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ARTICAINE AS PRIMARY LOCAL ANAESTHETIC AGENT – A REVIEW

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Abstract:

Local anesthesia is avital part of the daily routines for a dentist. The recently available local anesthetic agents are efficient in providing high quality nerve blockade in a wide variety of clinical circumstances. There are many local anesthetics available of which the most frequently used is lidocaine but as our understanding of chemistry is expanding newer and safer chemicals for providing anesthesia are also emerging. The aim of this paper is to review the use of articaine in dentistry. The literature review shows articaine is well tolerated and useful local anesthetic agent than lidocaine. Certain added advantages like shorter time of onset, longer duration of action and greater diffusion property makes it an ideal anesthetic agent to be used in dentistry.

Key-words: Articaine, Lidocaine, Local anesthetics,Pharmacology, Drug toxicity, Dentistry.

INTRODUCTION:

Pain control in clinical dentistry is mainly attained using local anaesthetic (LA) drugs. A revolutionary advancement of the late 1800s was the discovery of local anesthetics that facilitated pain prevention without the loss of consciousness. Since that time, a broad spectrum of local anesthetics has been moderately developing. These advancement in pain control have permit the selection and use of local anesthetic drugs based on the individual need of patients and the type of procedures.

Articaine was initially synthesised in 1969 and was used in clinical practice in Germany in 1976 (1). The name was changed in 1984 and it was released in Canada (2). It then entered the United Kingdom in 1998, (1) the United States in 2000 (3) and Australia in 2005 (4). Recently, articaine is available as a 4% solution containing 1:100, 000 or 1:200, 000 adrenaline.

PHARMACOLOGY

Articaine (4-methyl-3-[2-(propylamino)- propionamido]-2-thiophene-carboxylic acid, methyl ester hydrochloride) is a unique amide LA which contains a thiophene, instead of a benzenering (Fig. 1). The thiophene ring facilitate greater lipid solubility and potency as a greater portion of an administered dose can enter neurons.(5) It is the only amide anaesthetic containing an ester group, allowing hydrolysation in unspecific blood esterase.(6) Articaine's amide linkage go through biotransformationin the liver, comparetively slow process, however articaine is additionally inactivated by serum esterases,a fast process starting immediately after injection.(6) About 90% of articaine metabolises rapidly via hydrolysis in the blood into its inactive metabolite articainic acid, which is excreted by the kidney in the form of articainic acid glucuronide.(7) Its metabolism is

age dependent, in which clearance and volume of distribution decreases with increasing age.(8) The elimination serum half-life of articaine is 20 minutes(6) and of articainic acid is 64 minutes.(7) Equal analgesic effectiveness and a lower systemic toxicity (a wide therapeutic range) allows articaine use in aamount higher than other amide LAs.(6) Following maxillary tooth extractions, a high articaine concentration in alveolus blood has been observed post extraction, with an increasing metabolic ratio of articaine to articanic acid.(9) It is believed that local saturation of serum esterases, causing slower and prolonged metabolism, may contribute to the superior relationship between persistence of the local anaesthetic effect and low systemic toxicity.(10) The increased duration of the local anaesthetic effect may also be related to the high degree of protein binding, where the increased tendency of articaine to bind securely to the protein receptor site may provide a longer duration of clinical activity. (11) There is no correlation between the serum concentration and local anaesthetic effect of articaine.(6)

