A Review of Special Patient Populations and Adverse Reactions using Dental Anesthetics

*Sponsored by **Pierrel**, makers of **Orabloc**®*

(Articaine hydrochloride 40mg/ml and epinephrine Injection)

Abstract

Every day, dental professionals administer millions of local anesthetic cartridges, as it is an everyday practice in dentistry. All dentists have expertise in local anesthesia and should consider the potential risks using local anesthetics (LA) in specific populations.

As a critical topic, we would like to provide a brief overview of special populations at risk when dental anesthesia is administered.

1. Overview of Local Anesthetics

Structurally, from a chemical perspective, local anesthetics have specific fundamental features in common. Today all local anesthetics available in dental cartridges belong to the amide class (namely articaine, mepivacaine, lidocaine, and prilocaine) that are formed by a lipophilic group joined by an amide linkage to a carbon chain, which is joined to a hydrophilic group.

The ester class is no longer available for dental anesthesia because of the high allergy incidence rate. Amides are not only less allergenic but safer than the esters.

Before considering potential risks, a brief comparison of the two most used amide local anesthetics, articaine and lidocaine, is presented.
Because articaine contains a thiophene ring, as opposed to the benzene ring in lidocaine and other amide local anesthetics, it is more soluble in lipids. Thus it diffuses better through nerve membranes.
Articaine is almost 4 times more likely to produce profound pulpal anesthesia in some areas of the mouth as compared to lidocaine. Articaine starts working more quickly and anesthesia may be more profound.

Articaine as a smaller molecule can suffuse into areas lidocaine can't reach. Thus mandibular infiltrations in dense bone perform better and one could speculate that individuals with denser maxillary bone would have the same results.

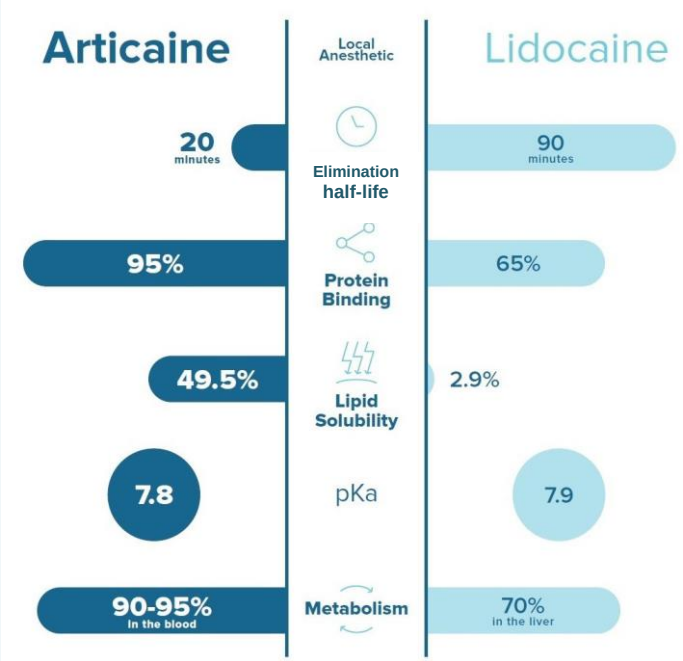
A systematic review of double blind, randomized clinical trials has shown that in adults with symptomatic irreversible pulpitis who are undergoing endodontic treatment, articaine was significantly more effective than lidocaine in reducing pain and incidence of adverse events.
There is a significant advantage to using articaine over lidocaine for supplementary infiltration after mandibular block anesthesia but no advantage exists when used for mandibular block anesthesia alone for maxillary infiltration. [1]

Articaine as compared to lidocaine, has a reduced elimination half life (the rate at which a local anesthetic is removed from the blood is described as its *elimination half-life*). Simply stated, the elimination half-life is the time necessary for a 50% reduction in the blood level of the LA.

