alveolar nerve has been considered the local anaesthesia technique of choice for performing mandibular dental procedures [3]. Though depth and profundity of anaesthesia have been the primary advantage of this technique [4], yet it is still known to be associated with several disadvantages especially among children. Inferior alveolar nerve block (IANB) is perceived as the most painful injection technique [5] and inducing a successful mandibular nerve block involves a degree of difficulty as a child has to open the mouth widely while administering the anaesthetic agent to allow the clinician to locate the position of the foramen which varies according to age [6]. Moreover, the prolonged duration of soft tissue anaesthesia [7] may result in self-induced trauma when a child bites the anesthetized lip, tongue and/or inner surface of the cheek [8].

On the other hand, infiltration anaesthesia which is recognized as a less traumatic technique for pain control in comparison to nerve block is highly recommended in paediatric dentistry [5]. Whereas infiltration anaesthesia has been used successfully to restore maxillary teeth; it is not commonly used in the mandibular molar regions because of the denser bone that does not allow adequate dissemination of the anaesthetic [3]. Though, in some studies, mandibular infiltration was found to be successful in restoring primary teeth [9,10], yet this technique was not as effective as nerve block in controlling pain during pulpotomy in primary molars [3,11].

Over the last two decades, the concept of using preoperative analgesic drugs to increase the effectiveness of local anaesthesia for pain control has been addressed in both children and adults [12–15]. Despite that, based on a recent systematic review, there is lack of robust evidence on efficacy of using pharmacologic agents for pain control in children during dental treatment [16].

Hence, the aim of this study was to evaluate and compare the effect of preoperative oral administration of two different analgesics ibuprofen and acetaminophen versus placebo on the efficacy of buccal infiltration during vital pulpotomy in mandibular primary molars

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Methods

The trial protocol was approved by the Research Ethical Committee, Faculty of Dentistry, Ain Shams University with an approval code FDASU-RECR 071607 and was registered in Clinical-Trials.gov with an ID no. NCT03423329. A randomized double-blinded controlled trial was conducted in accordance with Helsinki Declaration and Good Clinical Practice guideline over a period of 4 months from January 2018 to end of April 2018 (Figure 1).

Based upon data from a previous study [17], the effect size regarding the outcome success of anaesthesia (elimination of pain) was found to be (0.9). Using alpha (α) level of 0.05 (5%) and beta (β) level of 0.20 (20%), i.e. power = 80%; the minimum estimated sample size was 14 subjects per group for a total of 42 subjects. Sample size calculation was performed using IBM® SPSS® Sample Power® Release 3.0.1 (IBM SPSS Statistics, Armonk, NY).

In the present study, the primary outcome was defined as 'pain intensity during access cavity preparation' at the point of unroofing the pulp chamber and anaesthesia was considered successful when no or mild pain was encountered during pulpotomy procedure. A total of 60 children with age range from 7 to 9 years were recruited from the outpatient clinic of the Paediatric Dentistry and Dental Public Health Department, Faculty of Dentistry, Ain Shams University, Cairo, Egypt to participate in the trial and one investigator (MH) screened and recruited all the participants.

Inclusion criteria

Only children who had at least one carious mandibular second primary molar indicated for pulpotomy and were classified as cooperative or potentially cooperative according to Wright's classification [18] for child behaviour were eligible to participate. Moreover, to qualify for the study a child should be able to understand the use of pain scales and communicate effectively.

Exclusion criteria

We excluded children with special health care needs or any systemic disorders that contraindicate dental treatment under local analgesia. In addition, children who had sensitivity or allergic reactions to any of the tested premedications or suffered abscess in relation to the designated molar or who used any analgesic medication in the 12 h preceding the treatment were also excluded.

Parents of eligible children were informed about the purpose of the study, the nature of the procedures and any possible discomfort or risks that might be encountered. One investigator (MG) also outlined to the children what would take place and this was done from a child's point of view in a language that was appropriate to both the child's maturity and age. Only children who agreed to participate and whose parents signed an informed consent were enrolled.

