Articaine: Opening up a New Vista For Pediatric Dentists

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Abstract

Lidocaine has remained the gold standard local anaesthetic agent to perform dental procedures both in the adult as well as in the pediatric patients. However, the invent of articaine has offered the clinicians with a newer and more potent local anaesthetic agent, which causes minimal side effects. Articaine is 1.5 times more potent and 0.6 times less toxic than lidocaine. Also, adequate anaesthesia achieved through infiltration route of administration of the drug, almost eliminates the need for the painful and difficult inferior alveolar nerve block in children, thereby minimising the side effects. Thus, achieving adequate anaethesia through the administration of a small volume of the drug has opened up a new vista for pediatric dentists in managing pain in children, although manufacturers do not recommend the usage of articaine in children less than 4 years of age due to paucity of evidence. So, this review article tries to throw light on the use of articaine in pediatric patients, citing evidence from literature and also tries to portray the recent advances in the research on articaine use in pediatric patients less than 4 years of age.

***Key words**: articaine, local anesthesia, pain, children*

Introduction

Pain management plays a crucial role in the success of any dental treatment in a pediatric patient [(1)]. Minimising the fear and anxiety, a proper management protocol employed, can help develop a positive attitude towards dental treatment in the patient. Though considered a painful and challenging procedure, the administration of local anaesthesia continues to be one of the most commonly used methods for managing pain in the pediatric age group [(2)]. Maximum efficacy through minimum number of injections with negligible adverse events effected, should be the objective of the local anaesthetic agent used [(3)].

The discovery of the first amide local anaesthetic agent Lidocaine (Proprietary name: Xylocaine), also known as Lignocaine, in the 1940s, marked a revolution in the arena of pain management in dentistry as it offered better potency and triggered less allergic reactions when compared to the then commonly used local anaesthetic Novocain (Procaine) [(4)]. Since its inception, Lidocaine has remained the "gold standard" local anaesthetic agent to perform dental procedures, all around the globe. However, the search for more effective local anaesthetic agents led to the discovery of newer local anaesthetic agents in the subsequent years. Articaine was one among the newer local anaesthetic drugs developed [(5)]. It was originally developed and

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synthesised as 'Carticaine HCl' by H. Rusching et al in 1969 [6]. It was introduced into clinical practice first in 1976 in Germany and Switzerland followed by the other European countries and Canada [7][8]. In the United States, the US Food and Drug Administration approved the use of articaine in April 2000 [9]. Gradually, articaine started to gain attention and clinicians began employing articaine in adult dentistry. However, the use of the drug in the pediatric age group has raised concern over times, though literature shows that the efficacy and safety of articaine is comparable to the other commercially available local anaesthetic including lignocaine [10,11] or even superior [12,13]. A survey among pediatric dentists in India concluded that the majority of the respondents still preferred lidocaine with epinephrine as local anaesthetic for use in children [14].

UNIQUENESS OF ARTICAINE

Articaine or Articaine HCl ("4-methyl-3-[2-(propylamino)- propionamido]-2-thiophene-carboxylic acid, methyl ester hydrochloride") is an amide type local anaesthetic. The molecular weight of articaine HCl is 320.84 and it contains a thiophene group instead of a benzene ring, a peculiar characteristic that differentiates it from the other local anaesthetic agents. The greater lipid solubility and potency offered by the thiophene ring helps in the entry of a greater amount of the administered anaesthetic solution into the neurons. It is also able to diffuse more easily through soft tissue surfaces and has a high degree of plasma protein binding of 95%, when compared with the other local anaesthetics. Though classified as an amide, owing to its linkage of intermediate chain, articaine also contains an ester side chain, which triggers the plasma esterases and the hepatic microsomal enzymes to bring about the biotransormation of articaine in plasma and liver respectively. This imparts articaine a half-life of 20 minutes and the primary metabolite obtained is articainic acid which is pharmacologically inactive. This accounts to the decreased systemic toxicity effected by articaine, thereby rendering itself as a safer alternative[15]. Articainic acid (64.2 ± 14.4%), articainic acid glucuronide (13.4 ± 5.0%) and the parent drug (1.45 ± 0.77%) are excreted via urine after the metabolism of articaine [16].

4% solution with 1:100,000 or 1: 200,000 adrenalines are the commonly manufactured forms of articaine and they are dispensed in 2.2ml and 1.7ml glass dental cartridges. The two articaine formulations have been used in both adults as well as in children.

