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Local anesthetic calculations: avoiding trouble with pediatric patients

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Local anesthetic systemic toxicity (LAST) is a rare but avoidable consequence of local anesthetic overdose. This article will review the mechanism of action of local anesthetic toxicity and the signs and symptoms of LAST. Due to physiologic and anatomic differences between children and adults, LAST occurs more frequently in children; particularly when 3% mepivacaine is administered. The calculation of the maximum recommended dose based on mg/lb body weight, *Clark's rule,* and the *Rule of 25* in order to prevent LAST will also be reviewed, as well as the appropriate treatment procedures for a local anesthetic overdose.

Received: July 17, 2013
Revised: October 30, 2013
Accepted: February 10, 2014

Key words: local anesthetic toxicity, systemic toxicity, maximum recommended dose, Clark's rule, lidocaine, mepivacaine

Approximately 1 million cartridges of local anesthetic are used each day in the United States.[1] Local anesthetic systemic toxicity (LAST) is dose-related and although rare, occurs more frequently in small children than adults. LAST occurs more frequently when the patient is administered concomitant central nervous system (CNS) depressants, such as opioid/sedative medications.[2-9]

The following case serves as a reminder to proceed cautiously when administering routine local anesthetic, always keeping weight-based dosing in mind. A 50-lb, 8-year-old girl with a history of extensive caries and dental fear—but otherwise no medical problems, diseases, or allergies—presented for multiple extractions. For the initial sedation, the patient received oral promethazine, as well as nitrous oxide-oxygen inhalational sedation. A half hour later, the sedation was supplemented with an intramuscular dose of meperidine. After another half hour had elapsed, the child received injections of 6 cartridges of 3% mepivacaine plain (without a vasoconstrictor). Seizures and respiratory distress followed 5 minutes later. Resuscitation efforts followed, but were unsuccessful, and the patient died of anoxic encephalopathy.[5]

The most common cause of morbidity and mortality due to LAST is respiratory depression or apnea.[10] LAST occurs more frequently in children when 3% mepivacaine is administered, with the false presumption that a local anesthetic without a vasoconstrictor will have a shorter duration of soft tissue anesthesia and prevent postoperative self-inflicted lip and cheek trauma.[10,11]

Local anesthesia: mechanism of action and toxicity

Local anesthetics are essential for intraoperative dental analgesia; they work by blocking sodium channels in neurons so that pain signals from the periphery cannot be transmitted to the CNS. LAST is mediated by the same mechanism when the maximum recommended dose (MRD) is exceeded. This dose-related toxicity is especially important as the sodium channels in the cardiovascular system are blocked along with those in the CNS.[12,13]

Regardless of which local anesthetic is administered, the same progression of effects on the CNS and cardiovascular system occur with increasing plasma levels of local anesthetic.[12,13] Symptoms of early toxicity consist of numbness and tingling of the mouth and lips, metallic taste, diplopia, tinnitus, nausea, dizziness, and drowsiness.[12,13] These reactions are usually self-limiting and often are due to a mild overdose or an inadvertent intravascular injection. As the plasma concentrations of local anesthetic increase, the inhibitory neurons in the CNS are blocked, leaving excitatory neurons unopposed. Clinically, this manifests as tremors and tonic-clonic (also known as *grand mal*) seizures. CNS arousal may stimulate the cardiovascular system, possibly resulting in hypertension, tachycardia, and increased cardiac output.[12,13] At higher plasma levels of local anesthetic, both excitatory and inhibitory neurons are blocked to such a profound level that CNS and respiratory depression, unconsciousness, and respiratory arrest can occur. At even higher plasma concentrations, systemic vasodilation results in significant hypotension and cardiovascular depression. Local anesthetics also block sodium channels in the myocardium, resulting in bradycardia. Bradycardia is a major cause of concern when bupivacaine is used, as it can induce a use-dependent blockade at normal heart rates.[12,13] Because of its extended duration of action, bupivacaine is rarely indicated for children. The sequelae of depressed cardiac conduction include atrioventricular block, ventricular arrhythmias, cardiac arrest, and ultimately, death. A local anesthetic overdose can result in significant morbidity and mortality unless life support interventions can be initiated following standard basic and advanced cardiac life support guidelines.[12,13] Concomitant opioid sedative administration will augment respiratory depression and decrease the seizure threshold of local anesthetics.[3,5,6,12-15]