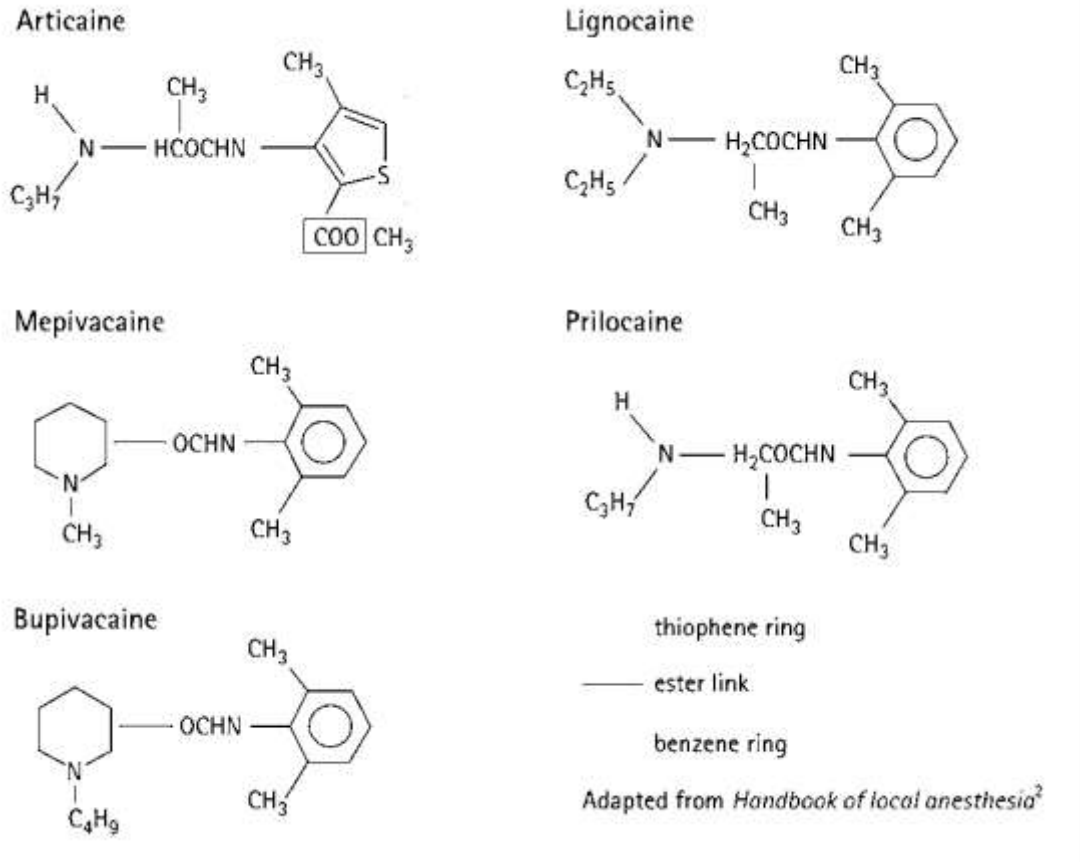

Fig. 1 Structure of amide local anaesthetics

Comparison with other anaesthetics:

It important to compare articaine with most commonly use local anaesthetic agent. Lidocaine was made clinical available in 1948, lidocaine hydrochloride became the first retailed amide local anesthetic (2). At that time, it substituted the ester-type local anesthetic procaine (Novocain) as the drug of choice in dentistry. Lidocaine hydrochloride has sustained its status as the most widely used local anesthetic in dentistry since its introduction. Proven efficacy, low allergenicity, and minimal toxicity through clinical use and research have proved value and safety of this drug. Thus, it is labelled as the "gold standard" to which all new local anesthetics are compared (5).

Clinical comparison on efficacy of articaine over lignocaine:

Articaine has been widely used in dental surgery. Dentists begin to use articaine around 1977 (12). In dentistry, articaine has been researched extensively. Clinical trials comparing articaine mostly with lidocaine have differed in study design and site of action. The majority of references in the literature describing the alleged neurotoxicity of articaideal with paraesthesia and prolonged numbness after dental procedures. An excellent review of the dental literature was published last year (14). The authors came to inference that articaine is a safe and effective local anesthetic drug to use in all aspects of clinical dentistry for patients of all ages, with properties comparable to other common local anesthetic agents. Although there may be debate regarding its safety and advantages in comparison to other local anesthetics, there is no conclusive evidence demonstrating neurotoxicity or significantly superior anesthetic properties of articaine for dental procedures. The choice whether to use articaine or another local anesthetic is based on the individual preference and experiences of

clinicians (15). Currently, articaine is available as a 4% solution containing 1:100,000 or 1:200,000 epinephrine. Clinical trials comparing 4% with 2% solutions show no clinical advantage of 4% over a 2% solution (16,17).