SAFETY OF ARTICAINE IN CHILDREN

Articaine is well tolerated and safe to use in children above 4 years of age. The potency of articaine is 1.5 times that of lidocaine, which enables the administration of a smaller volume of the drug. The reduced volume may help decrease the discomfort felt by the child during anaesthesia administration, especially in cases where an inadequate co-operation of the child is experienced. It is also 0.6 times less toxic as compared to lidocaine [17]. There is also a lesser need for supplemental injections in articaine. Articaine can be given via buccal infiltration to children requiring pulp therapy and extractions and can thereby be used to replace inferior alveolar nerve block (IANB). The high risk of inferior alveolar and lingual nerve damage can be avoided by replacing IANB. The extent of soft tissue analgesia experienced by the patient can be reduced and therefore the incidence of complications like lip biting can be minimized [18,19]. When buccal and palatal infiltration with other local anaesthetic agents was replaced by a single buccal infiltration using articaine, it yielded favourable results during the extraction of primary molars in the maxillary arch. Also, articaine delivered via intraligamentary injection can be used to replace IANB to extract primary molars [20].

According to Lemay et al, the onset of anaesthesia by articaine was 168±131 sec (nerve block) and 85±60 sec (infiltration) in children; for adults it was 170±131 sec (nerve block) and 119±84 sec (infiltration) [21]. For maxillary infiltration, the duration of action on soft tissues ranges from 2.6 to 4.5 hours whereas for nerve block, it ranges from 4.3 to 5.3 hours [6,8]. The volume of distribution of articaine is inversely proportional to the patient's age. For children between ages 4-12 years, the dosage of articaine ranges from 5-7 mg/kg body weight,

however a lower limit of ≤5mg/kg was advocated in children aged 4-12 years by authors who performed studies using articaine in conjunction with sedative agents [22]. In any case, it should always be remembered that the concentration of articaine can be considered double as that of lidocaine, and thus will require half the safe number of cartridges.

COMPARISON WITH OTHER LOCAL ANESTHETIC AGENTS IN PEDIATRIC DENTISTRY

Multiple investigators have reported their findings and conclusions on the use of articaine as a local anaesthetic agent in pediatric population.

Malamed in 2000 [6] compared the pain control property of "4% Articaine HCl (with 1: 100,000 epinephrine)" with "2% Lidocaine HCl (with 1: 100,000 epinephrine)" in children under the age of 13 years, by employing the Visual Analogue Scale (VAS). He found Articaine to be comparable to Lidocaine and gave a green signal to its use in the branch of pediatric dentistry citing its safety and efficacy.

Ram and Amir in 2006 [11] compared Articaine and Lidocaine during operative procedures in children aged 5-13 years. They stated that "Articaine 4% with 1:200 000 epinephrine is as effective as lidocaine 2% with 1:100 000 epinephrine". However, articaine produced a longer lasting anaesthetic effect on the soft tissues as compared to lidocaine.

Yilmaz et al in 2011 [23] compared Articaine 4% with (1:100000 epinephrine) and Prilocaine 3% (with felypressin) in 162 children belonging to the 6 to 8 age group, undergoing primary molar pulpotomy. Similar intensity of pain was reported during administration of both the anaesthetic solutions. However, coronal pulp amputation, prilocaine gave a pain score which was 1.5 times higher than that of articaine. The adverse events reported were also comparable.

In a review by Leith et al in 2012 [17], it was also reported that 4% articaine showed better pain control than 2% lidocaine for both simple and complex dental procedures.

In 2012, Odabaş [24] compared 4% articaine with 3% mepivacaine, to study the pain reaction and duration of soft tissue numbness during the administration of local anaesthesia in children. A "randomized, double-blind, split-mouth" design was adopted for the study which included a sample size of 50 children (25 girls and 25 boys) belonging to the 7- to 13-year-old age group, who required comparable operative treatment needs in symmetric primary teeth. The objective evaluation of the children was carried out by the modified behaviour rating scale and the subjective evaluation by using the Wong-Baker FACES pain rating scale which helped assess the post injection and post treatment experience. The duration of numbness felt was recorded by the parents by asking the children. Articaine (140.69±49.76 minutes) presented with a prolonged time period of soft tissue anaesthesia than mepivacaine (117.52±42.99 minutes). Neither did the efficacy of the anesthesia nor did the heart rate, blood pressure, or oxygen saturation show any significant differences during all evaluation spans for both anaesthetic solutions. The two anaesthetic solutions also showed similar post treatment experience. It was concluded that same efficacy and identical child behaviour was observed with 4% articaine and 3% mepivacaine, though articaine reported longer soft tissue numbness.