LAST: a greater tendency in pediatric patients

There are some important physiological differences between children and adults that play a role in the greater tendency for LAST to be reported in the pediatric population. Seated in the dental chair, a child may appear deceptively large. The reason that the child appears to be larger is that in the dental chair—with a bib, napkin, or blanket—only the child's disproportionately large head is visible.[4] This

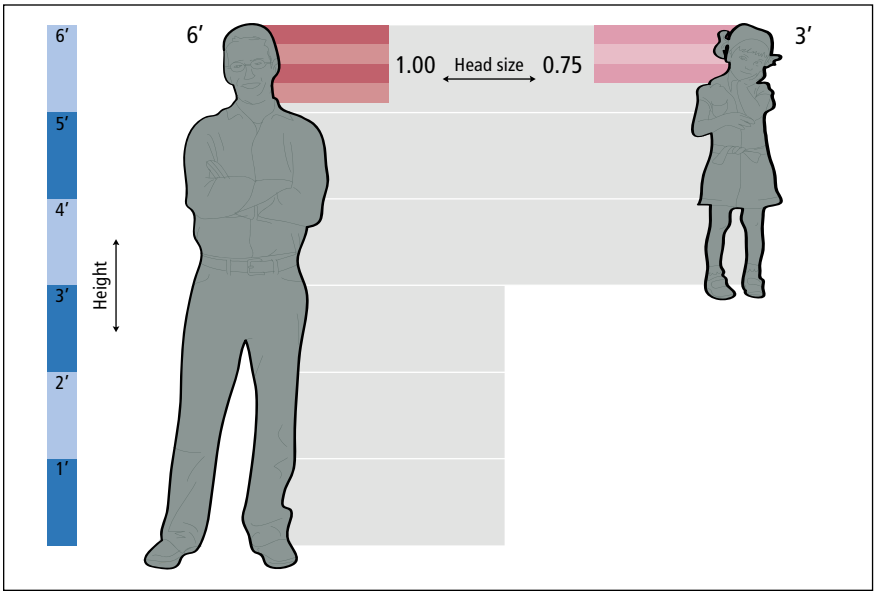

Figure. Diagram comparing the relative proportions in height vs head size between a 3.5-year-old child and an adult.

Table 1. Local anesthetic calculation: amount of local anesthetic in cartridges.

2% anesthetic = 2 grams/100 ml in volume = 2000 mg/100 ml = 20 mg/ml
3% anesthetic = 3 grams/100 ml in volume = 3000 mg/100 ml = 30 mg/ml
1 cartridge of local anesthetic is 1.8 ml in volume (exception: 4% articaine has 1.7 ml)
Therefore…
2% cartridge: 20 mg/ml x 1.8 ml/cartridge = 36 mg/cartridge
3% cartridge: 30 mg/ml x 1.8 ml/cartridge = 54 mg/cartridge

makes it more critical to determine the maximum dose and number of cartridges based on the child's actual weight.

The following example of a 3.5-year-old child illustrates the point that children often appear deceptively large and how this may prompt the dentist to overestimate the child's size based solely on appearances.[4] Because the head develops quickly during early childhood, children have disproportionately large heads; at the age of 3.5, a child's head is nearly 75% of the size of his/her adult counterpart.[4,5] However, the same child has only 50% of the height, 25% of the blood volume, and 20% of the weight compared to his/her adult counterpart (Figure).[4] The child's airway is also different, with narrower nasal passages, larynx, and trachea. Meanwhile, children have relatively larger tongues, tonsils, and adenoids than adults. These anatomic differences—coupled with the heightened susceptibility to CNS and respiratory depressants—render children more vulnerable to losing airway patency.[4]

