



Concise Clinical Review

Local Anaesthesia in Dentistry: A Review

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ABSTRACT

Over the past century, there is perhaps no greater contribution to the practice of clinical dentistry than the development and application of local anaesthesia. What were once considered painful procedures have now been made routine by the deposition and action of local anaesthetics. This article will serve as a review of basic pharmacological principles of local anaesthesia, subsequent sequelae that can arise from their use, considerations when using local anaesthetics, and recent advances in the delivery of local anaesthetics.

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Introduction

An average dentist will administer over 1,500 cartridges of dental local anaesthetic a year.¹ As such, anyone administering this drug should be intimately familiar with what the drug does to the body, as well as what the body does to that drug. This article will serve as a review of the pharmacokinetics and pharmacodynamics of local anaesthetics, possible consequences and adverse events from their use, and emerging technologies pertaining to the use of local anaesthetics.

Pharmacology

Chemical structure

Modern local anaesthetics are typically differentiated based on their chemical structure, specifically the linkage (an amide versus an ester linkage) between common elements of the compound. The majority of commonly used dental local anaesthetics fall into the amide category (lidocaine, mepivacaine, bupivacaine, prilocaine), though there are some amide-type local anaesthetics that also contain an additional ester linkage (articaine). While both types of local anaesthetics have the same mechanism of action, they differ slightly in their metabolism as described below. It is rare in dentistry that ester-type anaesthetics are used for local

anaesthesia purposes, though these types of anaesthetics are used more commonly for topicalisation prior to injection to reduce discomfort associated with mucosal needle puncture.

Mechanism of action

Local anaesthetics all act in the same manner – they bind to cellular sodium channels and inhibit the influx of sodium into the cell which prevents cell depolarisation and subsequent transmission of the previously propagating action potential.² This is beneficial in that the action potential of a painful stimulus, such as drilling into the dentin of a tooth, can be stopped from reaching the higher processing centres of the brain and otherwise painful procedures can be completed with relative patient comfort.

Onset

The onset of local anaesthesia is contingent on two factors: the lipid solubility and the pKa of the local anaesthetic. The more lipid-soluble a local anaesthetic is, the greater its potency.³

For the local anaesthetic base to be stable in solution, it is formulated as a hydrochloride salt.³ At that time, the molecules exist in a water-soluble state and thus are unable to penetrate the neuron.³ Therefore the time for onset of local anaesthesia is directly related to the proportion of molecules that convert to the lipid-soluble structure when exposed to physiologic pH (7.4). This proportion is determined by the ionisation constant (pKa) for the anaesthetic and is calculated using the Henderson-Hasselbalch equation.³ This implies that the higher the pKa for a local anaesthetic, the fewer molecules are available in their lipid-soluble form and thus the

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further is the delay in the onset of action.^{2,3} This is why it is harder to anaesthetise a patient with an infection, as the environment pH is much lower (around pH of 5.2) and this favours the water-soluble state.

For instance, bupivacaine is the most lipid-soluble local anaesthetic so a lower percent of drug dissolved in solution is required to cause nerve blockade compared to a less lipid-soluble local anaesthetic like mepivacaine. Thus, for a rapid onset of action, the lower the pKa of a local anaesthetic, the more ionised drug is present in normal tissue and the faster the onset of blockade.

Duration of action

The duration of action of a local anaesthetic is contingent on two factors: the protein binding and redistribution of the local anaesthetic. Protein binding of the local anaesthetic is an inherent drug characteristic – the more protein-bound a drug is, the longer the duration of action.⁴ Duration of action on dental pulp and soft tissues is contingent almost completely on diffusion away from the site of action of the local anaesthetic. If an area is more vascular, the faster the drug will be absorbed into systemic circulation and away from the target tissue.

Metabolism and elimination

Amide-type local anaesthetics are biotransformed into water-soluble metabolites in the liver by hepatic microsomal enzymes and subsequently excreted by the kidney.⁵ Articaine is primarily metabolised via its ester linkage by plasma esterases in the blood.^{6,7}

Vasoconstrictors

Knowing that the duration of action of a drug is determined by its protein binding and redistribution, cartridges of local anaesthetic can be modified to have additional components present in the cartridge in order to increase the duration of action. Specifically, a vasoconstrictor such as epinephrine or levonordefrin can be added so that when the solution is deposited at the site of action, the surrounding vascular beds will vasoconstrict, the drug will be more slowly absorbed into the circulating bloodstream, and the duration of action of the local anaesthetic will be increased.⁸ Local anaesthetics with vasoconstrictors should be used carefully for patients with pre-existing hypertension or cardiac irritability as their presence in the body may further increase blood pressure or cause cardiac dysrhythmias.

