Myth: Atropine should be administered before succinylcholine for neonatal and pediatric intubation

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ABSTRACT
Succinylcholine is often used to facilitate neonatal and pediatric rapid sequence intubation in the emergency department, and most relevant literature recommends administering atropine prior to succinylcholine to reduce the risk of bradycardia. Given the potential complications associated with combining these medications, we searched the published literature for evidence supporting this practice. Most studies recommending atropine premedication were undertaken in the operating room setting and pertained to repeated succinylcholine dosing. Furthermore, there is little published evidence to indicate that succinylcholine-related bradycardia is a clinically important side effect. Several authors have called for the practice to cease, but, to date, these calls have gone unheeded. We found no evidence supporting atropine’s use in pediatric patients prior to single-dose succinylcholine. Atropine premedication for emergency department rapid sequence intubation is unnecessary and should not be viewed as a “standard of care.”

Key words: atropine; succinylcholine; pediatric intubation

RéSUMÉ
On a souvent recours à la succinylcholine pour faciliter l’intubation en séquence rapide chez les nouveau-nés et les enfants au département d’urgence et la majorité des écrits pertinents sur le sujet recommandent l’administration d’atropine avant la succinylcholine afin de diminuer le risque de bradycardie. Compte tenu des complications possibles associées à la combinaison de ces deux médicaments, nous avons cherché dans la littérature publiée des données probantes qui appuient cette pratique. La plupart des études qui recommandent la prémédication à l’aide d’atropine ont été menées en salle d’opération et se rapportaient à des doses répétées de succinylcholine. De plus, il existe peu de preuves publiées qui appuient la notion selon laquelle la bradycardie liée à la succinylcholine représente un effet indésirable cliniquement important. Plusieurs auteurs ont recommandé l’abandon d’une telle pratique, mais jusqu’à maintenant, ces recommandations ont été ignorées. Nous n’avons trouvé aucune preuve appuyant le recours à l’atropine chez les patients pédiatriques avant l’administration d’une dose unique de succinylcholine. La prémédication à l’atropine pour l’intubation en séquence rapide au département d’urgence n’est pas nécessaire et ne devrait pas être vue comme «une norme de diligence.»

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Introduction

Prior to the 1970s, most medical care in emergency departments (EDs) was administered by physicians without specialty training in emergency medicine. As a result, airway interventions were often performed by anesthesiologists called to the ED. With the advent of emergency medicine residency training programs in the 1970s, emergency physicians gained airway management skills and developed rapid sequence intubation protocols. Adapted from anesthesiologists’ rapid sequence anesthesia induction, rapid sequence intubation uses sedation and paralysis to facilitate intubation of unprepared patients without causing adverse physiologic responses such as hypoxemia, hypertension and elevated intracranial pressure.1,2

Articles in the emergency medicine and pediatric literature have repeatedly recommended that children receive atropine before succinylcholine to prevent bradycardia and asystole.3-5 Atropine is thought to prevent bradycardia related to 2 different mechanisms. First, succinylcholine itself causes bradycardia, although the exact mechanism of this is unclear. McLeskey and colleagues suggest that stimulation of parasympathetic postsynaptic receptors in the heart may cause bradycardia,6 while Mathias and coworkers suggest that succinylcholine acts on vagal pathways or causes a reflex bradycardia by stimulating peripheral sensory receptors.7

Second, the process of intubation causes bradycardia. Proposed theories include parasympathetic stimulation involving the vagovagal reflex due to stimulation in the pharynx, esophagus and respiratory tract8,9; and stimulation of the baroreceptor reflexes by an increase in arterial blood pressure during laryngoscopy.10 The former is the most widely accepted theory because cardiac vagal activity protects against sudden onset of ventricular fibrillation. Experimental studies have demonstrated that inhibiting vagal activation with atropine or vagotomy eliminates this protection against sudden death;11 therefore, using atropine in this setting is not without risk. Atropine administration has been associated with ventricular arrhythmias,12,13 and atropine-mediated tachycardia limits the ability to use pulse as an indicator of hypoxia in the post-intubation period.

