

Original Article

Clinical Effectiveness of Egyptian Articaine (4% Artpharmadent) Versus Imported Articaine (4% Artinibsa) in Extraction of Primary Molars: Randomized Clinical Trial

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Abstract

Objective: the objective of this study is to compare the clinical effectiveness of a relatively new locally manufactured articaine (Artpharmadent 4% 1/100.000, made in Egypt) versus imported articaine (Artinibsa 4% 1:100.000, made in France) in buccal infiltration anesthesia during extraction of primary molars.

Subjects and Methods: A prospective, randomized, split-mouth comparative study was conducted on children aged from 6 - 10 years old having bilateral badly decayed mandibular or maxillary primary molars. Children were randomly chosen from the outpatient clinic of paediatric dentistry department, Cairo University. Split-mouth technique was followed to give buccal infiltrations of Artpharmadent on one side and Artinibsa on the other at separate visits. Child pain and behaviour were assessed using Wong–Baker FACES pain rating scale and face, leg, activity, cry and consolability (FLACC) Behavioural Pain Assessment Scale.

Results: Both anaesthetic types showed comparable and high clinical effectiveness in pain control during extraction. FLACC behavioural pain scale showed insignificant difference with both local anaesthetics.

Conclusion: locally manufactured articaine buccal infiltration anesthesia is effective as imported one. It showed deep and painless alternative to anaesthetize primary molars and related supporting tissues.

Key words: Articaine; Extraction; Primary teeth; FLACC; Pain scales

Introduction:

Children could carry negative feelings toward dentistry into adulthood if they face painful experiences during dental procedures ⁽¹⁾. It is important for pediatric dentists to make every

effort to minimize pain and discomfort during different dental procedures ^(1,2).

The direct effective method for controlling pain during dental procedures is injection of effective local anesthetic. Fear and anxiety during injection

were reflected on child behaviour They may exhibit negative behavior before, during and after the injection process ^(1,2,3) . Dental fear and anxiety affect the pain perception of the child where is a high correlation between the fear of pain and the activity of the area of the brain that regulates and evaluates responses to pain. Fear, anxiety, and a sense of loss of control contribute to patient suffering ⁽⁴⁾.

An ideal local anesthetic agent provides maximum efficacy with minimum number of injections and least adverse effects. Articaine, mepivacaine and lidocaine are the most widely used anesthetic solutions in the dental clinics. Several studies have claimed that articaine has superior success rate to Lidocaine, which is considered the gold standard anesthetic solution. Mepivacaine is the third most widely used anesthetic solution in dentistry only after articaine and lidocaine ^(5,6).

In the early 1970s Articaine was developed in Germany. It began to be widely used in 2006 in Ireland and United Kingdom. It has become popular for adults. Articaine usage was limited in children before 4 years old ^(1, 2, 3, 4)

Articaine hydrochloride is one of the amide local anaesthetics. It has a unique chemical structure over traditional amide analgesics ⁽⁷⁾. It has a thiophene ring that makes it more potent and more lipid-soluble, thus allowing it to diffuse more easily through both hard and soft tissue. Local anesthetic would have high potency and fast onset of action and long duration of action if it has more lipid solubility ⁽⁸⁾.

Articaine has high affinity for plasma protein binding but it contains an ester group which allows it to be rapidly broken down into its inactive state so decreasing systemic toxicity ^(9,10,11). Articaine has a low ionization constant; pKa (7.8). The maximum recommended dose of

4% articaine HCl should not exceed 3.2 mg/lb of bodyweight ⁽¹²⁾.

Articaine is manufactured as a 4% solution with 1:100,000 or 1:200,000 adrenaline. Both concentrations offer a rapid onset of analgesia and a similar degree of pulpal (approximately 1 hour) and soft tissue analgesia (3-5 hours) ^(9,10).

Articaine 4% 1:100,000 local anaesthetic reported to be safe, effective and well tolerated local analgesia for use in children older than 4 years old. It can be administered in a smaller volume of solution giving a higher concentration of drug ^(11,13, 14). Reduced local anaesthetic volume could decrease the discomfort of analgesia administration. That is beneficial especially with uncooperative children.

Wright et al., 1989 tested articaine usage for paediatric dental patients less than 4 years of age proving promising results. However, the manufacturers do not recommend articaine for children younger than 4 years ^(14,15). A systematic review found that there was insufficient data to support the use of articaine in very young children. Precautions during articaine administration are similar to other amide products. Dosage should be calibrated on a mg/kg basis for children ⁽¹⁶⁾.