Local anaesthetic cartridge additives

In addition to the local anaesthetic, the distilled water in which it is dissolved, and potentially a vasoconstrictor, there is the possibility of an oxidant included in the cartridge. Local anaesthetics are generally stable and are resistant to degradation, but vasoconstrictors present in the cartridge are much more susceptible to degradation from the presence of molecular oxygen, light, elevated temperature, heavy metals, and an increase in pH.⁹ As such, antioxidants such as

metabisulfite are added to the local anaesthetic cartridge to reduce the rate of deterioration of the vasoconstrictor.

Previously, methylparaben (an anti-fungal) was included in local anaesthetic cartridges as it was originally included in the formulation of multi-dose vials of local anaesthetics used for medical purposes. When single-use cartridges were introduced in the dental setting, methylparaben was included until it was appreciated that it was no longer necessary to ensure an additional infection control measure, and it was then phased out of dental cartridges in North America with the last amount of methylparaben included in 1984.¹⁰ It should be noted that there are still countries where formulations of local anaesthetic exist with the addition of methylparaben.¹¹

Adverse events

Systemic toxicity

While local anaesthetics have the ability to produce anaesthesia of intended nerves and anatomic areas, they are not exempt from Paracelsus' law, 'Only the dose makes the poison'. That is, they too can be toxic in higher doses. When systemic concentrations of circulating local anaesthetic become high enough, there can be unintended and severe consequences which are neuralgic and cardiac in nature. Inhibitory neurons in the nervous system are generally those first affected, which when blocked will produce excitatory symptoms such as visual and sensory disturbances, seizures, and muscle toxicity.¹² As plasma concentrations continue to rise, depressive clinical manifestations begin to appear such as decreased level of consciousness possibly leading to coma and respiratory arrest. Following increased plasma concentration leading to adverse neurological events, cardiac conditions can arise from heightened concentration of the drug. Local anaesthetics will again act to block sodium channels, but this time in areas of the heart required for propagation of cardiac conduction. A variety of sequelae can manifest from tachyarrhythmias to bradyarrhythmias, up to the point that plasma levels of the drug will inhibit cardiac function altogether and cause an arrest.¹³

The best means of avoiding local anaesthetic systemic toxicity is awareness of the patient's weight, the maximum per kilogram (or absolute) dose of the local anaesthetic being administered (see [Table 1](#)), and careful calculation so as to avoid systemic concentrations of the drug that could disrupt regular cell membrane function. Included in the [Table](#) is a list of the most commonly used local anaesthetics in dentistry as well as their associated maximums that can be administered to patients on a per kilogram basis. In order to determine the maximum dose for a patient, one must simply multiply the patient's weight by the per kilogram maximum specific to the local anaesthetic being used by the dentist.

In order to determine how much local anaesthetic is in a cartridge (see the example in [Table 2](#)), the percent solution of the local anaesthetic expressed in mg/mL must be multiplied by the amount of solution in the cartridge. Of note, percentage of local anaesthetic represents the number of grams per 100 mL, or mg per mL. For example, a 2% solution represents 20 mg/mL

Table 1 – Recommended Canadian maximum doses of local anaesthetics^{1,13}

Drug	Maximum
Articaine WITH vasoconstrictor	7 mg/kg (up to 500 mg) 5 mg/kg in children
Bupivacaine WITH vasoconstrictor	2 mg/kg (up to 200 mg)
Lidocaine WITH vasoconstrictor	7 mg/kg (up to 500 mg)
Mepivacaine WITH vasoconstrictor	6.6 mg/kg (up to 400 mg)
Prilocaine WITH vasoconstrictor	8 mg/kg (up to 500 mg)
Mepivacaine WITHOUT vasoconstrictor	6.6 mg/kg (up to 400 mg)
Prilocaine WITHOUT vasoconstrictor	8 mg/kg (up to 500 mg)