Local anesthetic selection: misconceptions about prolonged soft tissue numbness

When treating children, it is important to inform parents or caregivers that close postoperative supervision is needed to prevent the child from biting their lips, cheeks, and tongue. While the soft tissues are still numb, significant trauma from lip and cheek biting can occur. There is a misconception that using a local anesthetic without a vasoconstrictor, such as mepivacaine 3% plain, will provide a shorter duration of soft tissue anesthesia than a local anesthetic with a vasoconstrictor, such as 2% lidocaine with 1:100,000 epinephrine.[11,12] Mepivacaine does offer shorter *pulpal* anesthesia (20-40 minutes) as compared to lidocaine with epinephrine (60-90 minutes), but *soft tissue* anesthesia is similar between the 2 anesthetics: 120-180 minutes and 120-240 minutes for mepivacaine plain and lidocaine with epinephrine, respectively.[11] Hersh et al found that "the onset of soft tissue numbness, peak numbness effects, and numbness duration were quite similar" when comparing 3% mepivacaine plain and 2% lidocaine with epinephrine.[11]

Using 3% mepivacaine plain instead of 2% lidocaine with epinephrine does not provide any benefit with respect to the prevention of postoperative lip/mouth trauma, but the higher concentration of local anesthetic in the 3% mepivacaine solution makes it easier to reach or exceed the MRD.[3,4,11,16,17] A brief review of local anesthetic calculations illustrates this point: a 2% formulation of a drug means that there is 2 grams of drug in 100 ml volume. If 2 grams are in 100 ml, then 2000 mg are in 100 ml, which means that 20 mg are in each ml. Since a dental cartridge contains approximately 1.8 ml volume, then there are 36 mg drug per cartridge (Table 1). Similarly, when a drug is in a 3% formulation, there are 30 mg per ml, thus there are 54 mg per 1.8 ml dental cartridge. Therefore, a cartridge of 3% mepivacaine contains 50% more local anesthetic than a cartridge of 2% lidocaine; thus it would take less volume (or fewer cartridges) of the more concentrated drug (3% mepivacaine) to reach its respective MRD.[11]

Preventing local anesthetic toxicity: calculating appropriate weight-based dose

Respecting weight-based dosing limits is essential, as previous cases of LAST have resulted in significant morbidity and mortality when dosing limits were exceeded.[3,4,12,16,17] In a 1983 retrospective study, pediatric dental patients that received local anesthesia and opioid sedation—either local alone or local plus narcotic dose—exceeded their combined MRDs by a factor of ≥3; the result was either permanent brain damage or death.[6] In a 1992 survey of local anesthetic use

Table 2. Local anesthetic calculations for a 50 lb child based on mg/lb.

1. Calculate the MRD for each drug for a 50 lb child.
2% lidocaine with 1:100,000 epinephrine = 3.2 mg/lb x 50 lb = 160 mg
3% mepivacaine plain = 2.6 mg/lb x 50 lb = 130 mg
2. Determine the maximum number of cartridges based on the MRD.
2% lidocaine with 1:100,000 epinephrine: 160 mg ÷ 36 mg/cartridge = 4.4[a] cartridges
3% mepivacaine plain: 130 mg ÷ 54 mg/cartridge = 2.4[b] cartridges

[a]In clinical terms, 4.5 cartridges.
[b]In clinical terms, 2.5 cartridges.
Abbreviation: MRD, maximum recommended dose.

Table 3. Local anesthetic calculation for a 50 lb child based on Clark's rule.

1. Calculate the MRD from each drug for a 50 lb child.
Patient's weight/150 lb adult x adult MRD = patient's MRD
Adult MRD:
2% lidocaine with 1:100,000 epinephrine: 500 mg
3% mepivacaine plain: 400 mg
Lidocaine with 1:100,000 epinephrine: 50/150 x 500 mg = 166 mg
Mepivacaine plain: 50/150 x 400 mg = 133 mg
2. Determine the maximum number of cartridges based on the MRD.
2% lidocaine with 1:100,000 epinephrine: 166 mg ÷ 36 mg/cartridge = 4.62[a] cartridges
3% mepivacaine plain: 133 mg ÷ 54 mg/cartridge = 2.46[b] cartridges

[a]In clinical terms, 4.5 cartridges.
[b]In clinical terms, 2.5 cartridges.
Abbreviation: MRD, maximum recommended dose.