Prolonged soft tissue numbness was reported as the most common adverse effect following articaine injection. Allergy to local analgesia in dental office is uncommon. Allergic reaction to articaine would be considered as other amide analgesia ^(9,10,15, 17, 18, 19).

Palatal soft tissue anesthesia requires a separate palatal injection, a technique that is often painful for the patient especially for children. Local anesthetic used for buccal infiltration but give palatal anesthesia would be of great advantage in dentistry. For procedures in the mandibular arch, in children especially under 6 years of age, the thickness of buccal cortical bone is less than

adult, that allow buccal infiltration approaches to produce pulpal or lingual soft tissue anesthesia and this can replace nerve block technique^(9,10,18). The use of nerve blocks has disadvantages compared to infiltration technique. It is more painful with greater incidence of complications such as trismus, hematoma or paraesthesia⁽¹⁸⁾.

Another drawback is the requirement of anesthetizing the entire branch of the inferior alveolar nerve, even if only one tooth is being treated^(10,18). For children, the lack of the anesthetized sensation of the lower lip would be preferable. Articaine has superior properties with respect to diffusion into tissue, which allows it to induce pulpal and lingual anesthesia in the mandible, and palatal anesthesia in the maxilla, when administered labially^(16,18).

Many studies have shown that 4% articaine can be successfully used in children of 4 to 10 years of age where the mean time of onset of anesthesia is shorter in children than adults. It was justified by the cancellous nature of the pediatric maxilla and mandible which allows the spread of the anesthetic agent^(5,20).

The aim of this study is to compare the clinical effectiveness of a relatively new locally manufactured Egyptian articaine (Artpharmadent) versus imported articaine (Artinibsa) in buccal infiltration anesthesia during extraction of upper and lower primary molars. The null hypothesis is that there is no difference in the clinical effect of both local anaesthetic drugs.

Subjects and methods:

PICO Question: Do children with badly decayed primary molars (P), indicated for extraction, and anesthetized by 4% Artpharmadent (I) compared to 4% Artinibsa (C): react similarly as regard to pain perception and behavior (O)?

Type of study: Triple blinded split-mouth randomized clinical trial was planned. The study was conducted on children selected according to inclusion criteria and received their treatment at Cairo University, Pediatric dentistry department, Out-patients clinics.

Sample size: We planned a study of a continuous response variable from matched pairs of study subjects. Previous data⁽²¹⁾ showed that the difference in the response of matched pairs is normally distributed with standard deviation 1.67. If the true difference in the mean response of matched pairs is 1, we need to study 24 pairs of subjects to be able to reject the null hypothesis that this response difference is zero with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05.

Informed consent: Parent guardians written approval were taken by signing the informed consent after discussing the treatment plan and all the possible outcomes.

Selection criteria: Twenty -five children were examined at the first visit for allocation in the study. Children aged from 6-10 years old with free medical histories and with normal intellectual development reasonable with their age. Children should be with no previous history for allergies to medications or local anesthesia to be included in the study. Included subjects had bilateral maxillary or mandibular primary molars indicated for extraction. Primary molars are either badly decayed beyond restoration, remaining roots at molar area or loose molars that are painful to the child to withstand till normal shedding without professional interference. Children classified rating I or II according to Modified Frankle Behavioural Rating Scale were excluded from the trial.

Clinical procedures:

Non pharmacological behaviour management techniques were followed; distraction and tell-do techniques. Children received an infiltration on one side using imported Artinibsa injection and Artpharmadent on the other. Treatment of both sides with the two types of anesthesia in the mandible or the maxilla was completed in two separate visits, at least 1 week apart. Left and right sides were randomly allocated to either groups. The selected subjects were treated using both techniques. At the first dental treatment visit; the child was allowed to pick a closed one paper from 24 white papers prepared and folded three times so as not to show its contents to assure random assignment. The picked paper was written in it either Artinibsa or Artpharmadent. The right side of the patient was treated first using the local anaesthetic agent according to the picked paper.

Area of injection was dried with tip of cotton bud then topical anaesthetic (OPAHL topical anaesthetic gel 20% benzocaine, Dharma research inc USA) was applied for 60 seconds. Injection of local anaesthetic using short (11mm) needle with 27 gauge. The needle was slowly inserted until the bevel was at or below the apex of the tooth to be anaesthetized. It was gently inserted in the depth of mucobuccal fold where the target site was centered between mesial and distal root apices of the tooth to be treated with one or two drops of anaesthesia administered during its path. After needle penetration toward the target site, anaesthetic solution was given at the rate of 1 ml/min.

