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UPDATES IN ARTICAINE USE IN DENTISTRY

АРТИКАИН ВО СТОМАТОЛОГИЈАТА - НОВИ СОЗНАНИЈА

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Abstract

Introduction: Most dental procedures require local anesthesia. Today, a variety of commercially available anesthetics are used in dental practice. One of the reasons science is constantly striving to improve these chemicals in terms of their effectiveness and safety is that an ideal local anesthetic has yet to be discovered. Articaine 4% solution is one of the newer amide anesthetics with an ester bond. Its popularity among dentists is growing rapidly, despite the fact that its the effectiveness and safety in comparison to other anesthetics is still unproven according to some authors. **The aim** of this paper is to summarize the current knowledge about articaine and to compare its potency, efficacy, and safety in use. **Material and method:** Existing works were researched using PubMed as our main source, as well as Web of Science and Google Scholar. We used the following keywords to search for the effectiveness and potency of articaine: "articaine and (comparative or compare or efficacy or potency)"; this yielded 145 results from papers published in the last 5 years. For the safety analysis, keywords were: "articaine and (safety or safe or toxic or toxicity or paresthesia or dysesthesia)", and 75 results were found from publications in the last 10 years. Our research also includes clinical trials and reviews from Google Scholar that do not have specific keywords and time frames. **Results:** The efficacy and safety of using 4% articaine are satisfactory, according to the summarized information from the existing literature. In comparison to other local anesthetics, articaine is a superior anesthetic. Its metabolic and pharmacokinetic properties improve performance in terms of anesthesia effectiveness, and duration, which is especially important in elderly and medically compromised patients. **Conclusion:** Articaine is widely used in surgical and non-surgical dental procedures, as well as in dental surgery, and its use has been extensively researched. Every clinician is free to use articaine or another local anesthetic, based on their own personal preference and experiences, as well as the most recent updates on articaine safety, potency and efficacy presented in this review. **Key words:** articaine, anesthesia, safety, potency, efficacy

Апстракт

Вовед: Локалната анестезија е неодвоива од најголем број од стоматолошките процедури. Во денешно време постојат голем број на комерцијално достапни анестетици кои се користат во денталната пракса. Фактот дека сеуште не е пронајден идеален локален анестетик, е една од причините што науката постојано се залага за унапредување на овие хемикалии во смисла на нивна ефикасност но и безбедност во исто време. Артикаинот како 4% раствор е еден од поновите амидни анестетици кој во себе содржи и естерска врска. Неговата популарност забрзано расте кај стоматолозите, иако ефикасноста и безбедноста во споредба со другите анестетици е според некои автори сеуште недокажана. **Целта** на трудот е сумирање на досегашните сознанија во врска со артикаинот и неговите компаративни анализи во однос на потентноста, ефикасноста и безбедноста при користење. **Материјал и метод:** Истражување на постоечките трудови на PubMed, како наш главен извор, Web of Science и Google Scholar. При пребарување за ефикасноста и потентноста на артикаинот ги користаевме следниве клучни зборови: "articaine and (comparative or compare or efficacy or potency)"; што покажа вкупно 145 резултати од трудови објавени во последните 5 години. За анализа на безбедноста при користење клучни зборови беа: "articaine and (safety or safe or toxic or toxicity or paresthesia or dysesthesia)", со пронајдени 75 резултати од објавите во последните 10 години. Во нашето истражување земени се предвид и клинички студии од Google Scholar без посебни клучни зборови и временски рамки. **Резултати:** Според сумираните информации од постоечката литература, ефикасноста и безбедноста при употребата на 4% артикаин се на задоволително ниво. Во споредба со другите локални анестетици, артикаинот може да се смета за супериорен анестетик. Неговите метаболички и фармакокинетски својства даваат подобри перформанси во однос на ефективноста и времетраењето на анестезијата и се особено важни кога станува збор за постари и медицински компромитирани пациенти. **Заклучок:** Артикаинот е широко користен во хируршки и нехируршки стоматолошки процедури, а неговата употреба е опширно испитувана. Секој клиничар има право да избере дали да користи артикаин или друг локален анестетик, врз основа на неговите лични преференци и искуства како и на најновите ажурирања за безбедноста, моќта и ефикасноста на артикаинот претставени во овој преглед. **Клучни зборови:** артикаин, анестезија, безбедност, потентност, ефикасност.

