

Pediatric Pharmacotherapy

A Monthly Newsletter for Health Care Professionals
Children's Medical Center at the University of Virginia

Volume 2 Number 12

December 1996

Medications for Neonatal and Pediatric Advanced Life Support

In 1993, a survey of houseofficers from the University of Wales was conducted to evaluate pediatric advanced life support knowledge following the implementation of a rigorous training program.¹ The results were less than ideal. When asked for the correct dosage of epinephrine to be given to a child during cardiac arrest, only 52% could provide the answer without using a reference text. Although this number may seem surprisingly low, it reflects the difficulty most health care providers have in gaining mastery over this body of knowledge.

For new practitioners and those not routinely exposed to patients requiring resuscitation, remaining current and knowledgeable on advanced life support skills is difficult. The purpose of this article is to provide a brief review of the current recommendations of the American Heart Association and the American Academy of Pediatrics for medication administration during advanced life support in infants and young children.^{2,3}

Medication Administration

Venous administration is the preferred route for drug delivery during advanced life support. However, during cardiovascular collapse, establishing access may be difficult. During neonatal resuscitation, it is recommended that the umbilical vein be used, since it is more easily cannulated than scalp or peripheral veins.² In older infants and children, peripheral access is usually more easily established than central access. Regardless of the route used, all doses should be followed by a 5 ml normal saline flush to help move the drug more rapidly into the central circulation.

In patients less than six years of age, an intraosseous (IO) catheter may be used if attempts to gain peripheral venous access are not successful. All resuscitation medications, including catecholamines, may be administered into the bone marrow. Intramuscular and sublingual routes of administration are not recommended during resuscitation due to

delayed drug delivery. Intracardiac injection is no longer recommended due to the risks of hemopericardium and vessel injury in the face of questionable drug absorption.^{3,4}

Epinephrine, naloxone, atropine, and lidocaine may be given endotracheally (ET) during advanced life support if venous or intraosseous access is unavailable. The optimal dosages of these medications has not been well established. The current recommendations for naloxone, atropine, and lidocaine are to begin with the IV dose (Table). Studies have shown, however, that the endotracheal dose of epinephrine should be higher than standard intravenous doses. To administer medications via the endotracheal tube, the dose should be diluted in 3 to 5 ml of normal saline (1 to 2 ml for neonatal resuscitation) or instilled through a catheter inserted below the end of the endotracheal tube and followed by 3 to 5 ml of saline. Each dose should be followed by several positive-pressure ventilations using a hand resuscitation bag to ensure drug deposition into the lungs.^{2,3}

Epinephrine

Epinephrine is the most frequently used resuscitation medication in infants and children. During cardiac arrest, the primary benefit of epinephrine is its alpha-adrenergic activity, which causes intense vasoconstriction and increases systemic vascular resistance. In addition, epinephrine's effects at alpha receptors cause a reduction in blood flow to renal, splanchnic, mucosal, and dermal vascular beds, preserving blood flow to more critical organs. The beta-adrenergic effects of epinephrine cause an increase in cardiac contractility and heart rate, while relaxing smooth muscle.^{3,5}

Epinephrine is used for cardiac arrest (with or without a pulse), asystole, symptomatic bradycardia, and hypotension unrelated to volume depletion. It can be administered every 3 to 5 minutes as needed. The optimal dosage of epinephrine for infants and children during advanced life support remains controversial.^{2,3}

In neonatal resuscitation, epinephrine is given in a dosage of 0.01 to 0.03 mg/kg (0.1 to 0.3 ml/kg of the 1:10,000 solution) IV or ET.² Little research has been done to establish optimal dosage ranges during resuscitation in the newborn. At this time, higher doses of epinephrine are not routinely recommended due to concerns over the potential increased risk of intracranial hemorrhage and hypertension.^{6,7}

In pediatric resuscitation, the recommended initial dose of epinephrine is 0.01 mg/kg (0.1 ml/kg of the 1:10,000 solution) IV for bradycardia and cardiac arrest. If pulseless arrest persists, the dose may be increased to 0.1 mg/kg (0.1 ml/kg of the 1:1000 solution).^{3,8} This is the same dose used for endotracheal administration. The use of higher IV doses has been extrapolated from data in adults and in animal models. Results from research in children are mixed. A retrospective study comparing outcomes in children receiving high dose (> 0.1 mg/kg) vs. standard dose (< 0.1 mg/kg) therapy failed to demonstrate any differences in the number of successful resuscitations or in long-term survival.⁹