Child pain immediately after anesthesia administration was assessed using Wong Baker face pain rating scale (FPS) (Figure 1). This face pain rating scale considered subjective method for pain records as it assesses the unpleasantness of child to pain experience after dental treatment. This scale can be used in children aged 3–17 years. Each child saw a set of six cartoon faces with varying facial expressions ranging from a

smile/laughter to tears. Each face in that scale has a corresponding numerical value. After explanation by the operator to the child on how to use the FPS, the children were asked to select the face which they feel deep down inside, not the face they showed.

Those faces were expressing various degrees of feeling pain; Face 0 doesn't hurt at all. Face 2 hurts just a little bit. Face 4 hurts a little more. Face 6 hurts even more. Face 8 hurts a whole lot. Face 10 hurts as much as you can imagine, although you don't have to be crying to have this worst pain⁽¹⁹⁾.

Extraction procedure started as soon as the probing revealed no pain. Treatment was planned to be discontinued if the child showed any signs of pain such as hand / body tension, eye movement indicating pain, verbal complaints, tears, hand and body movement. If the child announces feeling pain during the dental procedure, he/she was immediately crossed over to a mandibular block or intrapapillary injection or palatal infiltration in accordance. Treatment was resumed after giving additional anaesthetic. With addition of local anesthesia care was taken not to exceed the maximum recommended dose of the drugs which is 7mg/kg body weight for articaine.

After profound anesthesia has been achieved, children's pain perception and behaviour during extraction were assessed using face, leg, activity, cry and consolability (FLACC) Behavioral Pain Assessment Scale (Figure 2). FLACC scale is objective measurement tool used to assess pain for children that are unable to communicate their pain. The scale is scored in a range of 0–10 where zero represents no pain. The scale has five criteria, each them is assigned either with score of 0, 1 or 2. Then interpreting the behavioral Score results in a total score of 0–10. Where 0: Relaxed and comfortable, 1–3: Mild discomfort, 4–6:

Moderate pain and 7–10: Severe discomfort or pain or both ⁽²¹⁾.

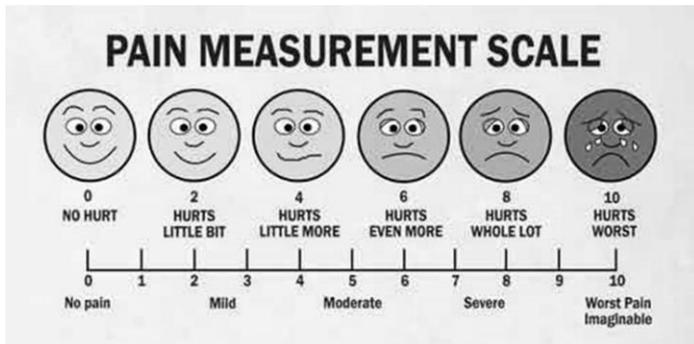


Figure1:Wong Baker face pain rating scale

Dental Assessor other than the operator observed the patient for 1 to 5 minutes. Legs and body were uncovered to assess body for tenseness and tone and initiate consoling interventions if needed. Then scoring was done according to five criteria mentioned in figure 2.

At the end of the dental visit; the child over all self-experience of pain from the dental procedure offered was assessed using the Wong–Baker FACES pain rating scale once more.

All data such as personal data, medical history, and dental history, chief complain, diagnosis and treatment plan, technique, type and amount of local anesthesia, the need for additional anesthesia and the technique of additional anesthesia used were recorded for each child on his chart separately.

Statistical analysis:

Pain scores data were presented as mean and standard deviation (\pm SD) values. Data scores are non-parametric so Wilcoxon signed-rank test was used to compare between the two groups specially that the study is a split-mouth design. Qualitative data were presented as frequencies (n) and percentages (%). McNemar's test was used to compare between the two groups. The

significance level was set at $P \leq 0.05$. Statistical analysis was performed with IBM® (Corporation, NY, USA) and SPSS® (Inc., an IBM Company) Statistics Version 20 for Windows.