The maximum recommended dose may vary from country to country. The maximum dosage means 'a single volume administered'; if additional cartridges are administered at a later time in the procedure then the calculation is no longer valid as one must incorporate redistribution and drug half-lives into current systemic dose. Many schools and organisations teach the maximum dose of lidocaine 2% with 1:100,000 epinephrine as 4.4 mg/kg but there is no consensus on the issue.^{61,62} There have been some investigators who advocate for abandoning the idea of maximum recommended doses⁶³ and instead taking patient and clinician factors into consideration such as the patient's age, the site of injection, the speed of injection, and the existence of other comorbidities.⁶⁴

and a 4% solution represents 40 mg/mL. A typical dental local anaesthetic cartridge in North America contains approximately 1.8 mL, while many countries use 2.2 mL cartridges.

Again, the amount of local anaesthetic being deposited should be less than the per kilogram maximum specific to the local anaesthetic being used and less than the absolute maximum associated with that local anaesthetic (Table 1).

Despite the best efforts of clinicians, drug errors occur when the patient receives too large a dose of local anaesthetic, or an intravascular administration of local anaesthetic occurs, and the patient demonstrates an abnormal reaction of systemic toxicity despite no pre-existing medical condition,¹⁴ or perhaps the patient had an unknown medical condition that predisposed them to local anaesthetic systemic toxicity.¹⁵ As such, astute clinicians should be ready to recognise and treat the symptoms of local anaesthesia systemic toxicity (tinnitus, metallic taste, circumoral numbness, altered medical status, slurred speech, hypotension, bradycardia, seizures, ventricular arrhythmias, and cardiac arrest). The management of local anaesthetic systemic toxicity includes (but is not limited to):

- Activating emergency medical services when in an ambulatory location in order to be able to transport and monitor the patient in a tertiary care facility

Table 2 – Example calculation of amount of local anaesthetic in a dental anaesthetic cartridge

Information	Calculation and amount
A 2% solution has a concentration of 20 mg/mL	20 mg/mL × 1.8 mL = 36 mg
The cartridge has 1.8 mL of solution	
A 4% solution has a concentration of 40 mg/mL	40 mg/mL × 1.8 mL = 72 mg
The cartridge has 1.8 mL of solution	

- Ensuring adequate oxygenation (may include administering supplemental oxygen and/or manual ventilation of the patient)
- Provided that intravenous access is established and the provider has been trained to administer intravenous rescue medications:
 - a. Administering of intravenous Intralipid 20% (1.5 mL/kg for a child or 100 mL bolus for an adult over 65 kg and a subsequent infusion of 0.25 mL/mh/min or more if hypotension persists) to treat the cardiac aspects of local anaesthetic systemic toxicity
 - b. Treating seizures, if present (titration of intravenous midazolam beginning with 100 mcg/kg for a child or 5 mg for an adult)
 - c. Treating bradycardia and/or hypotension with an intravenous vasopressor
 - d. Monitoring for ventricular fibrillation or ventricular tachycardias and treating as appropriate
 - e. Anticipating acidosis, hypercarbia, hyperkalemia, and treating as necessary.

Allergy

True documented allergy to amide-type local anaesthetics is exceedingly rare.¹⁶ While some literature reports an incidence of allergy from 0.1% to 1%,¹⁷ recent data suggest a possible increase in the incidence of this allergy (specifically to lidocaine).¹⁸ When an allergy to local anaesthetic is suspected, there exist several complex means of investigating whether the symptoms present are a true anaphylactic reaction. The patient should be referred to an allergist or immunologist in order to determine if indeed an allergy exists and, if so, to determine the allergenic components of the local anaesthetic cartridge. It is now understood that an allergist-administered intradermal administration test, followed by subsequent provocation challenges (if necessary), can demonstrate adequate predictive value in order to rule out possible local anaesthetic allergy.¹⁸

While some patients may note allergy-like symptoms from a dental injection, it is likely that these symptoms appear from either a psychogenic reaction, which can mimic allergy and even anaphylaxis, or it could be that the patient does have an allergy to one of the contents in the local anaesthesia cartridge other than the local anaesthesia itself. Historically, local anaesthetic multi-dose vials were re-used between patients and so an agent, such as methylparaben – a bacteriostatic, anti-fungal agent – was also present in these vials. It was not uncommon for patients to experience allergic reactions from these types of agents. Today's commonly used dental local anaesthetics with vasoconstrictors contain the preservative sodium metabisulfite, which some case reports note can cause allergic reactions.