In pediatric patients with continued hypotension, epinephrine may be given as a continuous infusion (drip). The recommended starting dose is 2 mcg/kg/min, with the infusion rate then reduced to maintain the desired response, usually to 0.1 to 1 mcg/kg/min. Infusion of doses greater than 5 mcg/kg/min may produce profound vasoconstriction at the site of administration.³

To calculate an epinephrine drip, a simple formula for children uses 0.6 multiplied by the child's weight in kg. This amount (in mg) is then added to enough IV solution to equal a total of 100 ml. When the resulting solution is infused at a rate of ml/hr, it will deliver a dosage of 0.1 mcg/kg/min.^{3,10}

Sodium Bicarbonate

The development of a mixed metabolic and respiratory acidosis is common during cardiopulmonary arrest as a result of anaerobic metabolism and carbon dioxide retention.^{2,3} Acidosis may cause a decrease in myocardial contractility, lowering of blood pressure, and a blunting of the response to catecholamines.⁷ The optimal method to reverse this situation is to provide adequate ventilation and systemic perfusion. Administration of sodium bicarbonate is reserved for children with severe metabolic

acidosis associated with prolonged arrest, hyperkalemia, or tricyclic antidepressant overdoses.³

The standard dose of sodium bicarbonate in infants and children is 1 to 2 mEq/kg IV or IO.^{2,3} The use of additional doses (0.5 mEq/kg) should be guided by assessment of laboratory values. Standard solutions of 8.4% (1 mEq/ml) sodium bicarbonate are very hyperosmolar (2,000 mOsm/L) and should be used with caution. In neonates, only the 4.2% (0.5 mEq/ml) solution should be used to avoid increasing the risk of intraventricular hemorrhage.^{3,7} The rate of administration should be no greater than 1 mEq/kg/min.^{2,7}

Sodium bicarbonate should not be given endotracheally, since it can cause substantial tissue injury. It should not be mixed with other medications. Precipitation of calcium and inactivation of catecholamines may occur if they are mixed with sodium bicarbonate.³

Atropine

Like sodium bicarbonate, the role of atropine in neonatal and pediatric resuscitation has diminished over the past decade. Atropine is a parasympatholytic which reduces vagal tone, increasing atrial pacemaker firing and conduction through the atrioventricular node.^{2,7} It is indicated for the treatment of symptomatic bradycardia, as a second-line therapy after epinephrine. It is also indicated in situations where bradycardia is known to be the result of increased vagal tone (such as during intubation) or in documented atrioventricular block.⁸

In children, the dose of atropine is 0.02 mg/kg IV, IO, or ET with a minimum dose of 0.1 mg to avoid paradoxical bradycardia. The recommended maximum single dose is 0.5 mg for a child and 1 mg for an adolescent or adult. This dose may be repeated once, if no response is seen within 5 minutes.³

Naloxone

Naloxone is a pure antagonist which reverses the effects of opioids such as morphine and fentanyl. In resuscitations, it is used to reverse the respiratory and central nervous system depression and hypertension caused by administration of opioids.³ Naloxone is also indicated for severe respiratory depression in neonates whose mothers received opioids within four hours of delivery.²

Naloxone acts within 2-3 minutes and has a duration of 30 to 60 minutes. The recommended dose of naloxone for total reversal is 0.1 mg/kg for infants and children up to 5 years of age or 20 kg body weight. Children over 5 years or 20 kg should receive a standard 2 mg dose. Smaller doses may be used if only partial opioid reversal is desired. Naloxone may be administered by rapid IV push, IO, or ET. Intramuscular or subcutaneous administration may be used, but may result in erratic absorption and reduced efficacy.^{3,7}

Clinicians should be aware of the relatively short duration of action of naloxone compared to many opioids. Repeat dosing is often necessary to avoid recurrence of symptoms of opioid toxicity. Use of naloxone may induce symptoms of abrupt opioid withdrawal (including seizures) in patients receiving chronic therapy or in infants of opioid-addicted mothers.³

Calcium Chloride

Calcium is used in advanced life support to enhance cardiac contractility and increase systemic vascular resistance.^{3,5} Its efficacy in pediatric life support is not clearly established. At this time, calcium administration is recommended only in cases of hypocalcemia, hyperkalemia, hypermagnesemia, and calcium channel blocker overdose.^{3,8}

The recommended dose of calcium chloride is 0.2 to 0.25 ml/kg of a 10% solution, to provide 5-7 mg/kg elemental calcium (20 to 25 mg/kg calcium salt). This dose should be infused at a rate no faster than 100 mg/min and may be repeated one time. Rapid infusion may result in bradycardia or asystole.³

Dopamine

In patients who remain hypotensive or poorly perfused after initial resuscitation, a continuous infusion of a catecholamine such as epinephrine, dopamine, or dobutamine should be considered.