Results:

The split mouth study was conducted on 25 children with the mean age of (7.88 ± 1.39) years. Artinibsa 4% anesthesia was mostly given in the lower arch 16 (64%), on the right side 16 (64%), with the higher percentage of extracted teeth being second primary molars 15 (60%), that was most likely extracted due to extensive decay 16 (64%), and the anesthesia was effective in all the cases with almost no need for nerve block or supplemental anesthesia except in 2 (8.0%) cases. Artpharmadent 4% anesthesia was mostly given in the lower arch 15 (60%), on the left side 16 (64%), with the higher percentage of extracted teeth being first primary molars 18 (72%), that was most likely extracted due to extensive decay 17 (68%), and the anesthesia was effective in all the cases with almost no need for nerve block or supplemental anesthesia except in 3 (12%) cases. There was no significant difference between both sides in all aforementioned features except for type of the extracted tooth ($p=0.021$). In case of utilizing Artpharmadent 4% anesthesia there was a higher Wong-Baker face pain scale (1.52 ± 1.12), FLACC score (3.32 ± 1.6) and self-experience of pain from the dental procedure offered (3.72 ± 1.86) in comparison to Artinibsa 4% (1.24 ± 1.27), (3.00 ± 1.29) and (3.32 ± 1.41), yet the difference was not statistically significant ($p=0.198$, 0.112 and 0.267) respectively. Frequencies (n) and percentages (%) for different features were presented figure (3), Summary statistics of different pain scores were presented in table (1).

	DATE/TIME			
Face 0 - No particular expression or smile 1 - Occasional grimace or frown, withdrawn, disinterested 2 - Frequent to constant quivering chin, clenched jaw				
Legs 0 - Normal position or relaxed 1 - Uneasy, restless, tense 2 - Kicking, or legs drawn up				
Activity 0 - Lying quietly, normal position, moves easily 1 - Squirming, shifting back and forth, tense 2 - Arched, rigid or jerking				
Cry 0 - No cry (awake or asleep) 1 - Moans or whimpers; occasional complaint 2 - Crying steadily, screams or sobs, frequent complaints				
Consolability 0 - Content, relaxed 1 - Reassured by occasional touching, hugging or being talked to, distractible 2 - Difficult to console or comfort				
TOTAL SCORE				

Figure 2: FALCC behaviour pain assessment scale.

Table (1): Summary statistics of different pain scores in both groups

Score		Artinibsa 4%	Artpharmadent 4%	p-value
Wong-Baker face pain scale (after anaesthesia)	Mean±SD	1.24±1.27	1.52±1.12	0.198ns
	Median(IQR)	1.00(2.00)	2.00(2.00)	
FLACC index (after extraction)	Mean±SD	3.00±1.29	3.32±1.6	0.112ns
	Median(IQR)	3.00(2.00)	3.00(2.00)	
Wong-Baker face pain scale (Self-experience of pain from the dental procedure offered)	Mean±SD	3.32±1.41	3.72±1.86	0.267ns
	Median(IQR)	3.00(0.00)	3.00(2.00)	

SD=standard deviation, IQR=Inter quartile range*; significant ($p \leq 0.05$) ns; non-significant ($p > 0.05$)

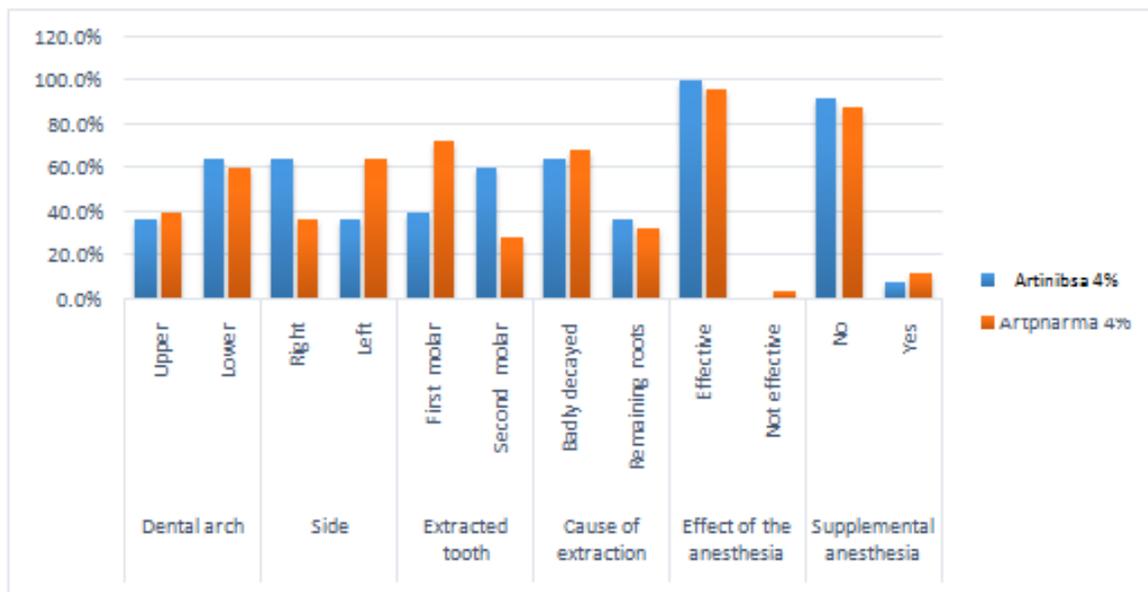


Figure (3): Bar chart showing differences in both groups according to the treated tooth and effectiveness of the local anaesthetic drug