It should be noted that ester-type local anaesthetics, such as benzocaine which is used in many formulations of topical anaesthetics, is one of the more allergenic agents found in a dental office after latex, non-steroidal anti-inflammatory drugs, and penicillin-type antibiotics. Dental practitioners should pay particular attention for the signs and symptoms of allergy or anaphylaxis after the application of any ester-

type topical anaesthetics.¹⁹ Benzocaine applied as a topical anaesthetic may cause aphthous ulcers in some patients (a possible sign of sensitivity or even allergy); should this occur, topical lidocaine would be more appropriate for future appointments.

With the above in mind, while noting that allergy to a local anaesthetic or a component in the cartridge is exceedingly rare, such an event is not altogether impossible and, as such, the prudent practitioner should therefore be prepared to recognise and treat the signs and symptoms of an allergic reaction. A conscious patient experiencing an anaphylactic reaction would generally have a constellation of symptoms involving the dermatologic (rashes, hives, urticaria, erythema, mottling), respiratory (wheezing, dyspnea from airway angioedema), and gastrointestinal systems (cramping, vomiting, diarrhoea). A patient who is in a state of sedation may have some of these clinical features masked and may instead present with cardiovascular collapse (significant hypotension or asystole) or respiratory compromise (hypoxia, dyspnea, tachypnea, coughing/bucking, bronchospasm).²⁰ The management of anaphylaxis includes (but is not limited to):

- Activating emergency medical services when in an ambulatory location in order to be able to transport and monitor the patient in a tertiary care facility
- Discontinuing or removing the anaphylaxis-inciting agent
- Ensuring airway patency (considering intubation) and administering 100% oxygen
- Administering epinephrine (0.3 mg for > 30 kg body weight; 0.15 mg for up to 30 kg, IM in lateral thigh as an initial dose of epinephrine).

These additional steps may be carried out provided the medications are available and the provider has been trained in their administration:

- Administering an H1 and H2 blocker (respectively: diphenhydramine 1 mg/kg IM to a maximum of 50 mg and ranitidine 1 mg/kg IM to a maximum of 50 mg)
- Administering a corticosteroid like hydrocortisone (2 mg/kg IM to a maximum of 100 mg)
- Provided that intravenous access is established and the provider has been trained to administer intravenous rescue medications:
 - a. Administering a bolus push of intravenous fluid (20 mL/kg to a maximum of 1 L, or more if necessary).

Psychogenic reactions

Pre-syncope and syncope (vasovagal reactions) are among the most common medical emergencies that occur in dental offices. Patients' anxieties about the deposition of local anaesthesia, or any other dental procedure for that matter, may manifest clinically with variations in heart rate and blood pressure, pallor, nausea, vomiting, and dyspnea.²¹ Care should always be taken to probe a patient's level of anxiety in the dental office so as to be able to implement pharmacologic

or non-pharmacologic techniques that will make patients comfortable for the duration of care in the office setting.

Lip/cheek/tongue biting

Another common issue for patients after having received local anaesthesia for a dental procedure is the associated soft tissue anaesthesia that persists and subsequent trauma to those anaesthetised tissues from lack of sensory feedback.²² Care must be taken to warn patients about this time of vulnerability to those tissues at risk. Additionally, cotton rolls or gauze can be used as a shield to prevent patients from gnawing chewing on these structures. If possible, the use of a local anaesthetic without epinephrine will reduce the amount of time that this soft tissue anaesthesia persists. Additionally, a practitioner may decide that the use of phentolamine mesylate would be appropriate, to be administered in order to cause local vasodilation in the area where a vasoconstrictor was previously administered, thus accelerating the rate of redistribution of the local anaesthetic, accelerating the offset of the drug, and subsequently accelerating the reversal of collateral soft tissue numbness. This medication is further discussed later in the paper.

Trismus

Trismus, a reduction in the range of mandibular motion, can occur after a dental injection. It is often caused by the needle passing through a muscle of mastication which in turn causes spasticity to the muscle.²³ It can also be caused by the accumulation of a haematoma (see below) impeding excursive movements that permit full opening. Analgesics and a soft diet are mainstay therapies in the acute phase of trismus following a dental injection, with a gradual return to function and physiotherapy if necessary.