Dopamine acts at a variety of receptors. At low doses, 2 to 5 mcg/kg/min, dopamine acts primarily on dopaminergic receptors, causing increased renal, coronary, splanchnic, and cerebral blood flow. As the infusion rate is increased above 5 mcg/kg/min, dopamine stimulates beta-adrenergic receptors and increases release of norepinephrine, producing an increase in cardiac contractility. At infusion rates greater than 10 to 20 mcg/kg/min, dopamine begins to act at alpha-adrenergic

receptors, producing vasoconstriction. At these doses, however, dopamine produces significant tachycardia.^{2,3}

Because of its rapid elimination, dopamine can only be administered as a continuous infusion. To calculate a dopamine infusion, multiply the child's weight in kg by 6. This amount of dopamine (in mg) is then added to enough IV solution to equal a total of 100 ml. When the resulting solution is infused at a rate of ml/hr, it will deliver a dosage of 1 mcg/kg/min.^{2,3,10}

As with epinephrine, extravasation of dopamine can result in severe tissue necrosis. Administration through a central line is preferred. If extravasation occurs, administration of 2.5 to 5 mg phentolamine intradermally at the IV site may help to reverse the intense vasoconstriction.

Dobutamine

Like dopamine, dobutamine stimulates beta-adrenergic receptors and produces a positive inotropic response. It does not, however, act on dopaminergic or alpha-adrenergic receptors. Unlike the vasoconstriction seen with high doses of dopamine, dobutamine produces a mild vasodilatation. Dobutamine is typically started at a dose of 5 mcg/kg/min and titrated to achieve the desired blood pressure response. Dobutamine infusions may be prepared in the same manner as described for dopamine.³

Adenosine

Adenosine is a pharmacologic alternative to defibrillation in patients with supraventricular tachycardia.^{3,8} Adenosine produces a transient block of the atrioventricular node. Its short elimination half-life (approximately nine seconds) makes it a safe medication, but also makes it difficult to get adequate drug concentrations at the site of action. The dose for infants and children is 0.1 to 0.2 mg/kg administered by rapid IV push, followed immediately by a 2 to 3 ml normal saline flush. The recommended maximum dose is 12 mg.³

Lidocaine

Lidocaine plays a less important role in pediatric advanced life support than in adult emergencies. It is used to control ventricular tachycardia or fibrillation, rare occurrences in children. The recommended method of administration is a 1 mg/kg bolus loading dose, followed by a

continuous infusion of 20 to 50 mcg/kg/min.³ The dosage should be reduced in children with low cardiac output or reduced hepatic blood flow or function to avoid lidocaine accumulation. Signs of lidocaine toxicity include drowsiness, confusion, tremors, and seizures.

Bretylium

The efficacy of bretylium has not been established in pediatric arrhythmias. It is reserved for cases of ventricular fibrillation refractory to defibrillation and lidocaine. The recommended dose is 5 mg/kg administered by rapid IV infusion. A repeat dose of 10 mg/kg may be given if the patient fails another defibrillation attempt.³

This brief review has highlighted several of the more commonly used medications for resuscitation. For more information, health care providers should consult the latest guidelines from the American Heart Association texts.^{2,3} The University of Virginia offers educational programs for qualified individuals interested in training or recertification in neonatal and pediatric advanced life support. For more information on pediatric advanced life support, contact Dr. Kathryn Weise, Medical Director of the Life Support Learning Center, at (804) 982-1707. For information on neonatal resuscitation training, contact Dr. John Kattwinkel, Director of the Neonatal Intensive Care Unit, at (804) 924-5428.

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The editors of *Pediatric Pharmacotherapy* wish to thank Dr. Kathryn Weise for reviewing this article.

Pharmacology Literature Review

Therapeutic Equivalence

This review provides a brief introduction to drug substitution policies. The author describes the methods used by the FDA for assessing bioequivalence and reviews some of the problems reported with substitution of medications. A list of medications with known bioequivalence concerns is included. Meredith PA. Generic drugs: Therapeutic equivalence. ***Drug Safety* 1996;15:233-42.**

Formulary Update

The following actions were taken by the Pharmacy and Therapeutics Committee at their meeting on 12/6/96:

- 1.
- 2.
- 3.
- 4.

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