



Articaine in Dentistry

S. Thaminee

*Student, Bachelor of Dental Surgery, Department of Pharmacology,
Saveetha Dental College and Hospitals, Saveetha University,
Chennai, Tamil Nadu - 600 113, India*

Abstract

Aims and objectives:

Articaine is an amide local anaesthetic, which is gaining popularity for use in dental and oral surgical anaesthesia in the United Kingdom. Hitherto there has been insufficient evidence to recommend articaine above the more commonly used lidocaine for dental procedures.

Back Ground:

Articaine is the most widely used local anaesthetic agent in dentistry in a number of European countries. The amide structure of articaine is similar to that of other local anaesthetics, but it contains an additional ester group which is quickly hydrolysed by esterases.

Reason:

To compare the efficiency of 4% articaine with 1:100,000 adrenaline (4AA) with that of 2% lidocaine with 1:100,000 adrenaline (2LA) administered as a buccal infiltration (for anaesthesia in mandibular permanent first molar teeth).

INTRODUCTION

Local anesthesia is any technique to induce the reversible loss of sensation in any part of the body. When it is used on specific nerve pathways, effects such as loss of pain sensation (analgesia) and muscle relaxation (paralysis) can be achieved. Local anesthesia commonly used to control the pain in dental procedures such as extraction, root canal treatment etc. Articaine, Lidocaine, Procaine, Marcaine, Mepivacaine, adrenaline are commonly employed in dentistry as local anesthesia for the purpose of various dental procedures. Among these, Articaine has advantageous due to its long duration of action and effective when compared to others. Hence, this reviews the effectiveness of Articaine in the arena of Dentistry.

PHARMACOLOGY OF ARTICAIN

Articaine is an intermediate-potency, short-acting amide local anesthetic with a fast metabolism due to an ester group in its structure. It has been reported that administration of Articaine to gingiva infiltrates rapidly and blocks the peripheral nerve in dentistry, when it administered as a spinal, epidural, ocular, or regional nerve block, or when injected intravenously for regional anesthesia. The use of articaine achieves successful pain control in low doses and it is safe and effective than lidocaine (Malamed, 1997). Articaine contains a thiophene ring which makes it more potent and more lipid soluble; thereby enabling it to diffuse more readily through both hard and soft tissue. In addition, articaine has a high affinity for plasma protein binding and it is the only amide analgesia to contain an ester group; this allows it to be rapidly broken down into its inactive state, thus decreasing systemic toxicity [Malamed et al., 2000a; Oertel et al., 1997].

In comparative trials, its clinical effects were not generally significantly different from those of other short-acting local anesthetics like lidocaine, prilocaine, and

chloroprocaine, and there is no conclusive evidence demonstrating above-average neurotoxicity. Articaine proved to be suitable and safe for procedures requiring a short duration of action in which a fast onset of anesthesia is desired, eg, dental procedures and ambulatory spinal anesthesia, in normal and in special populations (Malamed SF, 1997).

HISTORY OF ARTICAIN

Articaine was originally synthesized as articaine in 1969 and entered clinical practice in Germany in 1976 (Malamed S F, Gagnon, et al, 2001). Articaine is 4-methyl-3(2-[propylamino]propionamido)-2-thiophenecarboxylic acid, methyl ester hydrochloride with a molecular weight of 320.84. It is the only amide local anesthetic that contains a thiophene ring. In addition, articaine is the only widely used amide local anesthetic that contains an additional ester ring. Biotransformation of articaine occurs in both the plasma (hydrolysis by plasma esterase) and the liver (hepatic microsomal enzymes). Degradation of articaine is initiated by hydrolysis of the carboxylic acid ester groups to give free carboxylic acid (Van Oss GE, 1989). Articaine acid is the primary metabolite, or M1.3 Additional inactive metabolites, or M2, have been detected in animal studies (Verma R., et al, 2011). Articaine is eliminated via the kidneys. Articaine is manufactured as a 4% solution with 1:100,000 or 1:200,000 adrenaline in 2.2ml and 1.7ml glass dental cartridges. Both concentrations impart a rapid onset of analgesia and a similar degree of pulpal (approximately 1 hour) and soft tissue analgesia (3-5 hours) [Malamed et al., 2000a].