Other difference are showed in the table below:

Table 1. Characteristics and Clinical Correlates

Characteristic	***Correlate***	***Explanation***
Lipid solubility	Potency	Greater lipid solubility enhances diffusion through neural coverings and cell membrane, allowing a lower milligram dosage.
Dissociation constant pKa	Time of onset	Determines the portion of an administered dose that exists in the lipid-soluble, tertiary molecular state at a given pH. Agents having a lower pKa have a greater proportion in the tertiary, diffusible state, and this hastens onset.
Chemical linkage	Metabolism	Esters are principally hydrolyzed in plasma by cholinesterases; amides are primarily biotransformed within the liver.
Protein binding	Duration	Affinity for plasma proteins also corresponds to affinity for protein at the receptor site within sodium channels, prolonging the presence of anesthetic at the site of action.



2. ADVERSE REACTIONS

Local anesthetics can be considered quite safe, but with the high number of injections given yearly, adverse reactions do occur.

When an adverse event occurs as a result of a dental local anesthetic injection, the true nature of the problem should be considered carefully. It is important NOT to suggest that an allergic response has occurred when the clinical events are consistent with well-recognized common causes of adverse reactions to dental injections. Most adverse reactions are avoidable with attention to technique.

Allergy to amide local anesthetics used in dentistry is extremely rare. If an acute reaction is strongly suggestive of an allergic response, early referral for thorough investigation is required. [7]

- **ALLERGIC REACTIONS**

Patient reports of allergic reactions to Las are fairly common, but investigation shows that most of these are of psychogenic origin. These facts should be known by the physician and by the dentist in order to minimize the frequent fears and "myths" about the use of local anesthetics at the dentist office. Allergic reactions to amide type local anesthetics agents are extremely rare. Since the majority of reactions are either psychosomatic or a consequence of intravenous administration, recommendations for screening suspect patients can be found in the literature and generally involve skin tests. [2]

- **PSYCHOGENIC REACTIONS**

Some people feel dental treatment as highly stressful. During its course the patient faces situations that can cause anxiety or fear, such as: the utilization of aggressive instruments (syringes, scissors), painful procedures applied to sensitized areas, bothering auditory stimuli (turbines, motors), offensive to taste or foul-smelling substances, maintaining uncomfortable positions during long procedures, etc.

The dental illness that caused the appointment, the dental procedure techniques and the psychic susceptibility of some patients, can generate a psychogenic vasovagal reaction during treatment. Anxiety, deep breath, pallor, sweat, nausea, confusion, loss of consciousness can be the symptoms present in such a situation. The patient can improve in minutes after being put in a supine position or in a Trendelenburg position.

Most of the adverse reactions found in one study (88 %) have been due to this cause. Four patients had a similar reaction during previous dental treatments as a manifestation of their psychic lability. These findings are similar to those of other authors who think that the psychic reactions are the most frequent adverse reactions that follow LA injection[3].

- **TOXICITY**

Overdose is also known as a toxic reaction, that is a function of systemic absorption. It occurs when the blood level of LA in either the central nervous system or myocardium is elevated to a point where the drug produces potentially life-threatening events. The overdose reaction persists until the blood level of the drug in these organs falls below the toxic level.

The following tables represent the most common causes of local anesthetic overdose in dentistry.

Table Etiologies of LA overdose.

- •Rapid intravascular injection
- •Administration of too large a dose of LA
- •Rapid absorption of the LA from site of administration
- •Inability to biotransform the drug normally
- •Inability to excrete the drug normally

Table Factors adding to increased risk of LA overdose in younger patients.

1. Treatment plan: all 4 quadrants are treated using LA in one visit.
2. LA administered is a plain (no vasopressor) solution.
3. Full cartridges (1.8 mL) administered with each injection.
4. LA administered to all 4 quadrants at one time.
5. Exceeding the maximum dosage based on patient's body weight.

Intravenous administration may be prevented by always performing an aspiration test prior to and during all LA injections. Of somewhat greater importance is the rate at which the LA is administered. The ideal rate of drug administration is 1 mL per minute. Recommendations for dental procedures are a rate not to exceed 1 cartridge (1.8 mL) per minute. [4]

- METHEMOGLOBINEMIA

Methemoglobinemia occurs when iron atoms in hemoglobin molecules are oxidized from their normal ferrous (Fe^{++}) to a nonfunctional ferric (Fe^{+++}) state, resulting in reduced oxygen delivery to the tissue level. This is an uncommon adverse reaction associated most notably with prilocaine, which poses a greater risk of increased methemoglobin in children in particular.