Discussion:

Studies have claimed that articaine has a high success rate when used in children of 4 to 10 years of age ⁽⁶⁾. The Egyptian articaine (Artpharmadent) was assigned as the intervention because of being locally manufactured thus available in the local markets with reduced cost in comparison to the imported articaine brands that are not guaranteed to be available in local markets any time. Articaine has an advantage of having high penetration capability due to the presence of thiopene ring in its chemical structure so achieving a rapid onset and faster dental anesthesia in comparison to others ^(22,23). The current research was a triple blinded study to increase the accuracy and objectivity of clinical outcomes, where the patient was blinded to avoid reporting bias and the outcome assessor was blinded to avoid detection bias and ascertainment bias. Blinding of a statistician was also important to minimize reporting bias and maximize the validity of the results ⁽²⁴⁾. Cooperative children

were chosen to get accurate assessment of perceived pain after local anesthesia and extraction. Selecting children with normal intellectual development was done because the Pain assessment depends on the cognitive development of the child being tested as for children older than age 6 years, pain assessment is based on a self-report pain intensity ⁽²⁵⁾. Psychological management and proper desensitization procedures were performed to reduce fear and anxiety that may also affect pain perception. Wong-Baker face pain scale was reliable and valid self-report pain tool. It can be used by children to report their perceived pain subjectively. Also, it was proven to be valuable, intelligible, and easy to use with children ⁽²⁹⁾. In case of utilizing Artpharmadent there was a higher Wong-Baker face pain scale (1.52 ± 1.12), FLACC score (3.32 ± 1.6) and self-experience of pain from the dental procedure offered (3.72 ± 1.86) in comparison to Articaine 4% (1.24 ± 1.27), (3.00 ± 1.29) and (3.32 ± 1.41), yet the

different was not statistically significant ($p=0.198, 0.112$ and 0.267) respectively.

Regarding the results for the need of supplemental anesthesia; Artinibsa was effective in all cases with almost no need for nerve block or supplemental anesthesia except in 2 (8.0%) cases. Artpharmadent was effective in all the cases with almost no need for nerve block or supplemental anesthesia except in 3 (12%) cases. This in agreement with ^(23,26) who stated that there was a failure in dental anesthesia while using 4% articaine in some patients as they did not achieve the 100% anesthetic success within their study and required an additional anesthesia.

The need for supplemental anesthesia means a failure of the anesthetic solution to guarantee a deep anesthesia for the mandibular teeth during the extraction procedure. A number of factors may contribute to the justification of failure of dental anesthesia, which may be related to either the patient or the operator. Patient-dependent factors may be anatomical, pathological, or psychological while operator-dependent factors may be the improper performance of the injection technique through inaccurate placement of the needle in the correct place or the operator did not wait enough time for the anesthesia to act before starting the treatment ⁽²³⁾. Regarding the presence of adverse effects in the current study, no adverse effects associated with the anesthetic delivery in group A (4% Artpharmadent) and group B (Artinibsa 4%). This is in agreement with *Allegretti et al.,2016* ⁽²⁷⁾ who reported that there were no adverse effects related to the administration of 4% articaine local anesthesia. This result may be explained by the adherence to recommended dosages to avoid adverse effects and systemic toxicity. Also, the articaine has the simplest and most rapid metabolism of the amides due to its carboxyl group ester linkage that easily breakdown by plasma cholinesterase ⁽²⁸⁾.

Conclusions:

From the results of this study, the following can be concluded: 1) Artpharmadent and Artinibsa are equally effective in the control of pain during extraction of primary molars. 2) There was no statistically significant difference in the need for supplemental anesthesia in both groups. 3) No adverse reactions following the anesthetic injection were reported either from Artpharmadent or Artinibsa

Recommendations:

- 1) Egyptian medical industries should be encouraged and properly marketed on national and international levels.
- 2) Egyptian businessmen should look forward for more local dental industries and should be eager for exportation.
- 3) More researches are needed to assess the effectiveness of local Egyptian brands in dentistry field to improve and support the local productions.

Conflict of interest:

The authors declare no conflict of interest.

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