PHARMACOLOGY OF ARTICAIN

Articaine, a 4-methyl-3(2-[propylamino]propionamido)-2-thiophenecarboxylic acid, methyl ester hydrochloride, originally named articaine was first prepared by Rusching et al in 1969. It entered clinical

practice in Germany in 1976 under the changed name of articaine (Malamed SF, Gagnon 2011). It is the only amide local anesthetic that contains a thiophene ring and an additional ester ring (Malamed SF, Gagnon, 2011). Its molecular weight is 320.84. The thiophene ring increases its lipid solubility (Verma R; 2011). It has a pKa of 7.8 similar to that of lignocaine while that of bupivacaine is 8.1 (Verma R; 2011). It is highly diffusible and penetrates tissues effectively. 95% is plasma protein bound. The presence of both an amide and an ester linkage minimizes the risk of overdose leading to toxic reaction as its biotransformation occurs both in the plasma (hydrolysis by plasma esterase) and the liver (hepatic microsomal enzymes) (Katyal, et al, 2010). Metabolism is initiated by hydrolysis of the carboxylic acid ester groups to generate free carboxylic acid (Katyal, et al, 2010). Articainic acid is the primary metabolite, or M1. Additional inactive metabolites, or M2, have been detected. Elimination is through the kidneys. 5 to 10% is excreted unchanged and 89% as metabolites (M1 87% and M2 (Hoizey G; J Pharm Biomed Anal, 2009). The elimination half life of most amide local anesthetics is 90 minutes while that of articaine is 27 minutes (Katyal V., et al, 2010). It was first used clinically in dentistry and is the most common local anesthetic used in dentistry today.

ARTICAINE USE IN DENTISTRY

Articaine is widely used in Germany, Canada and many other countries. Articaine is the most widely used local anaesthetic agent in dentistry in a number of European countries. Complete anaesthesia can be observed in nearly 90% of all cases using articaine 4% 60–80 mg with adrenaline 5 mg/ml (Scott DB, et al, 1972). Articaine diffuses through soft tissue and bone more easily than other local anaesthetics. Systemic toxicity is rare and, for example, an unintentional intravascular injection of articaine 80 mg did not cause any toxic symptoms in healthy individuals. Haas and Lennon³⁷ used a postal survey to obtain data on the annual use of local anaesthetics in dentistry was sent to each of the 6,271 certified dentists in Ontario in 1993. A total of 2,426 dentists responded to the survey. It was estimated that more than 11 000 000 cartridge ampoules of local anaesthetic were administered annually by dentists in Ontario (Gupta A, Kaur S, 2001). Lidocaine with 10 mg/ml adrenaline accounted for 23.4% of all ampoules used, followed by articaine with 5 mg/ml adrenaline (19.9%), articaine with 10 mg/ml adrenaline (17.9%). A retrospective study of paresthesia following the injection of local anaesthetic in dentistry was conducted by examining every report of paresthesia recorded by Ontario's Professional Liability Program from 1973 to 1993. Only those cases in which surgery was not conducted were considered in this study. From 1973 to 1993, there were 143 reports of paresthesia not associated with surgery (Mikesell P., et al, 2009). No significant differences were found with respect to patient age, patient gender, or needle gauge. All reports involved anaesthesia of the mandibular arch, with the tongue most frequently reported to be symptomatic, followed by the lip. Pain was reported in 22% of the cases. Paresthesia was reported most often following the injection of articaine and