- PARESTHESIA

Paresthesia is defined as a persistent anesthesia or altered sensation that extends beyond the expected duration of anesthesia. It is usually un unpreventable complication in patients undergoing oral surgical procedures including implant placement.

If it is determined that paresthesia is due to surgical trauma, then consultation with an oral and maxillofacial surgeon should be considered to help determine if a surgical approach to repair is warranted. If it is determined that paresthesia is due to local anesthetic injection, then consider the following patient management strategy

i. Reassure patient

- Practitioner should speak to the patient personally
- Explain how paresthesia occurs and the expected timeframe for resolution
- Book an examination appointment with the patient
- Record incident in the dental record

ii. Patient examination

- Discuss phenomenon of paresthesia with patient
- Explain paresthesia may take time to resolve and can take months, although rarely it may persist indefinitely
- Determine degree and extent of paresthesia patient is experiencing
- Record examination findings in the chart

iii. Follow-up with patient

- Re-examine patient within one month, and then in 1 – 2 month intervals, or more often if appropriate, for as long as the paresthesia persists. An improvement in the signs and symptoms, however gradual, is often a promising sign of eventual complete resolution.
- If paresthesia persists at this first follow-up appointment, offer to refer the patient to an oral and maxillofacial surgeon or other appropriate specialist for an assessment

iv. Dental Treatment

- Dental treatment may continue in other areas of the mouth
- If further treatment is required in the area of the sensory deficit, avoid injecting local anesthetic into this region – consider alternative techniques to deliver anesthetic [5-6]

- VASOCONSTRICTORS (epinephrine effects)

Vasoconstrictors are used in LA solution to improve the depth and duration of anesthesia, reducing systemic toxic effects and providing hemostasis to achieve a bloodless surgical procedure. But patients suffering from uncontrolled systemic diseases might have a life risk situation if vasoconstrictor is used improperly. Systemic epinephrine has a brief duration of action (approximately 10'), so if more is required, injection can be repeated. If multiple quadrants are being treated, the timing of the injections should be spread out. Minimizing the likelihood of systemic effects of vasoconstrictors is another reason why aspiration before every injection is so important. [8]

Examples of calculations of doses of Vasoconstrictors

Ratio concentrations represent grams per milliliter
1:100,000 = 0.01 mg/mL or 10 µg/mL
1:200,000 = 0.005 mg/mL or 5 µg/mL
1:50,000 = 0.02 mg/mL or 20 µg/mL
1 cartridge of epinephrine 1:200,000 = 9 µg
1 cartridge of epinephrine 1:100,000 = 18 µg
1 cartridge of epinephrine 1:50,000 = 36 µg
1 cartridge of levonordefrin 1:20,000 = 90 µg

2. SPECIAL PATIENT POPULATION

- PREGNANT AND LACTATING WOMEN

Use of LA, as well as dental treatment during pregnancy, does not represent a major teratogenic risk." [9.] There is no reason not to use local anesthetics during pregnancy, even those types with epinephrine. We have known the safety of epinephrine since 1977. Risk Factors (A, B, C, D, X) have been assigned to all drugs, based on the level of risk the drug poses to the fetus. Risk Factors are designed to help the reader quickly classify a drug for use during pregnancy. They do not refer to any breast-feeding risk.

The definitions used for some risk factors are presented below:

Category	Description
Cat. A	Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester (and there is no evidence of a risk in later trimesters), and the possibility of fetal harm appears remote.
Cat. B	Either animal-reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women or animal-reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester (and there is no evidence of a risk in later trimesters).
Cat. C	Either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal, or other) and there are no controlled studies in women or studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the fetus.
Cat. D	There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).
Cat. X	Studies in animals or human beings have demonstrated fetal abnormalities, or there is evidence of fetal risk based on human experience, or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.