Intravascular injections

In order to administer local anaesthesia, a loaded syringe with an attached needle is inserted into the desired location of deposition. New needles have an associated bevel that are sharp in order to comfortably puncture oral mucosa, but that same quality reducing initial discomfort of mucosal puncture and travel through connective tissue can lead to puncture of surrounding vascular structures. When a dentist has reached their intended endpoint where local anaesthesia is to be deposited, it is recommended that, at minimum, one aspiration manoeuvre is performed. This act (via either pressing an aspiration ring or withdrawing from a cartridge that has a harpoon inserted into the cartridge's rubber stopper) introduces negative pressure into the local anaesthetic cartridge and serves the purpose of aspirating whatever matter is at the tip of the needle. If a needle tip is located inside a vascular structure, the negative pressure into the cartridge should in theory draw visible blood into the cartridge and alert the dentist of the needle's tip inside a blood vessel.

Unfortunately, there are times when an aspiration manoeuvre is carried out while the needle tip is indeed in a blood vessel but there is a false negative aspiration (that is, no blood is visualised in the cartridge). This false negative

event could be due to either the bevel of the needle being positioned in such a way that the action of aspiration draws the wall of the vascular structure to the bevel instead of blood, or because the gauge of needle was too small. In either case, if the contents of the cartridge are deposited directly into the bloodstream, patients can experience immediate symptoms from both the local anaesthetic and vasoconstrictor.²⁴ While these symptoms are often related to the blood flow from vessels adjacent to the block being performed, they may present as palpitations, headaches, visual disturbances, and vertigo. While patient reassurance that these symptoms will resolve is first-line management of an intravascular injection, the dental practitioner would be prudent to continue to monitor level of consciousness and vital signs until the local anaesthetic has redistributed away from the site of injection and the patient has returned to their baseline state. Anecdotally, just one cartridge of lidocaine can and in cases has produced seizures, illustrating how the speed attending intravascular injection may be the decisive factor in the severity of local anaesthetic systemic toxicity.

Haematoma

As the needle is passing through connective tissue, it is not uncommon for the tip to puncture a vascular structure. Occasionally, blood will extravasate from this breach of endothelium into the surrounding extravascular area and accumulate locally. This can be associated with facial swelling, soreness, and trismus from the expansion of the potential space where the bleeding from the insult occurred.²⁵ If a haematoma is suspected, a dentist should immediately apply pressure to the area in order to aid in haemostasis of the punctured vessel and to attempt to reduce the amount of extravasation in the area. The patient should only be dismissed once the dentist is confident that the bleeding has ceased.

Ocular complications

There have been case reports published for over 50 years about various ocular complications arising from the administration of inferior alveolar blocks. There may be one or more symptoms including, but not limited to, amaurosis, diplopia, total ophthalmoplegia, mydriasis, ptosis, and blanching of the periorbital skin.²⁶ The common belief of the cause of this phenomenon is the variable anatomy of the maxillary artery in which there is a subsequent intravascular injection which could carry the local anaesthetic in a retrograde manner from the middle meningeal artery through the foramen spinosum and back to the lacrimal and optic arteries resulting in anaesthetisation of cranial nerves 3, 4 and 6. Generally supportive measures and tincture of time suffice to resolve this complication, but a differential diagnosis should be formed and referral to the appropriate sub-specialist if necessary.

Non-surgical paraesthesia

There are extremely rare cases in the literature and closed-claim analysis where patients who had completed nerve blocks subsequently experienced permanent paraesthesias of associated nerves when there was no surgical procedure

involved.²⁷ Given the rarity of such events, the study of non-surgical paraesthesias is very difficult and almost exclusively retrospective in nature. With that being said, speculation exists that a combination of trauma to the nerve from the needle and higher percentages of local anaesthetics like articaine and prilocaine are the most likely causes of such paraesthesias from direct neurotoxicity to nerve trunks.²⁸ Additionally, the number of respective nerve fascicles and the ratio of nerve fascicles affected may correlate to the severity of paraesthesia (e.g. higher incidence of lingual nerve paraesthesia and a lower number of nerve fascicles generally present for the lingual nerve).²⁹ However, this topic does remain controversial as there has been other literature published noting that this hypothesis may not be the case.^{30–32} In any and all cases of deposition of local anaesthetic, the dental practitioner must weigh the pros and cons of choice of drug and route of administration prior to the injection.