Study procedures

In the current study, three orange-coloured syrups were used as follows:

- Group I: ibuprofen BP 100 mg/5 mL syrup (Brufen, Kahira Pharm. & Chem. Ind. Co., Cairo, Egypt),

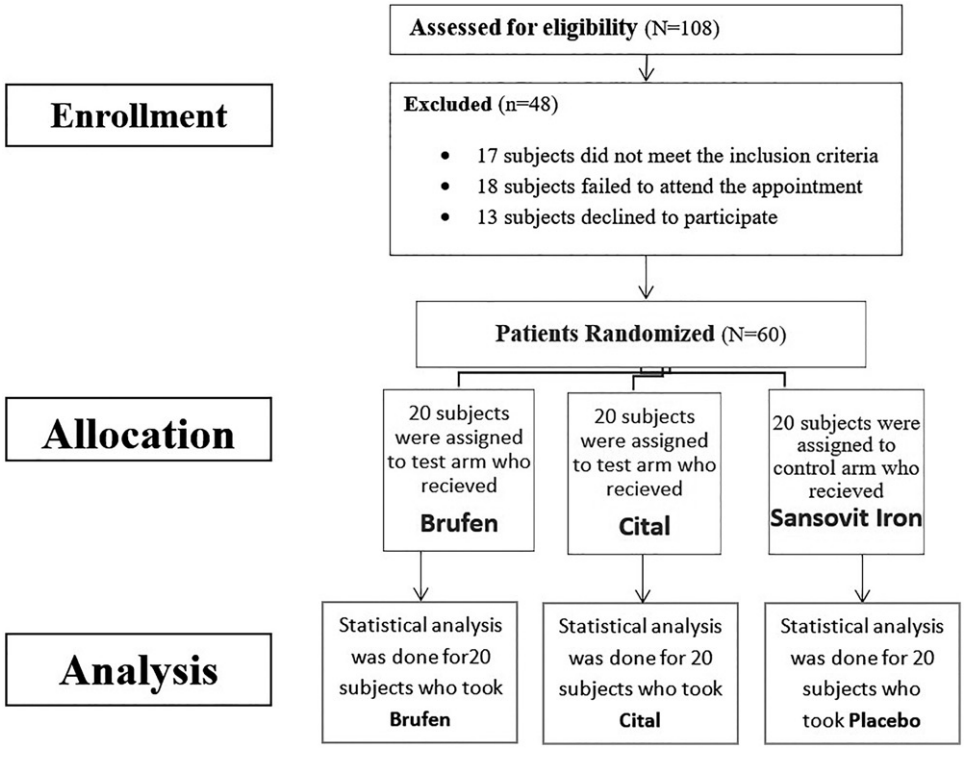

Figure 1. CONSORT flow diagram of the study.

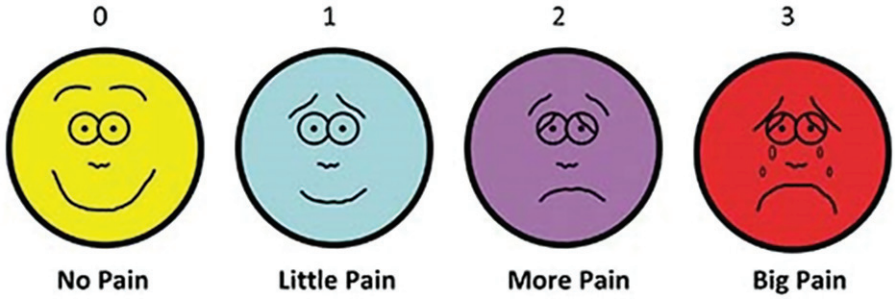

Figure 2. Modified Wong–Baker FACES Pain Rating Scale.

- Group II: acetaminophen 200 mg/5 mL syrup (Cital, Delta Pharma, Cairo, Egypt),
- Group III: multivitamin Sansovit Iron (AUG Pharma, Cairo, Egypt).

Preoperative periapical radiographs were taken prior to inclusion in the study. Only children with no signs of internal or external resorption or periapical or furcation radiolucency in relation to the designated molar were invited to participate in this study. For the purpose of randomization and allocation concealment, allocation was predetermined by using a computer-generated randomization list with a balanced allocation ratio of 1:1:1. The numbers of patients were written on slips of paper and kept in a sealed opaque envelope. Each child was asked to choose one paper and was then randomly assigned to one of the three groups (20 patients each) according to the chosen number and the randomization list (Figure 1). In order to ensure double-blinding, all drug solutions were placed in identical medicine bottles and were randomly assigned a letter by one researcher (RA).

