

The Myth of a Minimum Dose for Atropine

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ABBREVIATION

PALS—Pediatric Advanced Life Support

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Since its first appearance, the Pediatric Advanced Life Support (PALS) course has recommended a minimum dose of atropine of 0.1 mg regardless of the body weight of the child. The most recent update of PALS, after the extensive International Liaison Committee on Resuscitation (ILCOR) process, designed to develop the evidence base of resuscitation recommendations, still contains this same recommendation.¹ This recommendation is frequently quoted by pediatric residents fresh from their PALS courses; I have often been informed that a lower dose causes “paradoxical bradycardia.” Indeed, the computerized printouts for resuscitation drugs and doses from our hospital information system are based on the PALS guidelines and give the same recommended dose. Thus, if the computerized printout were to be followed, a 2-kg infant would receive 0.1 instead of 0.04 mg of atropine. If the indication persisted and a second dose were to be given, potentially lethal overdosage could occur.

This minimum dose is widely repeated. The 12th edition of *The Harriet Lane Handbook*² states that the preanesthesia dose (30–60 minutes before operation) for a child is “0.01 mg/kg/dose SC/IV/IM, max. dose: 0.4 mg/dose; min. dose: 0.1 mg/dose; may repeat Q4–6 hr” and for “Cardiopulmonary resuscitation (see remarks): Child,” the recommended dose is “0.02 mg/kg/dose IV Q5 min × 2–3 doses PRN; min. dose: 0.1 mg”; the remarks to which the authors refer included: “Doses < 0.1 mg have been associated with paradoxical bradycardia.”

In contrast, the 14th edition of the *Pediatric Dosage Handbook*³ states under the heading “usual dosage” the following: “Note: Doses <0.1 mg have been associated with paradoxical bradycardia”; however, the authors then state under the dose recommendations for neonates for pre-anesthetic administration that “use of a minimum dosage of 0.1 mg in neonates <5kg will result in dosages > 0.02 mg/kg, there is no documented minimum dosage in this age group.” Subsequently, under dose recommendations for bradycardia, the minimum dosage for intravenous, intraosseous, and intratracheal administration is said to be 0.02 mg/kg, minimum dose 0.1 mg, without any comment. The widely used Neofax,⁴ on the other hand, makes no mention of a minimum dosage.

The recommended dose for atropine in most circumstances, including in PALS, is 0.02 mg/kg; therefore, the minimum dose recommendation only affects infants with a body weight of <5 kg and leads to a progressive increase in the dose administered on a per-kilogram basis as the body weight of the infant in question gets smaller. It should be noted that although the PALS course also still recommends this minimum dosage, the PALS recommendations are not consistent: 0.03 mg/kg for endotracheal use “higher than the vascular dose” is recommended, and no minimum is mentioned. It should also be noted that the International Liaison Committee on Resuscitation task forces did not address the issue of a minimum dose.

I could think of no rational or physiologic reason why a 1-kg infant should receive a fivefold overdose of atropine compared with a 5-kg infant, so I decided to pursue the source of this recommendation.

In the latest edition of PALS, the reference is a 1971 article written by Dauchot and Gravenstein.⁵ This interesting physiologic study demonstrated that very low doses of atropine, dosed on a per-kilogram basis, of 0.0036 mg/kg (3.6 µg/kg) or less may cause a mild slowing of heart rate. It should be noted that there were no premature infants included in the study; the youngest studied infants were between 6 weeks and 3 months of age, and in these infants the cardiac slowing effect was not statistically significant. The most markedly affected children were the 7- to 12-year-olds who had an average decrease in heart rate from 79 to 70 beats per minute; above this dosage, heart rate was increased by atropine. This effect was later demonstrated to be a result of blockade of M1 muscarinic receptors, whereas the familiar tachycardic response is a result of blockade of the M2 and M3 receptors.⁶

The article in question, which seems to be the only source for the recommendation and which has been requoted on multiple occasions, presumably without a careful check of the primary source, provides absolutely no justification for an overall dose minimum. It does suggest that doses of 0.0036 mg/kg or less will not reliably block M2 and M3 receptors; therefore, to have this effect and prevent vagally mediated bradycardia,

the dose should be more than this minimum per-kilogram dose.

It seems that the strict, universal, often-repeated, minimum absolute dose of atropine is derived from an unsupported and irrational statement in the discussion of the aforementioned article in which the authors stated, “we therefore give a minimum dose of 0.1 mg of atropine to our patients.” This minimum total dose is completely out of keeping with the results of the careful physiologic investigation that they performed but has developed a scriptural correctness.

This approach to atropine dosing may be dangerous; a neonate who developed a toxic reaction (lethargy, opisthotonus, seizures, periodic breathing, dilated unresponsive pupils, dry mucous membranes and skin, and urinary retention) after 2 “minimum doses” of atropine (which calculated as 0.09 mg/kg) over 5 hours has been reported.⁷ Although several children have survived accidental overdosage with large amounts of atropine by mouth (16–40 mg/kg), Gillick⁷ underlined that death in children from atropine poisoning has occurred with doses as small as 0.05 mg/kg intravenously.

A dose of 0.1 mg would be toxic for some of our neonatal patients. There is no justification for this minimum dos-

age. For infants of <5 kg body weight, 0.1 mg is an overdose; this dose is probably not of much significance for infants of, say, ≥3.5 kg, but for an infant of 0.7 kg it could be disastrous.

A recent study of preterm newborns⁸ with an average weight of just over 1 kg used an appropriate dose of 0.01 mg/kg (that is an average one-tenth of the recommended minimum) and revealed a shortening of the R-R interval and no “paradoxical bradycardia.” Several prospective studies of neonatal intubation have used a dose of either 0.02 mg/kg^{9–11} or 0.01 mg/kg¹² and have carefully monitored heart rates. These studies routinely show an increase in heart rate after atropine and prevention of laryngoscopy-induced bradycardia and have never demonstrated paradoxical bradycardia. In these studies, all of the subjects had received doses that are less than the “minimum dose” recommended by PALS, which is the minimum dose calculated by many hospital information systems.

Precalculated resuscitation drug charts, pediatric reference books, the PALS program, and computer-based drug calculators should be revised to remove this erroneous and dangerous recommendation.

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