We conducted an ancestral search to identify studies examining the practice of administering atropine prior to succinylcholine and to determine whether there is consensus support for this practice in the research literature. MEDLINE search terms of “succinylcholine,” “children” and “atropine” were used.

Evidence for atropine use

In 1950, Burststein and cohorts found that the primary cardiac response to tracheal intubation was transient tachycardia.16 The following year, King and collaborators replicated this study, noting a tachycardic response in the absence of other physiologic factors such as coughing, hypercapnia or anoxia.17 Both studies were limited because the majority of participants were premedicated with scopolamine, atropine or cocaine; therefore the tachycardia could have been drug-induced.

In 1957, Leigh and coauthors reported 4 cases of bradycardia in children who received succinylcholine.1 In 3 of these the duration of bradycardia was not reported; nevertheless, the authors recommended intravenous atropine to correct succinylcholine-related bradycardia.

In 1960, Craythorne and colleagues monitored the ECGs of 35 children after administration of succinylcholine.18 All but 4 of these children were premedicated with scopolamine, scopolamine–secobarbital or scopolamine–secobarbital–morphine. Three of the 4 participants who did not receive premedication developed bradycardia, in 1 case profound, with the pulse dropping from 150 beats/min to 41 beats/min within 15 seconds.

A 1960 study described heart rate responses in 41 patients who received repeated doses of succinylcholine.4 By the fifth dose, 39 patients had slowing of the heart rate, two-thirds were bradycardic and the remainder had arrhythmias. Five bradycardic patients received atropine prior to their next dose of succinylcholine. Their heart rates increased to 100 beats/min, and they did not develop bradycardia following the next dose of succinylcholine. Based on these findings, the authors recommended atropine prior to the second injection of succinylcholine when large doses are given repeatedly.

In 1964, Lipton and coworkers analyzed the cardiac and respiratory responses of 42 infants to nasogastric tube feedings as well as to yawning, defecation and hiccupping.19 Yawning provoked bradycardia in 57 of 59 episodes recorded in 24 infants. Defecation caused intermittent respiratory pauses, immediately followed by bradycardia, and in 1 case the heart rate fell from 160 to 80 beats/min. Hiccupping also caused variable degrees of bradycardia, as low as 33 beats/min in 1 infant. Intermittent nasogastric intubation (for feeding in 3 premature infants) caused abrupt bradycardia during tube passage and when it was present in the esophagus, but no adverse outcomes were reported.

Marshall colleagues looked at changes in systolic blood pressure, heart rate and transcutaneous oxygen tension in...
10 preterm infants during intubation for respiratory failure. Six infants experienced bradycardia (defined as a heart rate less than 100 beats/min), and 1 infant’s heart rate increased during intubation. The lowest heart rate recorded for the 10 infants was 76 beats/min. The authors noted that 4 of the 6 infants who developed bradycardia were hypoxemic and concluded that the hypoxemia probably contributed to the bradycardia. Again, there were no clinically relevant adverse outcomes.

Kelly and Finer randomized 30 infants to receive atropine, atropine plus pancuronium, or no medication before intubation. Controls and atropine recipients had significant decreases in heart rate (52.2 beats/min and 36.2 beats/min; \( p < 0.01 \)), but no clinically important adverse outcomes were seen.

Green and cohorts studied heart rate changes in 26 anesthetized children being paralyzed with succinylcholine. Ten were premedicated with glycopyrrolate, 10 with atropine, and 6 served as a control group. The patients received a median of 3 doses of succinylcholine. Bradycardia occurred in 2 of 10 glycopyrrolate recipients, 3 of 10 atropine recipients and 3 of 6 controls, but these differences were not statistically significant. The authors concluded that patients who receive multiple doses of succinylcholine should be pre-treated with intravenous anticholinergics.