Wong–Baker FACES pain rating scale (PRS) [19] was used in this study for subjective evaluation of pain sensation. The scale was modified to include four cartoon faces which depict different facial expressions articulated as 'No hurt', 'Little hurt', 'More hurt' and 'Big hurt' (Figure 2). Initially, before taking the premedication, children were introduced to the PRS and verbal instructions were given to them in simple Arabic language to explain what they would be asked to do. Afterwards, each child was instructed to choose the image that closely corresponds to the degree of pain/discomfort felt at that moment. The bottles were shaken well and each child, then, received an age-dosed volume (10 mL) of one of the tested drugs 1 h before starting the treatment. Throughout the whole trial, all the preoperative medications were administered by one investigator (MH) who did not give any injections or evaluated any pain sensations.

Topical anaesthetic gel (20% benzocaine; DEFEND, Mydent International, Hauppauge, NY) was passively placed at the injection site for 60 s by using a cotton-tip applicator. 1.8 mL of 4% articaine with 1:100,000 epinephrine [20] (Septanest; Septodont, Saint-Maur-des-Fossés, France) was administered in the mucobuccal fold adjacent to the mandibular second primary molar. All local anaesthetic injections were delivered by 27-gauge short needle (Septoject; Septodont, Saint-Maur-des-Fossés, France) which was gently placed into the alveolar mucosa and advanced until the needle was estimated to be at or just superior to the apex (apices) of the tooth. The anaesthetic solution was deposited during a period of 1 min. In all cases, the investigator was asked to administer the full cartridge of the anaesthetic solution to ensure standardization. Seven minutes after administering the anaesthetic agent, each patient was asked about any signs of soft-tissue anaesthesia. Throughout the whole study, all patients followed the same protocol and anaesthesia was administered by one investigator (MG) who was 'blinded' to randomization.

Children and their parents were also 'blinded' to the administered premedication. Only when a child reported profound lip numbness, the clinician started caries removal and afterwards the child was asked to rate the level of pain experienced at the point of unroofing the pulp chamber during access cavity preparation using the PRS. Since an operator's clinical skills and approach in behaviour management skills could influence results, all patients were operated on by the same paediatric dentist (MG) to ensure comparability.

Statistical analysis

Statistical analysis was performed with IBM® SPSS® Statistics Version 20 for Windows (IBM SPSS Statistics, Armonk, NY). Data were presented as frequencies (*n*) and percentages (%). Chi-square test or Fisher's exact test when applicable was used to compare the three groups. Friedman's test was used to study the changes by time within each group. Age data (numerical data) were presented as mean and standard deviation values. Age data showed normal (parametric) distribution according to the results of normality tests (Kolmogorov–Smirnov and Shapiro–Wilk tests). Student's *t*-test was used to compare between mean age values in the three groups. The significance level was set at $p \leq .05$.

Results

Twenty-five boys and 35 girls with an average age of 7.5 years participated in the current trial. All patients reported lip numbness 7 min after the injection of local anaesthesia. Throughout the course of the study, none of the participants needed an additional amount of anaesthesia and none was excluded from the study due to pain during treatment. In

addition, none of the patients exhibited any adverse reactions to any of the tested premedications. Since measurement of the study outcome was performed at the same visit while operating, all enrollees were expected to complete the trial without any dropouts.

The baseline demographic variables including age and gender as well as the level of children's cooperation at the dental clinic were not significantly different between the three groups ($p > .05$) (Table 1). Within each of the three groups, the prevalence of 'No Pain' has significantly increased such that articaine buccal infiltration success rate was 40% for the ibuprofen, 55% for acetaminophen and 65% for the placebo group. However, no statistically significant difference could be detected between the three studied groups with respect to severity of pain both before starting treatment and during access cavity preparation as well as presented in Table 2 and Figure 3.

Table 1. Baseline characteristics in the three groups.

Characteristics	Group I	Group II	Group III
Age (mean ± SD)	7.4 ± 1.9	7.8 ± 0.7	7.6 ± 0.7
Gender (*n*, %)			
Boy	7/20 (35)	7/20 (35)	11/20 (55)
Girl	13/20 (65)	13/20 (65)	9/20 (45)
Cooperation level (*n*, %)			
Cooperative	15/20 (75)	14/20 (70)	15/20 (75)
Potentially cooperative	5/20 (25)	6/20 (30)	5/20 (25)

Discussion

Pain control through provision of profound analgesia is fundamental while performing dental procedures especially in children. In the current study, ibuprofen, a non-steroidal anti-inflammatory drug (NSAID) and acetaminophen were tested as supplementary preoperative medications since both are safe and fast-acting analgesics. It has been postulated that the anti-inflammatory and analgesic effects of NSAIDs are attributed to blocking the cyclooxygenase enzymes in the pathway of prostaglandins and thromboxane A2 production. The mechanism of action of acetaminophen, on the other hand, is more complex and multiple theories were suggested indicating that it acts both centrally and peripherally to inhibit the activity of cyclooxygenases and reduce pain sensations [21]. The anaesthetic efficacy of the two drugs was assessed by rating pain at the point of access cavity preparation per se as this was proved clinically reliable in other studies [22].