The use of local anesthetics is necessary and acceptable during pregnancy. The clinician should be aware that local anesthetic agents may exhibit a more rapid onset and longer duration of action during pregnancy. Local anesthetics freely cross the placenta, and the potential for fetal toxicity is also a concern.

The use of vasoconstrictors with local anesthetics during pregnancy is controversial. Judicious use of a vasoconstrictor, however, is permissible.

Obtaining profound local anesthesia and thus, preventing extensive endogenous catecholamine release is the objective. A major concern with the use of local anesthetics containing epinephrine involves the inadvertent intravascular injection.

Accidental intravascular injection of epinephrine can cause uterine artery vasoconstriction and decreased uterine blood flow.[10] Proper aspiration techniques and limitation of alpha-adrenergic agents (such as epinephrine) is advised to avoid this complication.

Clinicians may consider using carpules with 1:200,000 concentrations of epinephrine as an alternative.

Use of local anesthetics during pregnancy

Drug	FDA category
Local anesthetics (injectable)	
Articaine	C
Bupivacaine	C
Lidocaine	B
Mepivacaine	C
Prilocaine	B
Vasoconstrictors	
Epinephrine 1:200,000 or 1:100,000	C (higher doses)
Levonordefrin 1:20,000	Not ranked
FDA = U.S. Food and Drug Administration	

- **CHILDREN**

The main concern in pediatrics is the relative ease of inducing an overdose. Before administering local anesthetic to a child, the dentist should determine the child's weight and calculate the maximum dose to help prevent inadvertent overdose.

Safety and effectiveness of Articaine in pediatric patients below the age of 4 years have not been established.

Using Mepivacaine and Lidocaine in pediatric patients, the maximum pediatric dose should be carefully calculated.

The calculations shown in the table below, indicate the ease with which a young child can be overdosed. Given the concerns regarding toxicity, selection of a low concentration solution appears prudent. [11]

Example calculations of maximum local anesthetic doses for a 15-kg (33-lb) child

Articaine
5 mg/kg maximum dose x 15 kg = 75 mg
4% articaine = 40 mg/mL
75 mg/(40 mg/mL) = 1.88 mL
1 cartridge = 1.8 mL
Therefore, 1 cartridge is the maximum.
Lidocaine
7 mg/kg x 15 kg = 105 mg
2% lidocaine = 20 mg/mL
105 mg/(20 mg/mL) = 5.25 mL
1 cartridge = 1.8 mL
Therefore, 2.9 cartridges is the maximum.
Mepivacaine
6.6 mg/kg x 15 kg = 99 mg
3% mepivacaine = 30 mg/mL
99 mg/(30 mg/mL) = 3.3 mL
1 cartridge = 1.8 mL
Therefore, 1.8 cartridges is the maximum.

- **ELDERLY PATIENTS**

There are no significant differences in the response to local anesthetics between younger and older adults. Therefore, the doses required for each category are the same regardless of patient age. Nonetheless, it is prudent to stay well below the maximum recommended doses, as elderly patients often have some compromise in liver function. Responses to vasoconstrictors should not be considered significantly different in elderly patients, but some degree of cardiovascular compromise can be expected, even without an overt history of heart disease. Therefore, reducing the dose of epinephrine may be prudent. [12]

CONCLUSIONS

Adverse reactions to dental local anesthetic injections are common, but the majorities are transient and may go unnoticed by the dental professional. The most frequent causes of significant reactions appear to be psychogenic (driven by anxiety). A smaller number of reactions, which cause concern, are caused by intravascular injections. Some patients suffer systemic reactions when larger amounts of solution are absorbed into the circulation.

A patient may suffer progression of his/her oral disease if treatment is not provided because of age, behavior, inability to cooperate, disability, or medical status.
Postponement or denial of care can result in unnecessary pain, discomfort, increased treatment needs and costs, unfavorable treatment experiences, and diminished oral health outcomes[13].

The importance of a complete medical history cannot be underestimated. Consultation with the patient's physician may also be appropriate for those patients with medically complex conditions.

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