Methaemoglobinemia

Exposure to some local anaesthetics (namely the ester-type local anaesthetics and principally prilocaine) can precipitate a change in the iron atom in the haemoglobin, specifically from a ferrous state to a ferric state to create a molecule called methaemoglobin. This is of concern as the ferric haemoglobin molecule has a much greater affinity for oxygen, so much so that the oxygen will not dissociate from the haemoglobin and therefore not be available for tissue and organ use. If an exposure causes enough haemoglobin to become methaemoglobin, the patient may experience signs and symptoms of hypoxemia such as cyanosis and shortness of breath. If this condition is suspected, supplemental oxygen should be administered (despite an ineffective oxygen-carrying capacity from the methaemoglobinemia) and emergency medical services contacted. Definitive treatment for this emergency is the intravenous administration of methylene blue.

Table 3 provides example calculations for maximum dose for local anaesthesia for various patients.

Interactions

Unless the patient is on a concomitant local anaesthesia infusion for an ailment (a potential risk for local anaesthetic systemic toxicity), there are no significant drug interactions with non-epinephrine-containing local anaesthetics. Drug interactions stemming from the contents of a local anaesthetic cartridge are almost exclusively from the included vasoconstrictor. The most notable interactions are noted in Table 4 below. As such, epinephrine should be used with great caution when concomitant use of one of the drugs is present, and levonordefrin should be avoided altogether when the patient is taking a tricyclic antidepressant.

Considerations

Anatomic considerations leading to local anaesthesia failure

While supraperiosteal injections are generally sufficient to achieve pulpal anaesthesia for maxillary dentition, these

Table 3 – Example calculations of maximum dose for local anaesthetic for various patients

Information	Calculation and maximum
20 kg patient (e.g. a 5-year-old) 2% lidocaine with 1:100,000 epinephrine in a 1.8 mL cartridge	20 kg × 7 mg/kg maximum = 140 mg maximum 140 mg maximum/36 mg per cartridge = 3.8 cartridges of 2% lidocaine with 1:100,000 epinephrine
20 kg patient (e.g. a 5-year-old) 4% articaine with 1:100,000 epinephrine in a 1.8 mL cartridge	20 kg × 7 mg/kg maximum = 140 mg maximum 140 mg maximum/72 mg per cartridge = 1.9 cartridges of 4% articaine with 1:100,000 epinephrine
60 kg patient (e.g. a 40-year-old) 2% lidocaine with 1:100,000 epinephrine in a 1.8 mL cartridge	60 kg × 7 mg/kg maximum = 420 mg maximum 420 mg maximum/36 mg per cartridge = 11.6 cartridges of 2% lidocaine with 1:100,000 epinephrine
100 kg patient 2% lidocaine with 1:100,000 epinephrine in a 1.8 mL cartridge	100 kg × 7 mg/kg maximum = 700 mg maximum BUT reported maximum is 500 mg 500 mg maximum/36 mg per cartridge = 13.8 cartridges of 2% lidocaine with 1:100,000 epinephrine

types of injections are significantly less successful for mandibular teeth due to the thickness of the bone cortex. As such, deposition of local anaesthetic adjacent to the inferior alveolar nerve (IAN) must be carried out via one of several approaches, all of which have varying rates of success,^{33,34} and none of which are able to accomplish nerve blockage 100% of the time.³⁵ This can be attributed to various hard and soft tissue characteristics creating uncertainty about the position of the needle tip relative to the IAN, fascial linings acting as a potential barrier to the diffusion of local anaesthetic solution, and the sphenomandibular ligament possibly impeding diffusion of local anaesthetic to the IAN (likely because the needle tip was too medial to the mandibular foramen).³⁶ Accessory innervation from the mylohyoid nerve, the long buccal nerve, the greater auricular nerve, and even a bifid IAN can also carry additional sensory fibres to mandibular dentition.³¹ Given the above information, all injections should be performed with prior examination of the patients' anatomical features to permit minor alterations to technique as necessary in order to maximise chances of success of a nerve blockade.