Using self-report measures for rating pain intensity is a highly indicated approach which provides reliable information in children [23] yet it requires a certain level of intellectual development to enable the child to correctly understand the questions asked and use the scale appropriately [24]. In the present study, we used the Wong–Baker FACES a quick, easy to use scale which requires minimal explanation to the participants and is preferred by children over other simple

Table 2. Comparison of success rates of buccal infiltration in the three groups.

		Group I		Group II		Group III		*p* Value		
Time	Pain	*n*	%	*n*	%	*n*	%	(between groups)	Effect size (*v*)	95% CI
Before treatment	No	7/20	35	5/20	25	7/20	35	.584	0.162	0.110–0.193
	Mild	10/20	50	8/20	40	10/20	50			
	Moderate	3/20	15	7/20	35	3/20	15			
During access preparation	No	15/20	75	16/20	80	20/20	100	.062	0.302	0.284–0.326
	Mild	5/20	25	4/20	20	0/20	0			
p Value (within group)		.007*		.001*		<.001*				
Effect size (*v*)		0.184		0.300		0.325				
95% CI		0.145–0.207		0.275–0.319		0.297–0.348				

*Significant at $p \leq .05$.

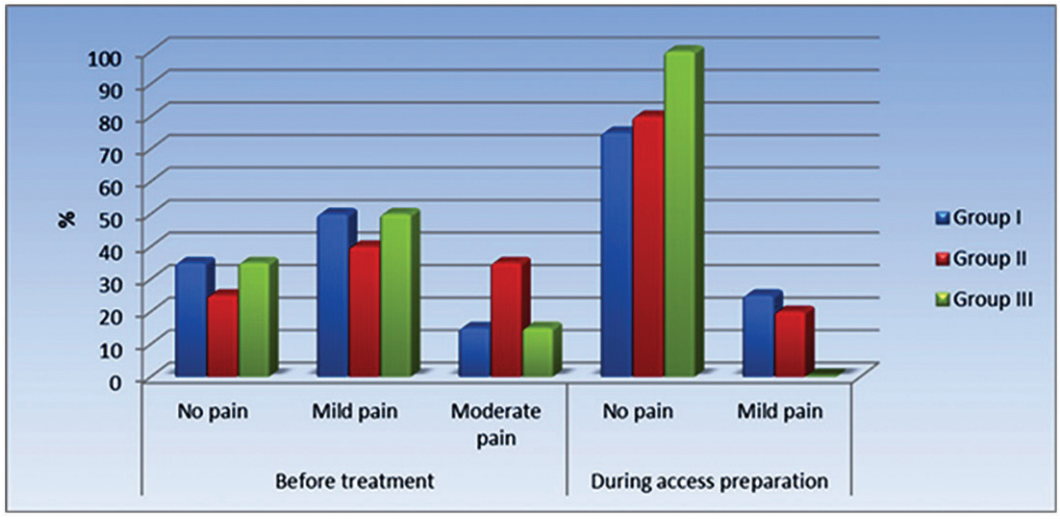

Figure 3. A bar chart illustrating severity of pain in three groups before treatment and at the point of unroofing the pulp (during access cavity preparation).

verbal, numerical and colour analogue scales [19]. Moreover, the PRS was found to be highly responsive in detecting any changes in children's pain perceptions after undertaking interventional procedures [25].

In a study for functional analysis of the PRS, it was revealed that children in two different age groups (6–8 years) and (9–11 years) failed to discriminate between the first two levels of the scale with smiling faces. Moreover, children in the younger age group were capable of differentiating between only three levels of facial expressions of pain in addition to the first level which denotes no pain. The authors, also, did not support scoring the facial expressions from 0 to 10 with equal intervals of two and suggested eliminating one or two of the 'Faces' according to age group [26]. Since the mean age, in the current study, in the three groups was around 7.5 years, in order to simplify the scale, we combined Faces 1 and 2 and Faces 4 and 5 and included only four levels of facial expressions.

According to Rowbothman [27], in a clinical trial, a 30% reduction in pain intensity is interpreted as a meaningful clinical improvement. The current study findings revealed that, though, there was meaningful improvement in the measured outcome where reduction in pain intensity was higher than 30% in all groups yet there was no significant difference between the effects of the two tested analgesics versus the placebo as measured by pain sensation at the point of access cavity preparation.