In 2012, Arrow [25] compared "4% Articaine (with 1: 100,000 epinephrine)" administered via buccal infiltration to "2% Lignocaine (with 1: 80,000 epinephrine)" administered via buccal infiltration (BI) or inferior alveolar nerve block (IANB) during standard restorative procedures in the posterior teeth of the mandibular arch among school children. The study assessed pain response via the Faces Pain Scale – Revised (IASP) and found no statistical difference in pain response between both the solutions. The study declared that both Articaine and Lignocaine, were declared equally effective in pain management in children for routine restorative procedures.

In 2014, Thakare [26] evaluated and compared 4% Articaine and 0.5% Bupivacaine through his randomized

controlled crossover clinical trial, in patients aged 10-18 years who had their premolars indicated for orthodontic extractions. The study showed that 4% Articaine presented with a quicker onset of action and lesser Visual Analog Scale scores as compared to Bupivacaine. However, Bupivacaine presented with a longer time period of analgesia and time to the first uptake of medication for rescue analgesia. Articaine was declared more potent and effective considering its quicker onset of action and low pain scale scores.

In 2015, Arali and Mytri P [27] studied the anaesthetic efficacy of "4% articaine (with 1: 100,000 epinephrine)" delivered via buccal infiltration and "2% lignocaine (with 1: 100,000 epinephrine)" delivered via inferior alveolar nerve block (IANB) by employing a "randomized, double-blind, cross over" study design in children aged 5-8 years, presenting with the clinical condition of irreversible pulpitis. The study also assessed the necessity for the administration of supplemental injections. The trial reported that the anaesthetic onset was quicker with 4% articaine than 2% lignocaine. A shorter span of anaesthesia was observed with articaine infiltration and with a lesser requirement for the administration of supplemental injections. The study concluded that 4% articaine can be given via buccal infiltration to children undergoing management for irreversible pulpitis. The study also highlighted the potential of articaine delivered via buccal infiltration to replace IANB to avoid complications such as lip biting.

A study by Zurfluh et al in 2015 [28] assessed whether an articaine solution could reduce the period of soft tissue anaesthesia and thereby reduce the risk of self-inflicted soft tissue lesions, while still providing an adequate anaesthesia. The study reported that owing to its high efficacy, tolerance, and reduced soft tissue anaesthesia, 4% articaine (with 1: 400,000 epinephrine) was considered safe for treatment in paediatric population.

In 2015, a study was performed by Mittal [29] in 112 children, to compare the anaesthetic efficacy of articaine with lidocaine during the extraction of primary molars in the maxillary arch and assess whether a buccal infiltration injection could achieve sufficient palatal anaesthesia as well. The study reported that buccal infiltration with articaine can be considered a potential substitute for lidocaine in achieving local anesthesia in children, though it did not succeed in achieving sufficient palatal anaesthesia.

In 2016, Chopra et al [30] compared the efficacy of buccal infiltration with articaine against inferior alveolar nerve block with lignocaine for primary molars in children aged 4-8 years, indicated for pulpectomy or pulpotomy. The efficacy of both the anaesthetic agents were assessed using the Pain Scores, the Facial Image score, Sound Eye Motor (SEM) scores and Heft- Parker Visual Analogue Score (HP-VAS). Buccal infiltration with articaine showed significant lower pain scores as compared to IANB ($p<0.001$). SEM scores at the time of pulp extirpation were also higher for IANB than infiltration ($p<0.001$).

Kolli et al in 2017 [31] stated that Articaine buccal infiltration can be used as an alternate to conventional local anaesthetic delivered via buccal and palatal infiltration, for extracting primary molars in the maxillary arch.

In 2018, Sharan et al [32] assessed the effectiveness of "2% lidocaine (with 1:80,000 epinephrine)" and "4% articaine (with 1:100,000 epinephrine)" to extract primary mandibular molars in children aged 6-10 years, by employing the intraligamentary injection technique. The study utilised the Sound eye motor scale to assess pain perception. The study showed 80% success rate in Articaine group and 30% success rate in lidocaine group. The study concluded that the intraligamentary injection technique using articaine might serve as an alternative to IANB during extraction of primary molars in the mandibular arch.