prilocaine. In 1993 alone, there were 14 reports of paresthesia not associated with surgery. This can be projected to an incidence of 1:785 000 injections. Articaine was administered in 10 of these cases and prilocaine in the other four. The observed frequencies of paresthesia following the administration of articaine ($P < 0.002$) or prilocaine ($P < 0.025$) were significantly greater than the expected frequencies for these agents, based on the distribution of local anaesthetics use in Ontario in 1993 (Malamed SP, 2004). These results are consistent with the suggestion that local anaesthetic formulations might have the potential for mild neurotoxicity. In the large dental patient material mentioned above, Malamed and co-workers also investigated the safety of articaine 4% with adrenaline (epinephrine) 1:100 000 and lidocaine 2% with adrenaline (epinephrine) 1:100 000. The overall incidence of adverse events in the combined studies was 22% for the articaine group and 20% for the lidocaine group (Simon MA., et al, 1997). The most frequently reported adverse events in the articaine group, excluding post-procedural dental pain, were headache (4%), facial oedema, infection, gingivitis and paresthesia (1% each). The incidence of these events was similar to that reported for subjects who received lidocaine. The adverse events most frequently reported as related to articaine use were paresthesia (0.9%), hypaesthesia (0.7%), headache (0.55%), infection (0.45%), and rash and pain (each) (Becker DE, 2006). Articaine appears to be a well-tolerated, safe and effective local anaesthetic for use in clinical dentistry. It is used for maxillary and mandibular infiltrations and block anaesthesia for routine dental treatments (Katyal, 2010). The reasons for its popularity are fast onset, short duration of action, good periosteal penetration and low degree of toxicity (Oertel R, Rahn R; Clin Pharmacokinet 1997). However, pediatric patients pose a difficulty, especially those with extensive restoration needs. Articaine should not be used in children < 4 years as they are at high risk of overdose. In addition, the children requiring extensive treatment are frequently sedated. The addition of depressant effects of high blood levels of local anaesthetic to the depressant effects of sedatives increases the incidence and severity of overdose reactions. Meticulous dose calculation is required so as not to exceed the maximum recommended dose for each patient. High blood levels can be avoided by spreading the dose injected over the entire period of single treatment rather than injecting the whole dose at the beginning. Negative aspiration should be carried out each time one injects and very extensive procedures should not be carried out in single sittings (Katyal, et al, 2010).

ADVANTAGES AND DISADVANTAGES OF ARTICAINE IN DENTISTRY

Pain control is a major component of patient comfort and safety. Local anesthetics form the backbone of pain control techniques in dentistry. Four percent articaine with epinephrine is an amide local anesthetic that will meet the clinical requirements for pain control of most dental procedures in most patients. The reluctance to use articaine for IANB in dentistry arose following initial reports of prolonged sensory disturbances with articaine use [Hass

and Lennon, 1995]. The incidence of adverse drug reactions is similar among all local analgesia agents [Malamed et al., 2001] and most commonly occur due to accidental intravascular administration of LA solution or direct trauma to the tissues. *Patients allergic to amide-type anesthetic. *Patients allergic to metabisulfites (preservative present in the formula to extend the life of the epinephrine). There is no cross-allergenicity between sulphites (preservatives), sulphur, and the “sulpha”-type antibiotics (Malamed SF. Handbook of local anesthesia. 5th ed. St. Louis: Mosby; 2004). *Articaine is not contraindicated in patients with sulfa allergies; there is no cross-allergenicity between articaine’s sulphur-bearing thiophene ring and sulfonamides (Becker DE; 2006).

CONCLUSION

Although there may be controversy regarding its safety and advantages in comparison to other local anaesthetics, there is no conclusive evidence demonstrating neurotoxicity or significantly superior anaesthetic properties of articaine for dental procedures. Articaine is a safe and effective local anaesthetic drug to use in all aspects of clinical dentistry for patients of all ages, with properties comparable to other common local anaesthetic agents. Therefore, at this time, the decision to use articaine cannot be based on any convincing evidence of superiority over other LA drugs, rather the choice will be based on the personal preference and experiences of individual clinicians (Van Oss GE, Vree TB, Baars AM, 1989). Four percent articaine with epinephrine 1:100,000 is a safe and effective local anesthetic for use in clinical dentistry. In this investigation consisting of three randomized, double-blind trials, we found articaine to be well-tolerated in 882 subjects, and that it provided clinically effective pain relief during most dental procedures. Furthermore, we observed no significant difference in pain relief between subjects in the 4 percent articaine with epinephrine 1:100,000 group and those in the 2 percent lidocaine with epinephrine 1:100,000 group. Articaine also provides the opportunity for research specific to dental hygiene practice. Dental hygiene researchers can build on the dental hygiene body of knowledge by examining articaine and other pain control agents and their effectiveness in dental hygiene practice. Dental hygienists should test this agent out when indicated and watch for future research to clarify its benefits and limitations (Malamed SF., et al, 2000b).