Introduction

Local anesthesia is the foundation of pain management in dental procedures. If used properly, local anesthetics are one of the safest and most effective drugs for the management of perioperative and post-operative pain[1]. Local anesthetics are one of the most commonly used substances in dentistry. Pain relief makes the patient more comfortable,

allowing the dentist to concentrate and work more efficiently. The normal sensation returns after a short period of time[2] Local anesthetics have been used since 1860, when cocaine was discovered. The Production of Lignocaine/Lidocaine significantly improves the local anesthesia procedure and quickly becomes the gold standard, against which all other new local anesthetics are compared[1]. Etidocaine, Bupivacaine, Mepivacaine, Articaine and other drugs were later discovered. Rusching discovered Carticaine in 1969, and the name was changed to Articaine in 1976 in Germany[3]. Its use gradually spread throughout the world. North America and Canada in 19834, the United Kingdom in 1998, and the United States and Australia in 2000 and 2005. Articaine is the first and only local anesthetic designed specifically for use in dentistry. Articaine is classified as an amide local anesthetic, but it has chemical properties of both the amide and ester groups. Wherever it has been made available, it has become an extremely popular local anesthetic. It was the second most commonly used local anesthetic in the United States (after lidocaine) in 2014[5]. Articaine is used by 70% of dentists in Australia[6]. Articaine was used by 97% of dental professionals in Germany in 2012[7] Articaine's use is rapidly increasing as it becomes one of the world's most popular local anesthetics[8].

The main benefits of articaine are its pharmacological properties. Its molecular structure contains an ester group, making it the only local anesthetic with both amide and ester groups, allowing the drug to be metabolized by plasma esterase and by microsomal enzymes in the liver. Numerous studies have been conducted since its discovery to compare articaine with various anesthetic agents.

Aim

The aim of this paper is to summarize current knowledge about articaine and to compare its potency efficacy, and safety in use. In everyday practice, summarizing this information can help you choose a local anesthetic.

Material and methods

To achieve our goal, we reviewed existing papers in the PubMed medical database, as our main source, as well as Web of Science, and Google Scholar search which cover a broader range of publications and provide easier access to full text documents. For each section of our research, we used a different search query. To compare the potency and efficacy of articaine with other local anesthetics we used the following search query: "articaine and (comparative or compare or efficacy or potency)", which yielded 145 results, with the only filter applied: "in the last 5 years". We searched for "articaine and (safety or safe or toxic or toxicity or paresthesia or dysesthesia)" to assess the safety of using articaine in our practice. We discovered 75 paper by, searching for studies published in the last 10 years. In our research on Google Scholar and other databases, there was no specific search query or time period.

Results and discussion

Potency and efficacy of articaine

Local anesthetics relieve pain by interfering with the propagation of peripheral nerve impulses,thereby inhibiting the generation and the conduction of action potentials. When the nerve membrane is at its normal resting potential, local anesthetics have no effect on it.

Articaine binds to the α-subunit of the sodium channels, preventing nerve conduction. As a result of the sodium influx not reaching the threshold potential, nerve conduction ceases. The action of binding with sodium channels to block conduction is state dependent, with the highest affinity for the open state, intermediate for the inactivated state, and lowest affinity for the resting state[9].

The diameter of the nerve has a significant impact on the degree of neuronal block. Fibers with larger diameter (usually for pressure, touch, motor) require higher anesthetic concentrations than small, myelinated fibers (pain conduction)[10].