among Florida dentists who routinely treated pediatric patients, a majority of the respondents used an absolute number of cartridges without accounting for the child's age or weight.[2] A clinician can prevent a local anesthetic overdose by calculating the MRD and the maximum number of cartridges by weight to appropriately administer local anesthetic in children; this dose per weight is contingent on calculations of a weight that is consistent with normal growth and development and normal lean body mass.[18]

Based on these calculations, the MRD of 2% lidocaine with 1:100,000 epinephrine is 3.2 mg/lb; for a patient ≥150 lbs, the adult MRD is 500 mg. The MRD of 3% mepivacaine plain is 2.6 mg/lb; for a patient >150 lbs, the adult MRD is 400 mg.[18,19] Table 2 illustrates the calculation needed to derive the absolute maximum number of cartridges of 2% lidocaine with epinephrine and 3% mepivacaine plain that can be given to a child weighing 50 lb. This number is approximately 33% of the adult maximum number of cartridges. A vasoconstrictor (such as epinephrine) reduces the systemic absorption of a local anesthetic, and several pharmacokinetic studies have demonstrated that the average peak blood levels following maxillary infiltration injections were 3 times higher with 3% mepivacaine plain in comparison to 2% lidocaine with epinephrine.[12,20,21]

Table 4. Local anesthetic calculation for a 50 lb child based on the Rule of 25.

1 cartridge/25 lb weight
1 cartridge/25 lb weight x 50 lb child = 2 cartridges of any local anesthetic or combination of local anesthetics for a 50 lb patient.

Clark's rule is another weight-based method for calculating the MRD.[12] According to Clark's rule, the dose of local anesthetic should be reduced by the ratio of the child's weight to an adult weight of 150 lb.[5] Thus, if a child weighs 50 lb, then he/she is 33% of the established adult weight. Therefore, the child's MRD for any local would be 33% of the 150 lb adult MRD for a given local anesthetic. As stated before, the MRD for 2% lidocaine with epinephrine for a 150 lb adult is 500 mg, and the MRD for 3% mepivacaine plain is 400 mg. Therefore, the MRD for a 50 lb patient is 33% of the adult MRD, which calculates as 166 mg of 2% lidocaine with epinephrine (approximately 4.5 cartridges) or 133 mg of 3% mepivacaine plain (approximately 2.5 cartridges.) (Table 3).[12]

It is important to note that the effects of all local anesthetics, including toxicity, are mediated at the sodium channel in a dose-dependent fashion. The effects of various local anesthetics are additive. Once the MRD for 1 local anesthetic is administered, the patient cannot receive any other local anesthetics, including topical applications.[22]

Moore & Hersh describe a simplified alternative for calculating safe maximum doses using a conservative guideline.[12] Described as the *Rule of 25*, this alternative calculation can be applied to all US dental local anesthetic formulations for healthy patients. The Rule of 25 states that 1 cartridge of any formulation marketed in the US may be used per 25 lb of weight. Therefore, 1 cartridge for a 25 lb patient, 2 cartridges for a 50 lb patient, 3 cartridges for a 75 lb patient, up to a maximum of 6 cartridges for patients ≥150 lbs (Table 4).[12] The end result of the Rule of 25 is a lower number of cartridges administered to the child in comparison to other weight-based calculations (Table 5). Since the vast majority of local anesthetic morbidity and mortality reports involve children ≤8 years of age, the Rule of 25 may be more appropriate in this population than in calculations used for adults.[12]

Table 5. Summary of dosing calculations in a 50 lb child.

	Adult MRD	Weight-based calculations	Clark's rule	Rule of 25
MRD 2% lidocaine with 1:100,000 epinephrine	500 mg	160 mg	166 mg	N/A
Maximum cartridges with 2% lidocaine with 1:100,000 epinephrine	13.5	4.5	4.5	2.0
MRD 3% mepivacaine plain	400 mg	130 mg	133 mg	N/A
Maximum cartridges with 3% mepivacaine plain	7.5	2.5	2.5	2.0

Abbreviation: MRD, maximum recommended dose.

When treating small children, it is advisable to determine the maximum number of local anesthetic cartridges needed for that appointment. Keep only this amount of cartridges on the tray, and do not discard any used cartridges until the appointment is over. This will precisely track the number of cartridges administered.