To the best of our knowledge, no previous studies have investigated the effect of preoperative administration of ibuprofen and acetaminophen on increasing the depth of pulpal anaesthesia following buccal infiltration in mandibular primary molars. On the other hand, there is controversy regarding the impact of preoperative administration of different analgesics on the effectiveness of IANB. Some studies have concluded that administering analgesics such as ibuprofen, ketorolac, acetaminophen or a combination of these drugs yield no significant effect on success rate of IANB for endodontic treatment of teeth with irreversible pulpitis [4,15].

Two systematic reviews, however, deduced that preoperative intraoral administration of NSAIDs could significantly increase the effectiveness of IANB [28,29]. Recently, Shantiaee et al. [30] have, also, indicated that the depth of inferior alveolar block has significantly improved when supplemented with ibuprofen administered as a premedication prior to endodontic treatment in teeth with irreversible pulpitis. Generally, it is much more difficult to achieve profound anaesthesia and control pain while operating in teeth with irreversible pulpitis than in those without pulpal inflammation owing to the effects of inflammatory mediators on nerve endings [31]. This might explain the contradiction between Shantiaee et al. results and our study findings. Whereas Shantiaee et al. [30] recruited adults with spontaneous pain in carious first permanent molars, in the current study; all included participants were children with carious second primary molars indicated for pulpotomy and the pain rating among participants before treatment ranged from no pain to mild or moderate pain but none of them suffered any history of active spontaneous pain.

For decades, the influences of the potency of the anaesthetic solution and its diffusion capabilities on the efficacy of infiltration anaesthesia have been well-recognized [9]. In the present study, 4% articaine hydrochloride with 1:100,000 epinephrine was the anaesthetic solution of choice. Owing to its thiophene ring, articaine was found to be more potent and more lipid-soluble when compared to other local anaesthetics and thus more capable to diffuse through both soft and hard tissues [32].

According to Wright et al. [33], the age of a child, also, affects the potency of anaesthesia and it has been well noted that the younger the age of children the less the density of bone in the mandibular arch thus enhancing a rapid and complete diffusion of the solution [34]. In the present study, the age of all enrollees ranged from 7 to 9 years and this might have further enhanced the diffusion of articaine and ensured adequate depth of pulpal anaesthesia. This goes in line with other studies which compared buccal infiltration with 4% articaine to IANB using either 2% lidocaine or lignocaine and concluded that both techniques proved efficacious and thus articaine infiltration could be a viable alternative for IANB while undertaking pulpotomy or extracting mandibular primary molars [35,36].

Furthermore, in various studies, it has been suggested that the location of the mental foramen has a significant role in the production of infiltration anaesthesia in the mandibular arch either through allowing the anaesthetic to diffuse to inferior alveolar nerve or by inducing mental nerve block [37]. According to Madeira, in young children, most commonly the mental foramen lies between the first and second primary molars [38] and this provides another plausible explanation for the efficacy of buccal infiltration in the area of mandibular primary molars in young children enrolled in the study.

It is, also, worth mentioning that paediatric pain assessment is a burdensome, complex process owing to children's cognitive level which might limit their capacity to thoroughly comprehend instructions on using a pain scale [39]. Since the mean age of children in the three studied groups was less than 8 years, there is a possibility that some of the participants might have failed to discriminate between different levels of pain and thus in turn articulated their sensations incorrectly. Besides, in children, perception of pain experience during dental procedures largely depends on the level of anxiety [40]. Thus, it is possible that the level of pre-emptive analgesia did not vary among the three groups since all the enrolled study participants were potentially cooperative and exhibited positive behaviour.

One limitation to consider is that, though the PRS is one of only six PRSs with well-established psychometric properties in terms of validity or reliability, [25] yet it is worth mentioning that while this scale has been translated into Arabic language [41] no psychometric analysis exists for the Arabic version. On the other hand, an advantage of the current study, was recruiting children of a well-defined small age range from 7 to 9 years as age is considered a proxy for level of development and thus the subjective perception of pain could vary considerably among children of different age groups [42].

In conclusion, articaine buccal infiltration produces adequate anaesthesia for pulpotomy in mandibular second primary molars with vital healthy pulps regardless whether or not a premedication is administered. Further studies are warranted to assess the efficacy of pre-emptive analgesia following preoperative administration of analgesics in children with history of spontaneous active pain in mandibular primary molars.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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