Inflamed dental pulps

As carious lesions increase in size and proximity to pulpal tissue, various biologic markers are produced and subsequent inflammatory mediators are recruited to the site.³⁷ This inflammation creates a localised area of inflammatory acidosis where the lowered pH value inhibits the action of local

anaesthetics due to the altered interaction with components of the liposomes.³⁸ Additionally, various isoforms of tetrodotoxin-resistant sodium channels (i.e. sodium channels on which lidocaine has a reduced antinociceptive effect)³⁹ are recruited in the inflammatory state.⁴⁰ This combination of factors can make reliable and profound anaesthesia very difficult to achieve, and practitioners should be prepared to administer adjunctive techniques such as intra-osseous or periodontal ligament injections in order to provide a comfortable experience for their patients.⁴¹

Pregnancy

At this time, only lidocaine and prilocaine have an FDA foetal risk classification indicating no risk of teratogenic effects based on the results of human and animal studies. Other commonly used local anaesthetics (bupivacaine, articaine, mepivacaine) have an FDA foetal risk classification indicating that teratogenic risk cannot be eliminated on the basis of human and animal studies.⁴² The first trimester of pregnancy poses the highest threat for teratogenicity and so only emergent dental work should be completed during this trimester. It is currently believed that the second trimester poses the lowest risk of foetal harm and local anaesthesia use should in theory be safe.⁴³ While it is possible to complete elective dental treatment during the third trimester of pregnancy, there is a higher risk of aortocaval compression and increased conduction blockade. If local anaesthesia is to be administered in the third trimester, lower doses should be used.

Table 4 – Drugs known to cause interactions with vasoconstrictors and potential associated effects

Drug	Effect
Beta blockers (drugs that end in -olol) Ex. metoprolol, propranolol, labetalol, bisoprolol, atenolol	Beta-blockers block beta-adrenergic receptors and can produce unrecognised and unopposed alpha-adrenergic receptor agonism with corresponding hypertension when epinephrine is present.
Volatile anaesthetics (drugs that end in -ane) Ex. halothane, sevoflurane, isoflurane, desflurane	Volatile anaesthetics sensitise the myocardium to catecholamines – cardiac arrhythmias can be induced with the injection of exogenous epinephrine.
Amphetamines (names vary) Ex. cocaine, methamphetamine	Amphetamines increase blood pressure and can cause cardiac arrhythmias by themselves with the potential for adverse event synergism from epinephrine.
Tricyclic antidepressants (names vary) Ex. amitriptyline, imipramine, trimipramine, nortriptyline, protriptyline, desipramine	Tricyclic antidepressants increase the systemic circulation of catecholamines and can lead to systemic hypertension when supplementary epinephrine is present.

Elderly

Current demographic data show that the North American population is aging, and projections suggest that the percentage of older people will continue to increase.⁴⁴ In those of advanced age, the pharmacokinetics and pharmacodynamics of many drugs are altered.⁴⁴ No significant differences in the response of the elderly to local anaesthetics are expected. However, as aging is accompanied by decreased liver and kidney function, doses below the maximum are recommended.⁴⁴

Also, geriatric patients commonly have cardiovascular disease and, thus, the dose of epinephrine contained in anaesthetics should be limited to a maximum of 0.04 mg.⁴⁴ Even without a history of overt cardiovascular disease, it is prudent to minimise the use of epinephrine in elderly patients simply because of the expected effect of aging on the heart. Monitoring blood pressure and heart rate is advised when considering multiple administrations of epinephrine-containing local anaesthetic.

Children

Children are at higher risk for soft tissue injury due to a relative lack of awareness after local anaesthetic administration. Children are at a higher risk for local anaesthetic systemic toxicity because they weigh significantly less than an adult patient so their absolute threshold for local anaesthesia deposition is much lower than that of adults.⁴⁵ Practitioners should also be wary of patient and personal safety when delivering local anaesthetic to a pre-cooperative or anxious child as needle-stick injury may be more likely given a mobile target for local anaesthesia deposition.

Patients on anticoagulants

It is currently understood that patients within therapeutic international normalised ratio (INR) ranges can receive local anaesthetic nerve blocks without cessation of the anticoagulant beforehand. Even if a haematoma does occur, local haemostatic measures are generally sufficient to produce haemostasis.