Rathi conducted a study in 2019 [33] among 100 children to compare the anaesthetic efficacy of articaine with that of lignocaine. It was concluded that a single buccal infiltration of 4% articaine with 1:100,000 epinephrine is more effective when compared to 2% lidocaine with 1:80,000 epinephrine for extracting

primary molars in children aged 7 to 12 years.

Massignan in 2020 [34] stated that though articaine reported a higher pain incidence during the injection, no difference in efficacy was observed when the anaesthetic administration of articaine was compared to lidocaine in the extraction of primary molars. In the study, the efficacy and the adverse events of "4% articaine with epinephrine 1:100 000" was compared with that of "2% lidocaine with epinephrine 1:100 000" during the extraction of primary molars, by employing anaesthesia via buccal infiltration in forty-three children belonging to the 6-10 age group. 21 children received local buccal infiltration with 4% articaine whereas 22 children received lidocaine 2%. The pain experienced during injection of the anaesthetic solution and during extraction of the tooth was the major outcome assessed. The anaesthetic efficacy of both the solutions was observed to be identical though a higher pain incidence was reported by children belonging to the articaine group. Similar adverse effects were observed in both the groups which included post-operative pain, edema and nausea.

It can be summarised that there is evidence to conclude that 4% articaine is comparable to or more efficacious than the other local anaesthetic agents used in children. However, the parents should be cautioned about self-inflicted soft tissue injuries that may arise due to the prolonged numbness, commonly reported with articaine administration. However, the evidence suggests that articaine is safe in chilren, as the administration of the drug triggers few adverse events, which are commonly noticed with lidocaine as well.

EVIDENCE FOR USE IN CHILDREN BELOW 4 YEARS OF AGE

Some studies have specifically reported the use of articaine in paediatric dental patients less than 4 years of age with positive results, however the manufacturers still do not recommend it for children younger than 4 years.

Wright et al in 1989 [22] conducted a retrospective research which analysed the usage of articaine hydrochloride as an anaesthetic agent in children aged less than 4 years of age. Records of articaine administration on 211 patients, with additional administrations of the agent on 29 patients was retrieved from two pediatric dentistry offices by a record audit. Some cases even reported administration of higher doses of the drug than recommended for older children. The clinicians have not noted the occurrence of any systemic adverse reactions. The report provided initial evidence for the use of articaine in children under 4 years of age.

Jakobs et al in 1995 [35] studied the pharmacokinetics of articaine on 27 children, 3 to 12 years of age, who underwent dental procedures under intubation anesthesia. They determined the serum concentrations after local anesthesia with 2% and 4% articaine solutions in this age group of children. They concluded that articaine shows age-related differences in the pharmacokinetics and hence there is no need to fix a lower mg/kg dose limit while administration in children.

A study was conducted in young children below four years of age by Elheeny in 2020 [36] to assess the efficacy and safety of 4 % articaine as a local anesthetic agent by comparing it with 2 % lidocaine hydrochloride. The study had an equivalent randomized control trial design, with two parallel arms including 184 young children (92 per group) aged from 36 to 47 months, in whom, pulpotomy of mandibular primary molars was indicated after administering anesthesia by buccal infiltration injection. The results of the study indicated that during pulpotomy, children who received articaine showed less pain as compared to their counterparts in the lidocaine group and no statistically significant differences were observed between both the drugs, considering the post-operative complications. It was concluded that the findings supported the efficient and safe use of articaine hydrochloride 4% with epinephrine 1:100 000 as a local anaesthetic agent during dental procedures in children aged between 3 and 4 years.

The evidence supports the use of articaine in children less than 4 years of age. However, limited research demands clinical trials on a larger sample size

to be performed before employing articaine as a local anaesthetic agent in children less than 4 years of age.

Conclusion

Articaine is a safe and effective local anesthetic drug which can be employed in pediatric patients to help achieve dental analgesia during invasive procedures. The evidence that articaine administered via infiltration technique can replace Inferior Alveolar Nerve Block makes it even more interesting. The ability of articaine to penetrate into deeper spaces by diffusing through bone and soft tissue should be understood by the clinicians as it helps to achieve excellent depth of anesthesia, while avoiding block and palatal anesthesia for dental treatment in children. However, advanced research and clinical trials is a necessity, as articaine is not recommended by manufacturers in children below 4 years of age.

Ethical Clearance - Not applicable (review article)

Source of Funding - Self

Conflict of Interest - Nil.

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