Aspiration and slow injection will allow for recognition of inadvertent intravascular injection before the entire cartridge is injected into a vessel.[22] Profound anesthesia can often be achieved in children with less than a full cartridge of anesthetic. Injecting slowly—approximately 30-60 seconds per cartridge—will minimize discomfort and allow retention of the local anesthetic at the target site rather than being flushed farther away.[22] Rather than giving the entire predetermined amount of local anesthetic at the beginning of a procedure, it is preferable to reserve 25% of the predetermined amount of local anesthetic in case an injection fails or if supplemental anesthesia is needed later.[5] With a reported 15%-20% failure rate for inferior alveolar nerve blocks, it is critical to use the proper technique in order to reduce the need for supplemental injections.[2,22] On average, a child's mandibular foramen is near the occlusal plane; by adulthood, the mandibular foramen moves posteriorly and is approximately 7 mm above the occlusal plane.[2,23] Therefore, if the inferior alveolar nerve block is missed in the treatment of a child but the MRD has not been exceeded, one can attempt to inject vertically higher.[2] While lip numbness is usually considered a sign of an adequate inferior alveolar nerve block, the lack of gingival response to stimulation is considered to be a more rapid and reliable indicator of anesthesia in young children than asking the patient about the presence or absence of lip numbness.[2,24] A possible alternative to mandibular blocks for procedures in young children is to utilize a buccal mandibular infiltration technique with 4% articaine plus 1:100,000 epinephrine, which appears to produce a high success rate of mandibular pulpal anesthesia.[25,26] If the injections fail and the predetermined maximum amount of local anesthetic has been administered, it is recommended to not attempt to supplement with more local anesthetic.[2,22] The best approach would be to reschedule the treatment appointment.

Local anesthetic systemic toxicity: warning signs and management

When providing emergency care, a dentist needs to immediately recognize signs and symptoms of LAST (such as tremors or convulsions). The dental procedure should be stopped as soon as any neurological, respiratory, or cardiovascular signs or symptoms of local anesthetic overdose become apparent.[5] The dentist should monitor vital signs (such as pulse and blood pressure), watch for coloration if pulse oximetry is not available, and assess breathing by looking for chest rise and movement of air. If necessary, initiate basic life support in the form of chest compressions and positive pressure ventilation with oxygen until medical assistance arrives.[5] In the event of an emergency, any delay may result in the patient's reserves of oxygen being consumed leading to poor oxygenation of key organs such as the brain and heart, and irreversible damage may occur. Three key interventions are necessary: 1) clear the airway of any obstructions including the tongue or foreign bodies such as gauze; 2) provide supplemental positive pressure oxygen; and 3) if the patient has no pulse, apply chest compressions so that oxygenated blood can reach the brain and heart.[4]

Basic life support skills are essential until the patient can be transferred to a hospital.[4] Someone on the dental team should call for medical assistance; another should manage seizures and respiratory depression.[5] The patient should be positioned on the left lateral side to facilitate suction, which should be applied to the pharynx to remove any saliva and foreign bodies, such as dislodged stainless steel crowns, rubber dam clamps, or pieces of gauze. An oxygen tank should be available to provide supplemental oxygen either by nasal cannula or nasal hood for a patient who is able to breathe, or by a bag-valve-mask if there is significant respiratory depression. According to Moore, "positive pressure oxygen ventilation is the most important element in managing local anesthetic overdose."[5] Although rarely required, advanced management of seizures may include the intravenous administration of a benzodiazepine such as diazepam or midazolam.[5,12] Following any convulsion, serious respiratory depression can occur, so it is critical to continue to monitor the patient and support the airway.[5,12]

Conclusions

While local anesthetics possess a wide margin of safety in adult patients, MRDs of these drugs can be easily exceeded in pediatric dental patients. The prevention of LAST in young children is best achieved by strictly adhering to weight-based MRD dosing guidelines. The more conservative Rule of 25, which states that no more than 1 cartridge of local anesthetic should be given for each 25 lb of patient body weight, will impart an added safety layer in children ≤8 years of age.

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