REFERENCE

1. Malamed SF. Handbook of local anesthesia. 4th ed. St. Louis: Mosby; 1997:63-4.
2. Van Oss GE, Vree TB, Baars AM, Termond EF, Booij LH. Pharmacokinetics, metabolism, and renal excretion of articaine and its metabolite articainic acid in patients after epidural administration. *Eur J Anaesthesiol* 1989;6(1):49-56.
3. Van Oss GE, Vree TB, Baars AM, Termond EF, Booij LH. Clinical effect
4. Verma R, Alladi R, Jackson I. Day case and short stay surgery: 2. *Anesthesia* 2011;66:417-3.
5. Gupta A, Kaur S, Khetarpal R, Kaur H. Evaluation of spinal and epidural anesthesia for day care surgery in lower limb and inguinoscrotal region. *J Anesthesiol Clin Pharmacol* 2011;27:62-6.
6. Malamed SF. Handbook of local anesthesia. 5th ed. St. Louis: Mosby; 2004. p. 320.
7. Becker DE, Reed KL. Essentials of Local Anesthetic Pharmacology. *Anesth Prog* 2006;53:98-109.
8. Scott DB, Jebson PJR, Braid DP, et al. Factors affecting plasma levels of lignocaine and prilocaine. *Brit J Anaesth*. 1972;44:1040-1049.
9. Boaro G, Mayer G. Clinical trials of a new local anaesthetic (Carticain) in orthopaedic and traumatologic surgery. *Minerva Anesthesiol* 1979; 45: 299-308.
10. Glatzl A. Regionalanästhesie des Plexus supraclavicularis mit Carticain. *Prakt Anaesth* 1974; 9: 165-7.
11. Vree TB, van Oss GE, Gielen MJ, et al. Epidural metabolism of articaine and its metabolite articainic acid in five patients after epidural administration of 600mg articaine. *J Pharm Pharmacol* 1997; 49: 158-63.
12. Eerola R. A comparative study of carticaine and prilocaine in regional intravenous analgesia. *Prakt Anaesth* 1974; 9: 171-5.
13. Simon MA, Gielen MJ, Alberink N, et al. Intravenous regional anesthesia with 0.5% articaine, 0.5% lidocaine, or 0.5% prilocaine: a double-blind randomized clinical study. *Reg Anesth* 1997; 22: 29-3.
14. Müller WPE, Weiser P, Scholler KL. Pharmakokinetik von.
15. Articain bei der Nervus-mandibularis-Blockade. *Reg Anesth* 1991; 14: 52.
16. Oertel R, Richter K, Weile K, et al. A simple method for the determination of articaine and its metabolite articainic acid in dentistry. *Methods Find Exp Clin Pharmacol* 1993; 15: 541-7
17. Malamed SF, Gagnon S, Leblanc D. A comparison between articaine HCL and lidocaine HCL in pediatric dental patients. *Pediatr Dent* 2000b; 22:307-311.
18. Malamed SF, Gagnon S, Leblanc D. Articaine hydrochloride: a study of the safety of a new amide local anesthetic. *J Am Dent Assoc* 2001; 132:177-185.
19. Meecham JG. Local analgesia, risks and controversies. *Dental Update* 2009;36:278-283
20. Mikesell P, Nusstein J, Reader A, Beck M, Weaver J. A comparison of articaine and lidocaine for inferior alveolar nerve blocks. *J Endod* 2005; 31:265-270.
21. Oertel R, Rahn R, Kirch W. Clinical pharmacokinetics of articaine. *Clin Pharmacokinet*. 1997; 33:417-425.
22. Katyal V. The efficacy and safety of articaine versus lignocaine in dental treatments: A meta-analysis. *J Dent* 2010;38:307-17.
23. Vree TB, Van Oss GE, Gielen MJ, Booij LH. Epidural metabolism of articaine to its metabolite articainic acid in five patients after epidural administration of 600 mg articaine. *J Pharm Pharmacol* 1997;49:158-63.