The efficacy and potency of local anesthetics are affected by several factors, including fiber type and size, ion balance, myelination, vasoconstrictor or vasodilator properties (vascular uptake), pH (lower pH causes greater ionization, which reduces efficacy), frequency of nerve stimulation, electrolyte concentration (hypercalcemia and hypokalemia can reduce nerve block), and other factors that are not directly related to the chemical composition of the anesthetic solution but to the overall condition of the organism, anatomical and morphological properties or the use or non-use of a vasoconstrictor with the anesthetic solution. Lipid solubility, protein binding affinity and vasodilator activity are the main factors that affect the potency and efficacy of local anesthetics and are dependent on their chemical structure and are frequently used to compare different local anesthetics. The lipid solubility of the molecules determines their ability to penetrate the nerve membranes[11].

The potency of local anesthetics is affected by lipid solubility. Because 90% of the membrane is lipid, increasing lipid solubility allows the anesthetic to penetrate the nerve membrane more easily[11]. Articaine has a different chemical structure than all other amide local

anesthetics.. It is based on thiophene. So, its molecule contains thiophene ring rather than a benzene ring, which is a structural component of other anesthetics. As a result, the molecule is more lipid soluble and can easily pass through lipid barriers, such as the nerve membrane[12].

Duration is affected by protein binding. When the protein binding ability is increased, the cations of the anesthetic can become more firmly attached to the proteins at the receptor sites, extending the duration of action. Articaine has remarkable ability to bind proteins. Vasodilator activity has a significant impact on the potency and duration of local anesthetics. When vasodilator activity is high, blood flow to a region increases, anesthetic molecules are quickly removed from the injection site. This is the cause of decreased anesthetic potency and duration. If both lidocaine and articaine are used without vasoconstrictor, they would be ineffective and more toxic because of their vasodilator activity. Adrenaline, a vasoconstrictor, is added to increase both the duration and safety.

According to some early studies, the potency of analgesia or relative analgesic potency of articaine is intermediate whencompared to lidocaine[13-15].

The high efficacy might be one of the main reasons why articaine became so popular in many countries. Dentists who use articaine for local anesthesia claim that they rarely miss with the IANB (inferior alveolar nerve block), and that maxillary buccal infiltration often is sufficient for extraction of a molar, because of articaine's excellent bone penetration properties. Many dentists from around the world report about the excellent efficacy of articaine, based on their clinical practice and experience. They claim that articaine works better and faster, that they do not miss as many times and can easily numb patients when other anesthetics fail[16,17].

However, the research findings concerning the reported advantage of 4% articaine over other anesthetics (often compared to 2% lignocaine) appear to be conflicting. In a clinical trial, it is difficult to demonstrate statistically significant superiority (evidence-based medicine) of 4% articaine over any other amide local anesthetic[16,17].

The methods used to compare two or more substances, such as articaine and lidocaine, are a critical issue. To obtain statistically significant data, we need a sample size with a sufficient number of subjects. It is possible that some studies cannot show significant differences because of this issue. That could be one of the reasons why articaine in several studies is slightly more effective than lidocaine, but the difference is not statistically significant.

Normally, the next step is to find literature support for some of these clinical findings. In one study, conducted by Malamed et al. (2001), they compared the efficacy of 2% lidocaine and 4 % articaine with adrenaline 1:100 000[18]. Articaine was injected in 882 subjects, and lidocaine in 443. For the determination of the efficacy a visual analog scale was used (VAS). There were no significant differences[18]. Similar findings were obtained by Vehetalo & al.[19].

Other studies also compared articaine to different anesthetics, such as the one conducted by Haas et al[20], who compared articaine with adrenaline 1:200 000 to prilocaine with same adrenaline concentration. The aim of their study was to test the claims that labial injection of articaine is enough to provide anesthesia for mandibular teeth (pulpal anesthesia) as well as lingual and palatal soft tissue. The determination was made by measuring sensation to electrical stimulation at the teeth, lingual and labial soft tissue for canines and second molars. There were no statistically significant differences[20].