Advances

Computer-controlled local anaesthetic delivery

There are now several electronic devices on the market that aid in the delivery of local anaesthesia, specifically with digital controls that can be manipulated to aid in aspiration and continuous delivery of local anaesthetic solution.⁴⁶ Many microprocessor-aided local anaesthesia devices will monitor the counterpressure exerted by the tissues into which the local anaesthetic is being injected and vary the rate of deposition of injectate accordingly.⁴⁷ In addition to assuming a less threatening appearance than a traditional syringe and needle armamentarium, these computer-controlled devices will ensure both appropriate aspiration and duration of delivery of the local anaesthesia which may reduce injection pain.

Phentolamine mesylate

Most local anaesthetic cartridges deposited worldwide contain epinephrine, so for patients at higher risk of traumatic injury to soft tissues or simply patients who wish to have their blockade reversed more quickly, phentolamine mesylate is a vasodilator that when deposited in a similar location to the original epinephrine-containing local anaesthetic solution can overwhelm the previous vasoconstriction and aid in the redistribution (and the clinical offset) of the local anaesthetic.⁴⁸ Recent studies suggest that it may have particular use in children in providing a more rapid recovery of lip sensation which may decrease the incidence of soft tissue trauma associated with local anaesthetic delivery in this age group.⁴⁹

Buffered local anaesthetics

It is believed that an increased pH of a solution being deposited could decrease the amount of discomfort associated with injections and increase the speed of onset of nerve blockade. Current studies show that the above claims above are increasingly likely to be true and dental manufacturing companies are creating devices that alkalinise, that is increase the pH of, local anaesthetic solutions prior to dental injection.⁵⁰ It should be noted that a recent meta-analysis shows that buffered local anaesthetics have 2.23 times greater likelihood of achieving profound anaesthesia in pulpally involved teeth.⁵¹

Inhaled local anaesthetics

A combination of local anaesthetics (tetracaine) and nasal decongestants (oxymetazoline) is being used to anaesthetise maxillary anterior teeth. This combination of drugs may demonstrate less successful pulpal anaesthesia and more adverse events compared to traditionally deposited local anaesthetics.⁵²

Liposomal bupivacaine

In an attempt to increase the duration of local anaesthetics, a formulation of bupivacaine has been produced where the local anaesthetic molecule is loaded in multivesicular liposomes. This slow-release formulation of drug is able to delay the release of local anaesthetic and therefore extend the duration of pain relief for the patient for up to 72 hours, compared to unaltered bupivacaine traditionally providing up to 8 hours of analgesia. It has been demonstrated to be suitable for local infiltration leading to increased duration of action and subsequent sparing of other analgesic medications (such as opioids).⁵³ The safety profile is currently being established and appears not to differ from that of bupivacaine with no additional incidence of adverse events being noted. Some trials have noted no difference in reducing the duration of analgesia of necrotic teeth from that of traditional bupivacaine.⁵⁴ That being said, additional trials with significant power are needed before its use can be recommended.

Local anaesthetic infusion pumps for localised deposition at the surgical site

Following surgical procedures, clinicians must determine the most appropriate means of controlling any post-operative pain associated with the procedure. This can be accomplished by a variety of localised or systemic means (some of which have been noted previously), one of which is an emerging method of patient-controlled localised deposition of local anaesthetic at the site of injury or surgery. There are many examples of a patient-controlled local anaesthetic infusion pump such as the ON-Q pain pump being used for general medical surgery,^{55–57} but there is still much research to be carried out about these infiltrating catheters and their potential benefit in treating the head and neck region,⁵⁸ and possible intraoral applications.

Ultrasound-guided IAN blocks

In order to negate mandibular anatomical differences in varied patient populations, the use of ultrasonography to visualise and direct the blockage of the IAN may prove worthwhile. Previous studies have either used Doppler ultrasound (i.e. indirect assessment) of the IAN position for local anaesthetic deposition⁵⁹ or injected coloured dye on cadavers to assess proximity of injectate deposition to the IAN.⁶⁰ There are currently ongoing studies using B-mode ultrasound (i.e. direct assessment) to directly visualise the IAN while using intraoral ultrasound to guide intraoral inferior alveolar blocks on patients with subsequent objective pulpal anaesthesia testing.

Conclusion

This paper provides a review of the pharmacology, techniques, and advances of local anaesthesia use in dentistry and should serve as a baseline for understanding that general dental practitioners possess for safe treatment of patients. Clinicians are encouraged to continue to expand both their didactic knowledge and practical clinical skills through advanced reading, discussion with colleagues, continuing education courses and treatment of patients.

Conflict of interest

None.

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