

Continuous Infusion In Pediatric Patients

The information provided herein is based on I-Flow®'s review of published medical literature, including textbooks. Always refer to the drug manufacturer's prescribing information when deciding whether to administer any drug with the ON-Q® Pain Relief System and for appropriate dosing information.

The safety and effectiveness of local anesthetics has not been established in controlled clinical trials with children. Nonetheless, continuous infusions of such anesthetics for postoperative pain management is used in pediatric patients in the practice of medicine.

The choice of local anesthetic depends on the desired onset time, duration of action and safety of the drug. The safety and effectiveness of local anesthetics depend on proper dosage, correct technique, adequate precautions and readiness for emergencies. Although the reasons for continuous infusions of local anesthetics for postoperative pain management in pediatric patients are similar to adults, dosing of these agents may differ. This difference is due to age-related changes in the pharmacokinetics and pharmacodynamics of local anesthetics. Practitioners who choose to administer local anesthetics to pediatric patients with the ON-Q® Pain Relief System should be familiar with the safety profile of the drug they choose and refer to relevant published information, especially including medical textbooks on this therapy in this population.

There are two classes of local anesthetics in clinical use: amides and esters. Amide-class local anesthetics include lidocaine, etidocaine, prilocaine, mepivacaine, bupivacaine, levobupivacaine and ropivacaine. Ester anesthetics include chlorprocaine and tetracaine.

Amide anesthetic agents are protein bound in the plasma. The free or unbound fractions of local anesthetic are considered physiologically active and responsible for cardiovascular and central nervous system (CNS) effects. Neonates and infants less than 6 months of age are at particular risk for higher levels of unbound local anesthetic due to their decreased levels of plasma proteins (albumin and α 1-acid glycoprotein). Adult levels of α 1-acid glycoprotein are reached at about 1 year of age. The enzymes mediating metabolism of amide local anesthetic in the liver's cytochrome P450 system also reach adult activity levels at about 1 year of age. Consequently, these factors place this age group at greater risk of toxicity. Amide local anesthetics, therefore, should be used carefully in children, in particular neonates and infants, because they lack the ability to distribute and metabolize these agents in a timely and effective manner.

Ester anesthetics such as chlorprocaine and tetracaine depend on plasma esterases for elimination. Neonates and infants also have decreased levels of plasma esterases thus the plasma half-life of ester local anesthetics may be prolonged.

Distribution and systemic absorption of the local anesthetic agents may also be greater in young children due to increased cardiac output and regional blood flow. This may increase the risk of toxicity.

Dosing with continuous infusion of local anesthetics in children is based on the weight and age of the patient. (Table 1) Due to the potential for toxicity, these dosages should not be extrapolated from adult experiences, which often use a generalized dosage regimen. In addition to weight and age, the dose of any local anesthetic administered varies with the anesthetic procedure, the area to be anesthetized, the vascularity of the tissues, the number of neuronal segments to be blocked, the depth of anesthesia and degree of muscle relaxation required, the duration of anesthesia desired, individual tolerance and the physical condition of the patient. The smallest dose and concentration required to produce the intended result should be administered.

Table 1.
SUMMARY OF MAXIMUM DOSING OF LOCAL ANESTHETICS IN CHILDREN BASED UPON AGE AND WEIGHT

Local Anesthetic	Single Dose (mg/kg)	Maximum Continuous Infusion Rate (mg/kg/hr)	Maximum Continuous Infusion Rate in Infants <6 months of Age (mg/kg/hr)*
Bupivacaine**	3	0.4	0.2 to 0.25
Levobupivacaine***	3	0.4	0.2 to 0.25
Ropivacaine***	3	0.4	0.2 to 0.25
Lidocaine	5	1.6	0.8

* 30% dose reduction after 48 hours recommended for newborns <3 months of age.

** Per the FDA approved labeling, until further experience is gained in pediatric patients younger than 12 years, administration in this age group is not recommended. Continuous infusions of bupivacaine in children has been reported to result in high systemic levels of bupivacaine and seizures; high plasma levels may also be associated with cardiovascular abnormalities.

*** Per the FDA approved labeling, safety and effectiveness in pediatric patients has not been established.

Table 1, above, is modified from *Smith's Anesthesia for Infants and Children* 7th ed. Allison Kinder Ross: Pediatric Regional Anesthesia Chapter 14, Mosby Inc. 2006. Medical practitioners should consult the manufacturer's prescribing recommendations and standard textbooks to determine the accepted procedures and techniques for the administration of continuous infusions of local anesthetics.

Additionally, it is recommended that all caregivers receive technical training on the early signs and symptoms of local anesthetic toxicity. The caregiver should ensure that there is the immediate availability of oxygen, other resuscitative drugs, cardiopulmonary resuscitative equipment, and the personnel resources needed for proper management of toxic reactions and related emergencies.

A bibliography of references regarding dosing of local anesthetics is available from I-Flow Corporation Clinical Services.

References:

1. Davis PJ, Lerman J, Tofovic SP Cook DR. Pharmacology of Pediatric Anesthesia and Ross AK. Pediatric regional anesthesia. In: Motoyama EK, Davis PJ, eds. *Smith's Anesthesia for Infants and Children*. 7th ed. St. Louis, MO: Mosby Inc., 2006: 202-203, 459-465.
2. Zeltzer LK, Krell H. Pediatric Pain Management. In: Behrman RE, Kliegman R, Jensen HB, Stanton BF. eds. *Nelson Textbook of Pediatrics*: 18th ed. Philadelphia, PA: Saunders Elsevier 2007: 479.
3. Mazoit JX. Pharmacology of local anesthetics. In: Bissonnette B, Dalens PJ, eds. *Pediatric Anesthesia: Principles and Practice*. New York, NY: McGraw-Hill, 2002: 303-331.
4. Matuszczak M. Continuous perineural infusion in children. In: Chelly JE,

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