On the other hand, in contrast to previously mentioned studies, Ruprecht & al. (1991) demonstrated the superiority of articaine by comparing equimolar concentrations of lidocaine and articaine, demonstrating significantly longer duration of pulpal anesthesia, regardless of the vasoconstrictor content[21].

An older study conducted by Winther & Nathalang (1972) found that articaine was significantly superior to lidocaine in terms of extent, frequency, and duration of analgesia[22]. Concentration of adrenaline is another critical issue. According to Tofoli & al. (2003), the anesthetic effects gained by 4% articaine with 1:100 000 or 1:200 000 adrenaline used for inferior alveolar nerve blocks are the same[23]. As a result, 1:200 000 is the recommended adrenaline concentration of local anesthetics for dental procedures (Jacob 1989)[24], with the exception of some other procedures (e.g., surgical interventions) that require larger degree of hemostasis. In these cases, according to some authors, the recommended adrenaline concentration is 1:50 000 (Buckley & al. 1984) or 1:80 000 as used in Scandinavia[25]. However, 4% articaine and 2% lignocaine both with 1:100 000 adrenaline demonstrated similar properties when used in surgery and a good tolerance and safety profile[26].

Articaine with adrenaline (1:100 000), used for buccal infiltration of mandibular molars, showed a higher success rate than lignocaine with same adrenaline concentration[27,28], but failed to anaesthetize teeth with irreversible pulpitis[29]. Comparable efficacy was demonstrated using 4% articaine with 1:100,000 adrenaline and 2% lignocaine with 1:100,000 adrenaline for intra-ligamentary injections[30]. In the attempt to anesthetize mandibular teeth with irreversible pulpitis using inferior alveolar nerve block injection, articaine and lidocaine had similar effects[31-33].

Some studies concluded that 4% articaine outperforms 2% lidocaine in terms of latency and duration of the local anesthetic effect, but did not show significant differences in anaesthetic efficacy[34]. Similar results were found when the success of inferior alveolar nerve blocks were compared. So, in case of inferior alveolar nerve block, articaine and lignocaine performed similarly[35]. In comparison to lidocaine infiltration, articaine infiltration produced a faster onset and longer duration of pulpal anaesthesia[36]. Supplemental vestibular (buccal) infiltration with articaine in an attempt to anesthetize mandibular molars with irreversible pulpitis, was more effective than lignocaine[37], which could be due to a concentration effect or the greater ability of articaine to diffuse through the bone.When their efficacy in maxillary buccal infiltrations in patients with irreversible pulpitis was compared, articaine had a statistically significant advantage over lidocaine[38]. This high success of articaine injections may be due to the higher lipid solubility and more molecules/ml injected when compared with lignocaine[39]. When used for periodontal surgery, 4% articaine mixed with 1:100 000 or 1:200 000 adrenaline provides excellent surgical pain control[40].

In a systematic review, articaine was found to be more effective than lignocaine, in providing local anesthesia in the first molar region, with similar adverse effects[41,42]. The conclusion of another meta-analysis study was that articaine had a higher probability of achieving local anaesthetic success than lignocaine[43], especially for infiltration, with an odds ratio of 3.81 (95 % CI, 2.71-5.36; P<0.00001), and although weaker, but still significant, for mandibular block anesthesia, with an odds ratio of 1.57 (95% CI, 1.12-2.21; P =0.009)[43].

Clinical trials comparing articaine to other local anesthetics have varied in study design and site of action comparing articaine with lidocaine in most of the cases, with lidocaine being known as the current standard for comparing all new local anesthetics[44]. In his report, Cowan revealed satisfactory clinical properties of articaine, but also a variable onset time and poor predictability for profound anaesthesia[45]. Maxillary teeth anesthesia has yielded varying results; articaine may have a significantly shorter latency and longer duration of anesthesia of the pulp than lignocaine in posterior teeth36 but not in anterior teeth[46]. Articaine showed better properties in maxillary lateral incisors than lidocaine but not in maxillary first molar[47]. There were no significant differences between articaine and prilocaine in anaesthetic duration and onset time[48], nor in the ability of these local anesthetics to induce pulpal anesthesia, buccal or palatal tissue anaesthesia in maxillary second molars[49] or canines.