**Evidence against atropine use**

**Prospective studies**

McAuliffe and collaborators compared the cardiovascular changes among 41 children aged 1–12 years who received either atropine with succinylcholine or succinylcholine alone. The patients’ heart rates and rhythms were recorded from 2 minutes before drug administration until 2 minutes after intubation. Heart rate increased in both groups, with the greatest increase in the children who received atropine. Only 1 incident of bradycardia was recorded during this study and it occurred in a child who received atropine. The authors reported that the incidence of bradycardia following administration of succinylcholine (without atropine premedication) was lower than previously thought. They suggested that the practice of administering atropine to children prior to single-dose succinylcholine be reconsidered. It should be noted that patients in this study were anesthetized with thiopentone, which may have had a protective effect against bradycardia.

In a 1998 study, Mirakhur and coauthors compared the effect of pretreatment with intravenous atropine, glycopyrrolate or placebo on cardiac arrhythmias during anesthesia with halothane and succinylcholine. While significantly more bradycardia was seen in children in the placebo group, it resolved spontaneously and without sequela. Conversely, 23 of 25 patients treated with atropine experienced persistent tachycardia. The authors concluded that routine anticholinergic premedication is unnecessary and that atropine should be reserved for children experiencing persistent bradycardia.

**Surveys**

In a survey of neonatal intensive care units in the United Kingdom, Whyte and colleagues looked at the use of premedication in infants being intubated. The survey found that only 37% gave any medication prior to intubation. Of the units that used sedation, 53% used succinylcholine and half of those used succinylcholine combined with atropine.

Fellows of the Faculty of Anesthetists in Australia were surveyed about their practices in the administration of prophylactic atropine. Most respondents did not administer atropine as a premedication, but more than 80% of the anesthetists believed that neonates, infants and children should be premedicated with atropine when repeated doses of succinylcholine were being administered.

Robinson and coworkers surveyed consultant anesthetists and senior registrars in Birmingham, UK, about their routine use of succinylcholine. The most recently trained reported the highest routine use of succinylcholine: all anesthetists with less than 10 years’ experience indicated that they use succinylcholine during routine intubations, compared with 81% with more than 20 years’ experience. Respondents were also asked about their experience with succinylcholine. Cardiac arrhythmias were the most frequent side effect reported: one-third of respondents reported self-limiting bradycardia; 24% reported bradycardia following the first dose of succinylcholine and 43% following the second dose. Anesthetists were also surveyed regarding their use of atropine in relation to succinylcholine administration. The pattern of use also varied with years of experience. Of respondents with more than 20 years’ experience, 35% reported routinely using atropine prior to administering any succinylcholine and 40% reported using atropine prior to the second dose of succinylcholine. Only 9% of respondents with less than 10 years’ experience reported routinely using atropine prior to administering any succinylcholine, whereas 65% reported using atropine prior to the second dose of succinylcholine.

**Conclusions**

Many relevant studies were conducted in the operating
room and involved succinylcholine combined with other anesthetic drugs, notably fentanyl, thiopentone, propofol, alfentanil or halothane, which confound the association between succinylcholine and bradycardia.\textsuperscript{27,28} Most studies suggesting a benefit to atropine involved repeated doses of succinylcholine; consequently, these recommendations for atropine administration should be considered specific to this type of use. In the ED, succinylcholine is normally administered in a single dose for emergency intubation, and there is no evidence showing that single-dose succinylcholine in the absence of other anesthetic agents is likely to cause clinically important bradycardia.

Atropine prior to single-dose succinylcholine during pediatric intubation increases the likelihood of ventricular dysrythmias, inhibits protective reflexes and masks bradycardia that results from hypoxemia. Atropine is rarely administered to prevent the bradycardia associated with yawning, hiccupping and defecating, and its routine use prior to intubation and succinylcholine should be re-evaluated.

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\textbf{References}


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