Articaine and Lidocaine: how their chemical properties can impact your clinical use

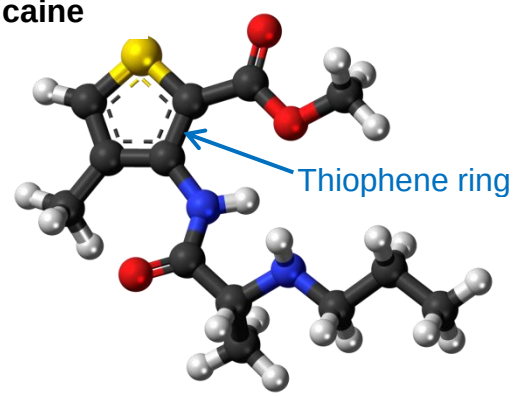
Introduction

Local anesthetics such as **lidocaine** and **articaine** are the most commonly administered medications in dentistry.

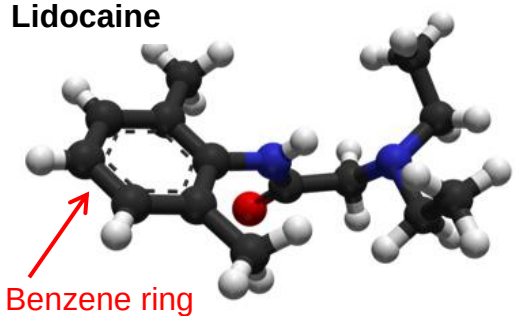
To appreciate the differences in these agents the chemical properties that differentiate them is important.

The chemistry and pharmacology of a local anesthetic can give valuable information about which clinical effect you can expect when you use them.

Articaine



Lidocaine



Key items

- Reinjection
- Drug potency
- Onset of action
- Duration of anesthetic effect
- Toxicity
- Use in patients younger than 4 years old
- Use in geriatric patients
- Complications

Reinjection & Elimination half-life

The half-life of a drug is the amount of time that it will take the plasma concentration of a drug to be halved. Articaine contains an additional ester group that is quickly (and mostly) hydrolyzed by plasma esterases. This gives articaine an elimination half-life of approximately 20 minutes. The half-life of lidocaine is approximately 90 minutes. Lidocaine is mostly hydrolyzed in the liver. The enzymes in the liver act slower than plasma enzymes.

This makes reinjection of articaine safer, since the majority of the initial dose is metabolized after approximately half an hour, and the reinjected dose will not be added to the initial dose.[1]

Local anesthetic	**Articaine**	**Lidocaine**
Elimination half-time	20 minutes	90 minutes

Drug potency & Lipid solubility

Lipid solubility affects the anesthetic potency. Potency represents the measure of a drug activity expressed in terms of the amount that is required in order to produce an effect of given intensity. The higher the lipid solubility, the greater the ability to cross the lipid membrane of the epineuria, which is 90% lipid. [2]

The lipid solubility of articaine is higher than lidocaine because it's molecular structure contains a thiophene ring whereas lidocaine contains a benzene ring. Thiophene is more lipid soluble than benzene.[3]

Local anesthetic	**Articaine**	**Lidocaine**
Lipid solubility	49.5%	2.9%

Onset of action & Dissociation constant (pKa)

The dissociation constant (pKa) affects the onset of action. A lower pKa means that more uncharged base molecules are present to diffuse through the nerve sheath and thus the onset time is decreased. Articaine has a lower pKa than lidocaine.[4]

Local anesthetic	**Articaine**	**Lidocaine**
pKa	7.8	7.9

Duration of anesthetic effect & Protein binding

Local anesthetics are bound in different degrees of intensity to the proteins found in tissues including the nerves. This parameter affects anesthesia duration. The more highly protein bound an agent is, the longer it will stay and have an extended duration of action. In addition, highly protein bound agents are not reabsorbed into the central circulation as quickly and therefore may have a lesser tendency towards systemic toxicity. Articaine protein binding is higher than that of lidocaine.[4]

Local anesthetic	**Articaine**	**Lidocaine**
Protein binding	95%	65%

Metabolism & Systemic toxicity

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 the liver of patients with normal liver function.

Articaine differs from lidocaine in that it is 90-95% metabolized in the blood and only 5 – 10% in the liver. Since articaine is not as dependent as lidocaine for liver metabolism, there is a higher degree of safety found with articaine in patients with hepatic disease.

The major metabolic product of articaine is articainic acid. It is inactive as a local anesthetic and systemic toxicity has not been observed.[5] This is important because an active metabolite may affect toxicity and may exert undesirable side effects. In comparison, lidocaine has an active metabolite, xylidide, which is a local anesthetic and potentially toxic.[3]

Local anesthetic	**Articaine**	**Lidocaine**
Metabolism	90-95% in the blood	70% in the liver

Use in pediatric patients

In order for a local anesthetic to become popular, it is important that it is useful in a wide range of situations.
Lidocaine has been used for both adults and children for more than five decades. Articaine, however, is not indicated in children younger than 4 years of age.

