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Articaine: A Comprehensive Review

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Abstract

Articaine is an intermediate-potency, short-acting amide local anesthetic with a fast metabolism due to an ester group in its structure. Articaine was developed in 1969, with reported advantages which are increased potency, increased duration of its anesthetic effect and superior diffusion through bony tissue. Hence, the aim of present review of literature is to discuss articaine in detail.

Keywords: Local anesthesia, Articaine, Lidocaine

Introduction

Pain and its successful management have been one of the cornerstones of dentistry worldwide since time immemorial.[1] The successful use of local anesthetic solutions and their diligent administration have helped patients overcome their fears and displeasure towards dentistry. The injection of local anesthetic is perhaps the greatest source of patient fear and inability to obtain adequate pain control with minimal discomfort remains a significant concern of dental practitioners. The achievement of good local anesthesia requires

knowledge of the agents being used, the neuroanatomy involved, best techniques and devices available. The agents and anesthetic delivery equipments available today provide the practitioner an array of options to effectively manage the pain associated with dental procedures.[2]

Lignocaine was marketed in 1948 and is up to now the most commonly used local anesthetic in dentistry worldwide. Proven efficacy, low allergenicity, and minimal toxicity through clinical use and research have confirmed the value and safety of this drug.[3] Thus, it has been labelled as the "gold standard" to which all new local anesthetics are compared. An amide solution was prepared by Rusching et al. in 1969 which was known as carticaine. When it entered clinical practice in Germany in 1976, its generic name was changed to articaine. It differed from other amides as it contains a thiophene ring with additional ester ring.[4] Articaine is able to diffuse through soft and hard tissues more reliably than other local anesthetics, and the maxillary buccal infiltration of articaine provides palatal soft tissue anesthesia obviating the need for a painful palatal injection.[4] Another advantage with articaine is that patients will be drug free more quickly than those who receive other local anesthetics.[5] In addition, superiority of articaine to lignocaine has been claimed in terms of fast onset, excellent quality of anesthesia, and low degree of toxicity.[6] Present review of literature aims to discuss articaine in detail.

History of Articaine

Cocaine was the first reported ester-type local anesthetic for clinical use, in 1886, followed by procaine in 1904. In the search for less allergic compounds with a faster onset, the amide-type local anesthetic lignocaine was synthesized by Swedish chemist Nils Löfgren in 1943 and marketed as lidocaine in 1949. Since then, other amide local anesthetics have been introduced and used clinically for their favourable onset time and duration, eg, mepivacaine, prilocaine, bupivacaine, etidocaine, and ropivacaine. Among this group, articaine, originally synthesized as carticaine, entered dentistry practice in 1973.[7] Epidural administration and comparison with lidocaine started in 1974.[3] In 1984, it was released in Canada, followed by the UK in 1998, the rest of Europe and the US in 2000, and Australia in 2005. Currently, articaine 4% with adrenaline 5 μg/mL is widely used in dentistry.[8,9]

Mechanism of Action

Articaine blocks nerve conduction by reversibly binding to the α-subunit of the voltage-gated sodium channels within the inner cavity of the nerve, similar to other local anesthetics. Binding of articaine to the sodium channel reduces sodium influx so that the threshold potential will not be reached and impulse conduction stops. The blocking action of articaine on the sodium channel is state dependent: it has the highest affinity for the open state, an intermediate affinity for the inactivated state, and the lowest affinity for the resting state. Articaine is an intermediate-potency, short-acting local anesthetic with a fast onset of action.[10,11]

Its chemical structure, different to that of other local anesthetics due to substitution of the aromatic ring with a thiophenic ring, and the presence of an additional ester ring, provides Articaine with increased liposolubility and intrinsic potency, as well as greater plasma protein binding versus other commonly used local anesthetic such as Prilocaine or Mepivacaine. These differential characteristics are in turn clinically reflected by a shorter latency and increased duration of anesthesia, as well as superior bony tissue diffusion.[12]

Figure 1: Articaine

Comparison of Articaine and lidocaine

Concentration of solution: Articaine is delivered as a 4 % solution in as opposed to lidocaine which is 2 %. It may be speculated that if there is a toxic local metabolite involved, it may manifest toxicity simply due to the higher concentration. This also means that when the same recommendations for the maximum doses are applied, one can inject twice as many carpules of lidocaine when compared with articaine. This is important to be aware of during situations where more anesthetics have to be re-injected.[13,14]

Lipid solubility: Lipid solubility affects the anesthetic potency. Increased lipid solubility permits the anesthetic to penetrate the nerve membrane, which itself is 90 % lipid, more easily. Articaine differs from all other amide local anesthetics, in that it is derived from thiophene. As a result, the articaine molecule does not contain a benzene ring like the others but instead contains a thiophene ring. This renders the molecule more lipid soluble and therefore better able to cross lipid barriers, for example the nerve membrane.[14]

Metabolism: Metabolism of local anesthetics is important, because the overall toxicity of a drug depends on a balance between its rate of absorption into the bloodstream at the site of injection and its rate of removal from the blood. Approximately 70 % of the dose of injected lidocaine undergoes biotransformation in patients with normal liver function. Significant liver dysfunction or heart failure represents a relative contraindication to the administration of amide local anesthetics. Articaine differs from other amide local anesthetics, in that it has an extra ester linkage (COOCH3). 90-95 % is metabolized in the blood, and only 5-10 % in the liver. The major metabolic product of articaine is articainic acid. It is inactive as a local anesthetic, and systemic toxicity has not been observed.[3,13]

Excretion: The kidneys are the primary excretory organ for both the local anesthetic and its metabolites. A percentage of a given dose of local anesthetic drug will be excreted unchanged in the urine, and this varies according to the drug. Articaine is largely excreted in the urine as the metabolite articaninic acid, followed by articainic glucuronide and the parent drug. For lidocaine the excretion is also via the kidneys; less than 10 % unchanged, more than 80 % various metabolites.[15]

Onset of action: The average time of onset for subjective symptoms for Articaine in study was 1.35 min (1–2 min) and objective symptoms 2.12 min (1.08–4 min). On comparison to Lidocaine it was subjective symptoms 1.40 min (1–3 min) and objective symptoms 2.15 min (1–4 min).