No significant difference was found in the anesthetic success rate in some trials where articaine and prilocaine were used for mandibular buccal infiltrations comparing pulpal, buccal or lingual anesthesia for mandibular canines or second molars[49], or when buccal injections were compared to buccal and lingual injection of articaine in mandibular first molars. Articaine buccal infiltrations have significantly higher anaesthetic success rates than lidocaine in lower first molars[50,51], premolars and molars and in the mental nerve block for mandibular premolars, canines and lateral incisors[52] .

There were no significant differences in the ability of articaine and lignocaine to achieve pulpal anaesthesia when a periodontal ligament injection was used in mandibular first molars[49]. If we want to provide a pulpal anesthesia for mandibular teeth, we usually use the inferior alveolar nerve block, but in 15 to 20% of the cases, adequate anesthesia is not provided. Lignocaine and Articaine had comparable success rates when used for inferior alveolar nerve block[53].

An additional buccal injection of articaine adjacent to a mandibular molar after an inferior alveolar nerve block has been shown to have a significantly higher success rate than lidocaine in mandibular posterior[54] and anterior teeth[55]. Some reports concluded that there is no significant increase of the effect of anesthesia of mandibular teeth when lignocaine is injected as a supplemental buccal or lingual infiltration[56] or mylohyoid nerve block after an inferior alveolar nerve block[57]. In one study, articaine was used for an inferior alveolar nerve block and buccal infiltration, both injections showed similar success rates in providing pulpal anesthesia for mandibular first molar; however, the buccal infiltration had a faster latency[58].

If articaine is used to extract impacted mandibular third molars, the period of postoperative anesthesia and duration of analgetic effects is significantly longer than when mepivacaine[59] and lignocaine are used. Articaine provided comparable duration of postoperative analgesia to bupivacaine[60], but had a significantly shorter duration and latency of soft tissue anesthesia.

When maxillary teeth must be extracted, palatal injection may not be necessary if articaine is injected in a buccal infiltration[61-63]. It is possible that most of the impacted maxillary third molar extractions can be performed without palatal anesthesia if articaine is used as the anesthetic of choice[64]. These results back up the findings of Badcock et al.[65]. They used lignocaine for buccal and placebo saline for palatal infiltrations in the extraction of maxillary third molars. The conclusion is that when lignocaine is infiltrated buccaly, a palatal injection may not be necessary. On the other hand, when the palatal diffusion of articaine in the maxillary first premolar and molar region was evaluated in clinical and magnetic resonance imaging study, there was no evidence of anesthesia following needle prick stimulation or articaine in the palatal tissues[66].

Safety

If we want to put a new local anesthetic on the market, it must go through various testing procedures such as in vitro studies, testing on animals and clinical testing. Some local anesthetics, such as lidocaine, are well known and their effects and side effects are documented. Articaine, on the other hand, is not as old as lidocaine, although it has been used for 30 years in some European countries.

The possibility of intravascular injection of local anesthetic in oral cavity is not so remote because of high vascularization in this area. The symptoms and signs of toxicity are commonly associated with the cardiovascular system and CNS. CNS intoxication causes disorientation, dizziness, anxiety, visual and auditory signs, muscular tremor etc. According to some studies, intravascular injection of lidocaine causes CNS toxicity more frequently and to a greater extent than articaine[67]. Other concluded that intravascular injection of 80mg 4% articaine (one cartridge) causes no signs of toxicity in healthy patients, which is confirmed by LD50, 37mg/kg for articaine and 33.2 mg/kg for lidocaine[68]. LD50 denotes lethal dose for 50% of the defined population.