Complications of articaine and lidocaine:

A vast range of complications can occur during or after the injection of local anesthesia. They can be divided into local complications, such as pain on injection, persistent anesthesia, trismus, hematoma, oedema and facial nerve paralysis, and systemic complications such as overdose and allergic reactions. Another crucial complication found common in patients is known as 'Paresthesia'.

Clinical comparison between articaine & lidocaine:

Malamed et al. (3) conducted a study to compare the safety between articaine 4 % with adrenaline 1:100 000, and lidocaine 2 % with adrenaline 1:100 000. The authors presented a report on three identical single-dose, double-blind, parallel-group, active-controlled multicentre studies. A total of 1325 subjects took part in these studies, 882 in the articaine group, and 443 in the lidocaine group. The adverse incident reported by 1 percent or more of patients are shown in table. The overall incidence of adverse events in the combined studies was 22 % in the articaine group and 20 % in the lidocaine group which are listed in Table (2).

Body system/adverse event	Treatment group	
	Articaine 4 % with adrenaline 1:100 000 (n = 882) % (n)	Lidocaine 2 % with adrenaline 1:100 000 (n = 443) % (n)
Body as a whole		
Face edema	13 (1)	6 (1)
Headache	31 (4)	15 (3)
Infection	10 (1)	3 (<1)
Pain	114 (13)	54 (12)
Oral system		
Gingivitis	13 (1)	5 (1)
Nervous system		
Hypoesthesia	7 (<1)	5 (1)
Paresthesia	11 (1)	2 (<1)

Table (2) showing incidence of adverse effects of articaine and lidocaine [Malamed et al. (3)]

USE IN CHILDREN:

Serum concentrations of articaine were similar adults well asin 3-12 years old children, with maximum concentrations of a 2% solution notably lower than that of a 4% one.(18) Numbness and soft tissue injuries, with prolonged numbness are commonly affecting children age under seven. (19) Manufacturer does not recommend use of articaine in children under the age of 4 (20) Yeta retrospective report on 211 children under four years of age gave initial evidence reporting no adverse systemic reactions. (21) A survey involving American dentist (22) reported that 21% of 373 dentists surveyed had used articaine in the 2-3-year-old group. In mandibular primary molars andcanines undergoing operative dentistry, a buccal infiltration of articaine achieved anaesthetic success for all procedures in a study of 50 children aged 4-12 years. (23) In children 3-6 years of age, no difference in the effectiveness of mandibular infiltration was found between articaine, mepivacaine and prilocaine. (24) Lignocaine infiltrations in primary molars were effective and reliable for amalgam and stainless-steel crown restorations but not for a pulpotomy. (25) . in patient aged 4-12 articaine has been as effective as lignocaine. (27) Articaine IO injections in 4-16-year-old children were able to provide successful anaesthesia for a high

proportion of deciduous and permanent teeth, with a significantly higher success rate in maxillary teeth. (28) The available literature
on articaine use in children shows that it is safe and effective for clinical procedures in children of all ages.

SAFETY:

Articaine is one of the safer local anaesthetics because of its rapid metabolism into an inactive metabolite, reducing the risk of systemic toxicity and overdose, even after repeated injection.(6) Early studies on articaine reported no toxic reactions from 100 injections,(12) in 211 paediatric patients(24) and a recent study reported a low number of adverse events comparable to that of lignocaine.(29) Articaine safety after non-surgical dental procedures with an IANB(Inferior Alveolar Nerve Block) is debatable, which advocate articaine having a higher incidence of paraesthesia (persistent anaesthesia or an abnormal or unprovoked sensation). A study using data when articaine was vastly available in the USA contradicted early results, with lignocaine being the most popular L A (35%), followed by articaine and prilocaine (30% each).(39) However, the most recent retrospective study(39) on voluntary reporting of adverse reactions following LA administration in the USA reported from the available data that 4% solutions of articaine and prilocaine were related with a higher frequency of paraesthesia than LAs of a lower concentration. The methodology of data collection needs to be carefully examined. All reports indicative of articaine having neurotoxic potential (31,32,46-49) included voluntary reporting or referral to the respective insurance board for paraesthesia assessment. As referral following paraesthesia was not mandatory, the collected data cannot be taken as representative sample. This has the potential for underreporting, which 'almost certainly exists'(49) and can bring change in the distribution and incidence of nerves affected and LA agents used. The reasons for reporting or not reporting an adverse outcome is beyond the scope of this paper and is an area that needs further research to reduce reporting bias. In addition, some studies did not include complete data and instead made presumption on the procedures involved. Paraesthesia following non-surgical dental procedures is uncommon and the mechanism of nerve damage is unknown,(17) however, suggested theories regarding susceptibility of the lingual nerve to damage include: direct needle trauma, intraneural haematoma formation, local anaesthetic toxicity and the fascicular pattern.(17,50) Incidences of lingual nerve damage due to mandibular block anaesthesia for non-surgical dental procedures have been reported to be between 0.15%(51) and 0.54%(52) and gross estimations of the incidence of paraesthesia after IANB administration for non-surgical procedures range from 1:26,762 to 1:785,000, with the presumption that half of all LA injections involve IANB injections.(29,39,47,48,) To date, there is only one record in the literature of maxillary paraesthesia involving articaine, however, it was following an extraction.(53) Only one record of maxillary non-surgical paraesthesia has been documented, following palatal-anterior superior alveolar nerve block with lignocaine and mepivacaine.(54) From the available literature, it is apparent that paraesthesia is an extremely rare occurrence and regardless of the LA used, most of the non-surgical paraesthesia cases affect the lingual nerve after IANB administration. Currently no scientific proof exists for this observation. Other reports have recommend that it is not the anaesthetic agent itself but instead the available concentration. (46,49,55) This is due to 4% articaine and prilocaine preparations being reported with increased incidences of paraesthesia, but these claims are empirical. Whilst there may be in vitro animal studies linking increased anaesthetic concentration and neurotoxicity, (56) it does not explain why the majority of non-surgical paraesthesia after IANB preferentially involve the lingual nerve. No scientific evidence exists supporting the claim that articaine is related with increased paraesthesia(57,58) and a clear causal relationship has not been established in the literature between anaesthetic agent and neurological complications, such as paraesthesia.(59) These statements currently remain true. In order to prove claims of increased paraesthesia, the current incidence of paraesthesia associated with other anaesthetics needs to be clearly established and further studies are needed to determine a significant increase in paraesthesia associated with articaine, if any. Gaffen and Haas concede that 'it would take an unrealistically large trial or cohort to detect statistically significant differences for an event as rare as nonsurgical paraesthesia' and, in reference to the current data on RCTs(Randomised Control Trials) using articaine, purpose that 'no conclusions regarding permanent paraesthesia should be made from these particular studies'.(49) To date there is only one RCT(3) comparing articaine with other LAs reporting adverse outcomes. This study compared 4% A100 and 2% L100 for simple and complex dental procedures, with respective sample sizes of 882 and 443 and respective incidences of paraesthesia of 1 and less than 1%, and did not offer any suggestion of articaine being related with an increased risk of paraesthesia. In light of this evidence, along with efficacy studies comparing IANBs of articaine with other LAs in sound teeth37 and teeth with IP (Irreversible Pulpitis),62-64 the literature shows that there is neither significant clinical advantage nor significant risk of developing a paraesthesia when using articaine instead of lignocaine for an IANB. Therefore, from the current available literature, there is no scientific proof demonstrating that articaine as a 4% solution is neurotoxic or unsafe to utilize in any aspect of clinical dentistry.

CONCLUSION:

Based on the results of this report, rare use of articaine was seen. An evidence-based approach to the recent available literature indicates that articaine is an effective and well-tolerated anaesthetic for dental use in

comparison to lidocaine. However, practitioners should be aware of a probable, yet unproven, link between 4% concentrations of local anaesthetic solution and nerve damage.

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