Duration of Anesthesia: Duration of anesthesia is proportional to its degree of protein binding. However, the duration of the effect of the local anesthetic is also dependent on the injection site or concentration of

vasoconstrictor present in the anesthetic solution, among other factors. Articaine presents one of the greatest protein binding percentages of all amide local anesthetics, comparable only to ultra-long action substances such as Bupivacaine, Ropivacaine and Etidocaine.[12]

Haas et al. (1990)[16], Vahatalo et al. (1993)[17] and Costa et al. (2005)[18] stated that 4 % Articaine with 1:100,000 epinephrine clinically presented the shortest onset and the longest duration periods.

The long period of analgesia for Articaine explained by Gregorio et al. (2008) in their study stated that the concentration of Articaine in the alveolus of a tooth after extraction is about 100 times higher than in systemic circulation. This saturable local Articaine mechanism has been considered as possibly contributing to the observed duration of the local anesthetic effect.[19]

Efficacy of Articaine: Tofoli et al. (2003) and Moore et al. (2007) reported that 4 % Articaine anesthetic formulations containing epinephrine provided excellent surgical pain control. For patients who can tolerate higher amounts of epinephrine, the 4 % Articaine 1:100,000 epinephrine formulations had the additional therapeutic advantage of providing better visualization of the surgical field and less bleeding.[20,21]

Potency of Articaine: Articaine is 1.5 times as potent and only 0.6 times as toxic as lidocaine and has been shown to be superior in achieving successful anaesthesia following infiltration.[12]

Safety of Articaine: The safety of articaine use in children under 4 years of age was documented in a 1989 retrospective report by Wright et al. reviewing 211 pedodontic cases using articaine. No adverse reactions were observed, therefore, the review stated that articaine is safe to use in children under age 4.[22] Articaine was recognised as safe and efficacious in children of all ages in a 2011 comprehensive review of articaine. A subsequent 2018 study found that there is no difference between articaine and lidocaine in frequencies of anaesthetic-related adverse events in children.[23]

Adverse effect of Articaine: A wide range of different 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/paresthesia, trismus, hematoma, oedema and facial nerve paralysis, and systemic complications such as overdoses and allergic reactions.

Among all, paresthesia is the most common. Paresthesia can be defined as persistent anesthesia (anesthesia well beyond the expected duration), or altered sensation (tingling or itching) well beyond the expected duration of anesthesia. The definition of paresthesia also includes hyperesthesia and dysesthesia. Hyperesthesia is defined as increased sensitivity to noxious stimuli, and dysesthesia as painful sensation to non-noxious stimuli. The symptoms are most commonly associated with mechanical trauma during surgical procedures. During the administration of anesthesia for a mandibular nerve block, the lingual or inferior alveolar neurovascular bundle can be traumatized by the sharp needle-tip, the movement of the needle, extraneural or intraneural hemorrhage from trauma to the blood vessels, or from neurotoxic effects of the local anesthetic.[3]

Advantage of Articaine[24,25]

- The clinical advantages of Articaine include the duration of its anesthetic effect - only surpassed by ultra-long acting anesthetics such as Bupivacaine, Etidocaine and Ropivacaine - and its superior diffusion through bony tissue

- Articaine showed faster onset and duration of anaesthesia than lidocaine for buccal infiltrations
- Articaine is an efficient and safe LA to treat children between ages three and four.
- Articaine's anaesthetic success rate was significantly higher than lidocaine's and mepivacaine's for supplemental buccal infiltrations.
- Articaine can be used as buccal infiltration for invasive treatment of mandibular molars in children ages eight to fifteen. There was no difference in anaesthesia success between lidocaine mandibular blocks and an articaine buccal infiltration.

Contraindication of Articaine[3]

- Allergy to amide-type anesthetics.
- Allergy to metabisulfites
- Idiopathic or congenital methemoglobinemia (not a concern in dental practice due to the small volumes of articaine used)
- Hemoglobinopathy, such as sickle cell disease

Discussion

Local anesthetic is both the savior and the bane of modern dentistry, which is ironic. It allows for nearly painless treatment. The emergence of articaine is generating considerable interest because of its considerable faster onset of action and longer duration of action and its comparable safety and potency. The advantages of articaine are as follows: Articaine causes a transient and completely reversible state of anesthesia (loss of sensation) during dental procedures; in dentistry, articaine is used both for infiltration and block injections, and with the block technique, it yields the greatest duration of anesthesia; also, in people with hypokalemic sensory overstimulation, lidocaine is not very effective, but articaine works well.[26]

Malamed compared both the anesthetics in a study and concluded that articaine was safe ,tolerated well and was effective in pain relief.[4] In another study done by Vahatalo et al. in 1993 articaine and lidocaine were compared and he found no difference in the duration of action and onset of anesthesia between the two.[27]

In tandem with the various studies, it can be said that 4% articaine hydrochloride is more effective than 2% lignocaine hydrochloride in dental procedure. It has proved its mettle as a safer alternative from a cardiovascular standpoint, making it better suited over lignocaine. The higher anesthetic efficacy makes articaine patient-centric, which helps maximise patient compliance.

Conclusion

The conclusion of this review of literature that articaine is a safe and efficacious LA for all routine dental procedures in patients of all ages.

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