Articaine has very low immunogenic potential. The frequency of allergic-type reactions is comparable to that of lidocaine, although there are several factors that alter the predictability such as age, genetics, frequency, and route of administration, etc.[69]

Patients that might be allergic to articaine may also be allergic to lidocaine or other amide local anesthetics. In the formulation of articaine, there is a vasoconstrictor preservative, sodium metabisulphite, which may cause allergic reactions in patients with sulphite sensitivity, such as some people with allergic-type asthma[18]. It is claimed that both articaine and prilocaine can cause methemoglobinemia. This type of side effect is very unlikely, when used in dental practice. No cases of methemoglobinemia have been reported when anesthetics are used at the recommended dosages[12]. Earlier formulations of articaine and other local anesthetics contained a bacteriostatic, antifungal and antioxidant preservative for the local anesthetic itself, called methylparaben, which is allergenic. It was part of articaine until the mid-1990`s.

All anaesthetics have the potential to be dangerous, causing different adverse effects such as symptoms of dizziness, disorientation, tremors, convulsions, seizures, and cardiac and respiratory depression[70,71]. Articaine might be one of the safer anaesthetics because of its rapid metabolism into an inactive metabolite, lowering the risk of systemic complications, even after repeated injection.

Some early studies on articaine from 100 injections in 211 paediatric patients reported no toxix reactions[72] and lower adverse events when compared to lidocaine. Some studies reported different adverse reactions to articaine such as ophthalmologic complications, hypersensitivity, chills and arthralgia, ischemic skin necrosis and fever[73-76]. Based on four retrospective reports, there is some controversy regarding the safety of using articaine, in non-surgical dental procedures with an inferior alveolar nerve block, in which articaine has a higher incidence of paraesthesia[77-80]. Articaine is the local anesthetic most commonly associated with paraesthesia (34–60%), the majority of cases involved the lingual nerve (71–93%) and no nerves in the maxilla were affected[77-80]. Prior to the release of articaine in the United States, similar studies revealed that the lingual nerve was mostly involved with similar incidence of involvement (71–83%) and lignocaine as the most commonly used local anesthetic (67%)[81,82]. Some later studies contradicted these early findings, with lignocaine still being the most used local anesthetic (35%), than articaine and prilocaine (30% each)[83]. However, according to one retrospective study from 2010, 4% solutions of local anesthetics (articaine and prilocaine) were more associated with cases of paraesthesia than local anesthetics with a lower concentration. Only one case of paraesthesia was linked to a Gow-Gates[8], with the rest being linked to an inferior alveolar nerve block.

Studies that have documented paresthesia after inferior alveolar nerve block included only non-surgical procedures, except for one, which included one simple dental extraction and another in which 64% of their sample were cases with unknown procedural details. When the methodology of data recruitment is not carefully examined and referral after paresthesia is not compulsory, then the collected data cannot be considered a representative sample, because this has the potential for underreporting, which certainly exists and can change the distribution and incidence of nerves affected and local anesthetic agents used.

Paresthesia as a complication of non-surgical dental procedures is extremely rare and its mechanism is unknown; however, there are few theories regarding susceptibility of the lingual nerve damage: direct needle trauma, local anesthetic toxicity, intraneural hematoma formation, and the fascicular pattern[85]. Incidences of lingual nerve damage caused by mandibular block anesthesia for non-surgical dental procedures have been reported to be between 0.15%[86] and 0.54%[87] and gross estimations of the incidence of paresthesia after inferior alveolar nerve block administration for non-surgical procedures range from 1:26,762 to 1:785,000, assuming that half of all injections involve inferior alveolar nerve injections[77].

There is only one report in the literature of maxillary paresthesia after articaine injection, following an extraction[88], and one report of maxillary non-surgical paresthesia, with lignocaine and mepivacaine[89]. According to the available literature, it is evident that paresthesia is an extremely rare occurrence that occurs regardless of the local anesthetic.

Most of the non-surgical paresthesia cases affect the lingual nerve after inferior alveolar nerve block. According to some reports, the concentration of the local anesthetic is more closely related to complications such as paresthesia than the anesthetic agent itself[90]. Although there have been some in vitro animal studies linking increased anesthetic concentration and neurotoxicity[91], this still does not explain the preferentially involvement of the lingual nerve. There is no scientific evidence to support the claim that articaine is more associated with paraesthesia than the other anesthetics[92,93] and there is still no clear causal relationship in the literature between anesthetic agent and paresthesia[94].

