CHAPTER 59

UPDATE ON LOCAL ANESTHETICS

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Local anesthetics are some of the most commonly-used drugs in podiatric medicine today. Local anesthetics allow minor surgical procedures to be carried out virtually pain-free in the office setting. They also have greatly decreased the inherent risks associated with surgical procedures that would normally require general anesthesia.

To effectively use a local anesthetic, it is important to understand its mechanism of action, side effects, and chemical properties. The physician must also be familiar with the different types of local anesthetics available (Table 1).

Table 1

AVAILABLE LOCAL ANESTHETICS

	Concentration	Concentration of Epinephrine
Carbocaine	1%	
	1.5%	
	2%	
Marcaine	.25%	
	.5%	
	.75%	
Marcaine w/Epinephrine	.25%	1:200,000
	.5%	1:200,000
	.75%	1:200,000
Polocaine	1%	
	1.5%	
	2%	
Sensorcaine	.25%	
	.5%	
	.75%	
Sensorcaine w/Epinephrine	.25%	1:200,000
	.5%	1:200,000
	.75%	1:200,000
Xylocaine	.5%	
	1%	
	1.5%	
	2%	
Xylocaine w/Epinephrine	.5%	1:200,000
	1%	1:100,000
	1%	1:200,000
	1.5%	1:200,000
	2 %	1:100,000
	2 %	1:200,000

HISTORY

The first recorded use of local anesthetics was by the South American Indians before the Spanish conquest. The Indians would use the saliva from chewed cocoa leaves and pour it into wounds. By 1860, the purified substance from cocoa leaves, known as cocaine, was identified. In 1880, von Anrep published a paper describing the physiologic effects that the administration of cocaine had on animals.

Eventually, the side effects of cocaine, such as seizure and respiratory arrest, became known. Wood proposed the concept of performing nerve blocks with cocaine. In 1889, Koller began using cocaine for ophthalmological procedures. Later on, cocaine was used in dentistry and for spinal anesthesia. As the use of cocaine in medicine increased, so did the reports of addiction, systemic toxicity, and death. Eventually cocaine was limited to its current use as a local anesthetic.

The negative side effects of cocaine led to the search for safer local anesthetics. In 1904, Einham produced Procaine. Later in 1929 came Dibucaine, the first amide local anesthetic. In 1931, Tetracaine was synthesized. The current types of local anesthetics exist as a result of the early studies performed with cocaine.

CLASSIFICATION

Local anesthetic agents used today can be classified into two broad categories, the amide group and the ester group. The basic local anesthetic molecule includes an aromatic ring, an intermediate chain, and an amino group. The major difference between the two types of local anesthetics is the bond between the aromatic ring and the intermediate chain. This bond can be either an ester or an amide.

In the amide group of local anesthetics, many subgroups exist. Amide anesthetics can also be further broken down by variations in the amine portions of the drug. Lidocaine is a tertiary amine, while Prilocaine is a secondary amine. By adding a

piperidine ring, mepivacaine and bupivacaine are made. The chemical structure of a local anesthetic is important because of its influence on the site and rate of metabolism. Amide agents are hydrolyzed by the liver, while ester agents are hydrolyzed by cholinesterases in the blood. Amide agents take longer to metabolize than ester agents do. As a result of the longer metabolism rates of amide agents, toxic reactions induced by these amide agents last longer than toxic reactions induced by ester agents. The terminal elimination half-life of amide agents ranges from 1.5 to 3.0 hours.

MECHANISM OF ACTION

Nerves communicate through conduction of impulses along nerve axons by the flow of ions through voltage gates. Local anesthetics work by blocking these gates to prevent nerve conduction. Currently it is believed that the local anesthetic either blocks the ion pore itself, or binds to a receptor affecting ion pore function.

CHEMICAL PROPERTIES

The chemical properties of local anesthetics determine the onset of action and lipid solubility. The non-ionized form of the local anesthetic is more lipid soluble, therefore, penetrating nerve membranes more easily. This results in a smaller quantity of local anesthetic required for nerve block. However, experiments on animals have shown that local anesthetic agents with low lipid solubility are less toxic than those that are highly lipid soluble. Greater toxicity is thought to be associated with the enhanced ability of highly lipid soluble anesthetics to penetrate central nervous system tissue. Local anesthetics, such as lidocaine and mepivacaine, are less lipid soluble than bupivacaine. It has also been shown that local anesthetics that are highly protein bound, such as bupivacaine, are potentially more toxic than those that are less protein bound, such as lidocaine.

Local anesthetics are also available with epinephrine. By using epinephrine, the absorption rate into the bloodstream is reduced, which keeps the local anesthetic in the desired area for longer periods of time, and reduces the chance of systemic toxicity.

It is important for the physician to be familiar with the maximum dosage of commonly-used local anesthetics, in order to prevent toxic side effects (Table 2).