When used in pediatric dentistry, it is important to remember that articaine is in a 4% solution and that the maximum dose for children is the same as for adults: 7 mg/kg (0.175 ml/kg). For simple procedures the recommendation is 0.04 ml/kg and for complicated procedures the recommendation is 0.07 ml/kg. It is important to remember that when you administer a local anesthetic to children with a small weight, the maximum dose can easily be reached.[4]

Local anesthetic	**Articaine**	**Lidocaine**
Pediatric patients	For children with a small weight, the maximum dose can easily be reached	

Use in geriatric patients

Aging is associated with physiologic changes that can alter the pharmacokinetics of drugs. Age-related changes in pharmacokinetics affect drug absorption, distribution, metabolism and elimination. Increase in body mass, decrease in lean body mass, total body water, changes in hepatic metabolism and renal elimination capacity in the elderly are of particular clinical significance. These changes should be taken into account when choosing drug therapy for older patients to minimize adverse effects and maximize potential benefits.

Taking into account that articaine shows an age independent metabolism there should be no reason to change the dosage in elderly patients.[4]

Local anesthetic	**Articaine**	**Lidocaine**
Geriatric patients	Aging and physiologic changes can alter the drug pharmacokinetics	

Local anesthetics & Complications

A wide range of different complications can occur during or after the injection of a local anesthetic. They can be divided into local complications such as pain on injection, persistent anesthesia/paresthesia, trismus, hematoma, edema, facial nerve paralysis and systemic complications such as overdose and allergic reactions.

Among these, we would like to highlight paresthesia, which is certainly not one of the most recurrent side effects, but many discussions are still on going in regard to the use of articaine in mandibular nerve block procedures and its increased risk of generating paresthesia.

Paresthesia can be defined as persistent anesthesia or altered sensation well beyond the expected duration of anesthesia. The symptoms are most commonly associated with mechanical trauma during surgical noxious stimuli. During the administration of anesthesia for a mandibular 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 anesthetics.

Haas and Lennon did a retrospective analysis of paresthesia after local anesthetic administration for nonsurgical dental procedures over a 20-year period,

from 1973 – 1993, in 1995. The analysis revealed a higher than expected frequency of paresthesia with articaine based on the number of cartridges used. There were no significant differences found with respect to patient age, patient gender or needle gauge.[6]

Subsequently in JADA, February 2001, Malamed, ET. Al. reported on three identical single-dose, randomized, double blind, parallel-group, active-controlled multicenter studies that were conducted to compare the safety and efficacy of articaine (4% with epinephrine 1:100,000) with that of lidocaine (2% with epinephrine 1:100,000). A total of 1,325 subjects participated in these studies, 882 of whom received articaine 4% with epinephrine 1:100,000 and 443 of whom received lidocaine 2% with 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. The most frequently reported adverse events in the articaine group, excluding post procedural dental pain, were headache (4%), facial edema, 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 percent), hypoesthesia (0.7%), headache (0.55%), infection (0.45%), and rash and pain (0.3% each).[7]

An interesting finding in the Haas and Lennon analysis is the different frequency between paresthesia of the lingual nerve and the inferior alveolar nerve. The lingual nerve (tongue) is approximately twice as often involved as the inferior alveolar nerve. The reason for this finding might be that in performing inferior alveolar nerve injections some practitioners change direction of the needle at the approximate depth of the lingual nerve. The sharp needle tip may lacerate the lingual nerve and/or artery on the initial or subsequent path. Another possible explanation might be that during a subsequent injection for the inferior alveolar nerve block, the needle might traumatize the more superficial lingual nerve but without the “electric shock” sensation because the nerve is usually anesthetized on the initial attempt. The cause of paresthesia may also be a combination of neurotoxicity of the local anesthetic and trauma to the nerve.

Local anesthetic	**Articaine**	**Lidocaine**
Paresthesia	Can be associated with the use of any local anesthetic. Controversial conclusions still exist in regard to articaine and its increased risks associated to paresthesia	

Conclusion

A range of local anesthetic drugs has been used in dentistry. Although lidocaine continues to be used more than articaine in the US, many dentists have begun using articaine as a more definitive means of achieving profound anesthesia.

Many dentists who continue to use lidocaine refer to the lower cost of lidocaine. Due to the fact that articaine is a 4% solution and lidocaine is a 2% solution, a dentist would theoretically only need to use one-half the volume of articaine to get the same level of anesthesia, which makes the cost of the two anesthetics very comparable.

The chemical and physical properties of articaine show that articaine has a higher lipid solubility, which permits the anesthetic to penetrate the nerve membrane. In

addition, the higher protein binding produces prolonged duration and slower release of the anesthetic into systemic circulation and a shorter elimination half-life, which makes reinjection safer. The combination of a higher dose of articaine, increased protein binding and increased lipid solubility may also provide a significant advantage over lidocaine in patients with local inflammation/infection which can make profound anesthesia more difficult to achieve.

Controversial conclusions still exist in regard to articaine and its increased likelihood, with respect to lidocaine, to cause prolonged paresthesia when mandibular nerve blocks are performed.

References

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