All of the studies that suggest that using articaine has an increased risk of neurotoxicity are retrospective and biased in data recruitment, lack high level evidence and consequently are unsuitable for strong recommendations[95]. In order to prove claims of increased paresthesia, the current incidence of paresthesia associated with other anesthetics needs to be clearly established and further studies are needed to demonstrate a notable increase in paresthesia associated with articaine. These claims should be randomized controlled trials that will contribute to the highest level of evidence, and their design can maximize control over the environment while providing convincing causal relationship[96]. According to Gaffen and Haas, it would take an unrealistically large trial to detect statistically significant differences for an event as rare as nonsurgical paresthesia and in reference to the current data on randomized controlled trials using articaine, they advocate that no conclusions regarding permanent paraesthesia should be drawn from these particular studies. To date there has only been one randomized controlled trial comparing articaine to other local anesthetics that has reported adverse outcomes. The comparation of 4% Articaine and 2% Lidocaine for various types of dental procedures, with respective samples of 882 and 443, did not offer any association of articaine with an increased risk of paresthesia. Considering this evidence, as well as efficacy studies comparing inferior alveolar nerve blocks of articaine with other local anesthetics in sound teeth and teeth with irreversible pulpitis[97,98], the literature demonstrates that there is neither clinical advantage nor higher risk of paresthesia when using articaine instead of lignocaine for inferior alveolar nerve block. Therefore, there is no scientific evidence from the current available literature demonstrating that articaine as a 4% solution is neurotoxic or unsafe to use in any aspect of clinical dentistry.

Articaine has been widely used in non-surgical dental procedures and dental surgery since aroud 1977, and its use has been extensively researched. In the clinical trials, articaine is usually compared with lidocaine. All these studies have varied in terms of study design and site of action. There are many controversial data regarding the association of articaine with neurotoxicity like paresthesia or prolonged numbness after dental procedures. Based on an excellent review of the dental literature, the authors[99], concluded that articaine is a safe and effective local anesthetic in all aspects of clinical dentistry for all patients of various ages, with suitable properties, comparable to other common local anesthetics. Although there could be some controversy about its safety and advantages over other local anesthetics, there is no convincing evidence demonstrating the connection with neurotoxicity or some significantly superior anesthetic properties of articaine over the other local anesthetic drugs for surgical or non-surgical dental procedures. Currently, articaine is available as a 4% solution containing 1:100,000 or 1:200,000 epinephrine. Although clinical trials have not found significant advantage of 4% anesthetic solutions (like articaine) over the other (2%) local anesthetics100, the number of dental practitioners who use 4% articaine is growing, and they feel more comfortable practicing dentistry with this local anesthetic where “chances of failing are lower”. It might be due to its superior diffusion through bony tissue or grater bone penetration. Its higher lipid solubility accelerates diffusion through the nerve membranes, resulting in faster anesthetic effect. Because articaine is hydrolyzed into the blood plasma by the action of nonspecific cholinesterase, it is the preferred anesthetic of choice in patients with impaired liver function. Its metabolic product, articainic acid, is inactive and systemic toxicity has never been observed.

Conclusion

According to the summarized information from the existing literature, it can be concluded that the efficacy and safety of using 4% articaine are at a satisfactory level. Articaine has superior diffusion through bony tissue (grater bone penetration) and greater lipid solubility that accelerates diffusion through the nerve membranes, resulting in faster anesthetic effect. Articaine is hydrolyzed into the blood plasma by the action of nonspecific cholinesterase and is a preffered anesthetic of choice in patients with impared liver function. The presence of an ester group makes articaine much less toxic

and thus an anesthetic of choice in patients with advanced age and chronic diseases. Every clinician is free to use articaine or another local anesthetic, based on their own personal preference, experiences and data from this review.

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