Table 2

MAXIMUM DOSES OF COMMONLY USED LOCAL ANESTHETICS IN PODIATRIC MEDICINE

Lidocaine (plain)	300 mg
Lidocaine (with epinephrine)	500 mg
Bupivacaine (plain)	175 mg
Bupivacaine (with epinephrine)	225 mg
Mepivacaine (plain)	400 mg

SYSTEMIC TOXICITIES

The site at which a local anesthetic is injected determines how quickly the drug enters the bloodstream. Direct intravenous injection produces an immediate peak blood level. Injecting highly vascularized areas, such as an intercostal space, is the second most rapid method for entrance of local anesthetics into the bloodstream. Injection into poorly-vascularized areas produces lower peak levels in the blood at a slower rate. Mineo found that when using local anesthetics for ankle blocks at near maximum dosages, blood levels reached only 1/5 of that considered to be toxic. Mineo concluded that when using local anesthetics for ankle blocks, a wide margin of safety exists.

Scott studied the effects of threshold dose for central nervous system toxicity and found that when a local anesthetic was injected at a slower rate, a higher blood level was required to produce a toxic central nervous system effect. The two main sites for toxicity to local anesthetics are the central nervous system and the cardiovascular system.

The general pattern of signs and symptoms of central nervous system toxicity are shown in Table 3. These signs appear in this general order when the infusion of the local anesthetic is slow. However, a bolus dose may produce more rapid side effects, and convulsions may appear first. Although it appears that local anesthetics excite the central nervous system, this is a dose-dependant effect. At low doses, local anesthetics depress the

central nervous system. At higher doses, local anesthetics suppress the inhibitory cortical synapses that prevent seizures and convulsions. As doses continue to increase, the facilitatory pathways become blocked, leading to overall central nervous system depression, and eventually coma and death.

Table 3

SIGNS AND SYMPTOMS OF CENTRAL NERVOUS SYSTEM TOXICITY OF LOCAL ANESTHETICS

1. Numbness of the tongue
2. Light-headedness
3. Tinnitus
4. Visual disturbances
5. Slurring of speech
6. Muscular twitching
7. Irrational conversation
8. Unconsciousness
9. Grand mal convulsions
10. Coma
11. Apnea

The cardiovascular system is more resistant to the effects of local anesthetics than the central nervous system. Local anesthetics can act as anti-arrhythmic agents at certain doses. Generally, local anesthetics depress the activity of the heart. Local anesthetics reduce myocardial contractile force and prolong intracardiac function.

Local anesthetics also act as vasodilators, helping to speed absorption into the bloodstream, and increase effects on the cardiovascular and central nervous systems.

ALLERGIC REACTIONS

Allergic reactions resulting from the administration of local anesthetics are rare. Local anesthetics in the ester group are derived from para-amino benzoic acid (PABA), which is a known allergen. Most reports of local anesthetic allergic reactions are dermatologic in nature, and a great majority are of the ester-type. Since the introduction of amide agents, the incidence of allergic reactions has decreased. However, some preparations of the amide agents employ methylparaben as a preservative. Methylparaben is chemically related to PABA, and is also an allergen. Therefore, local anesthetics without preservatives should be used in patients who relate an allergy to methylparaben.

LOCAL ANESTHETIC USE IN PREGNANCY

The toxic effects of local anesthetic use in pregnancy have been extensively studied in sheep. It was found that pregnant ewes were more susceptible to the toxic effects of bupivacaine than were the non-pregnant ewes. When lidocaine was studied, no difference was shown to exist between the pregnant and non-pregnant ewes. Bupivacaine appears to be more toxic when used during pregnancy than does lidocaine or mepivicaine.

EFFECT OF INFLAMMATION ON LOCAL ANESTHETIC ADMINISTRATION

Inflammation can impair the effectiveness of a local anesthetic block. Local inflammation has been shown to cause tissue acidity. The acidic environment in the extracellular space reduces the amount of local anesthetic that exists in a lipophilic state, thereby preventing enough of the local anesthetic from crossing the cell membrane.

The vasodilation associated with inflammation may also play a role in the decreased effect of local anesthesia. As the blood flow to the area increases, so does the uptake of the local anesthetic into the blood stream.

CARBONATED LOCAL ANESTHETICS

It has been shown that CO_2 potentiates the blocking action of local anesthetics by enhancing diffusion through the nerve membrane. As the rate of diffusion increases, so does the onset of anesthesia. As the carbon dioxide enters the intracellular space, it decreases the pH. The decreased intracellular pH increases the concentration of the cationic form of the local anesthetic, which is the active form. The local anesthetic in its charged form cannot cross the cell membrane, so it remains within the neuron for longer periods of time, resulting in longer anesthesia.

To produce the maximum clinical effect, the carbonated local anesthetic must be injected soon after opening the vial because the carbon dioxide rapidly diffuses out of the solution, resulting in a

diminished effect. Another method of carbonating local anesthetics is the addition of sodium bicarbonate to the solution. In one test, it was found that carbonated lidocaine with epinephrine reached onset of anesthesia 3 minutes faster than lidocaine and epinephrine without carbonation.

CONCLUSION

Local anesthetics provide anesthesia that can be effectively used in both the office and the operating room. By having a thorough understanding of the basics of local anesthetics, these drugs can be used as a safe, effective tool in the care of the podiatric patient.

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