Sedation for Nonemergent Neonatal Intubation

Scott L. DeBoer RN, MSN, CFRN
Lisa V. Peterson RN, MSN

Abstract

A newborn lies wide-awake, about to be intubated. The infant is able to feel everything, to hear everything—but cannot do anything to change the situation. Big people hold down the newborn and place a laryngoscope blade into the mouth, then a large endotracheal tube into the trachea. As the baby struggles, coughs, chokes, gags, and cries, blood pressure and intracranial pressure increase dramatically, and the heart rate plummets.

Infants, like adults, do feel pain and anxiety. Yet recent studies show that NICU staff continue neonatal intubation utilizing only force. In pediatric emergency/critical care settings, rapid-sequence intubation (RSI), once confined to the environment of the operating room, is now the standard of care. An understanding of commonly administered RSI medications is essential to bring this practice to standard use in the NICU as well.

In the pediatric and adult critical care population, rapid-sequence intubation (RSI)—the use of sedatives and chemical paralytics to facilitate tracheal intubation—is considered the standard of care. Use of these medications optimizes intubating conditions and helps to minimize the adverse physiologic effects of intubation. Neonatology has yet to embrace this trend, however. This article addresses the issue of sedation for intubation in the neonatal population.

Intubation is a commonly performed procedure in the neonatal intensive care unit, with the urgency of the procedure determined by the hemodynamic status of the child. The technique of intubation involves placing an endotracheal tube (ETT) into the trachea via the nares or mouth with the assistance of a laryngoscope blade. Intubation is often associated with a vigorous/crying/moving/drooling infant, not ideal intubating conditions. The tube itself and the blade can stimulate vagal and mechanical pressure reflexes, resulting in severe bradycardia. Prolonged intubation attempts or, in some cases, placement of the blade in the oral cavity alone can result in hypoxia.[1] Airway trauma, increased number of attempts and time until the tube is correctly placed, increased blood pressure, and increased intracranial pressure (ICP) can also result.[1,2]

PREMEDICATION FOR INTUBATION

Medications to help minimize the adverse physiologic effects and to maximize the chances for successfully intubating on the first attempt are available. In critical situations when the infant is unstable, endotracheal intubation must be done immediately. In most other situations, however—if IV access is in place or is easily obtainable—rapid sequence intubation (RSI) can be a much better technique for the patient and staff.[3] Use of a combination of medications from the categories of atropine, sedatives and/or analgesics, and neuromuscular blockers (chemical paralytics) can minimize or abolish the adverse effects of tracheal intubation.

Anticholinergics

Atropine (Table 1) is administered early in the intubation process to increase heart rate, block the vagal response to placement of the laryngoscope blade and ETT, and minimize oral secretions. The drying of secretions not only allows for easier visualization of the glottis with intubation, but also makes securing the ETT after confirmed placement easier.[4] Administration of succinylcholine in infants can be associated with bradycardia, and pretreatment with atropine can greatly lessen this side effect.[5]

Concerns about atropine administration with intubation

Accepted for publication January 2001. Revised March 2001.

TABLE 1 ■ Atropine

Action	Dose	Onset	Peak	Duration	Considerations
Anticholinergic parasympatholytic mydriatic Blocks ACH at parasympathetic neuroeffector sites, thus blocking vagal stimulation to the heart and increasing cardiac output and heart rate Dries secretions and decreases salivation	IV: 0.01–0.03 mg/kg/dose over 1 minute	IV: 2 minutes	IV: 12–16 minutes	IV: 4–6 hours	Should always be given before succinylcholine to block decreases in heart rate Can mask bradycardic signs of hypoxia Can decrease gastrointestinal motility; follow closely with abdominal exam Requires continuous monitoring of heart rate

Adapted from: Young T, and Mangum B. 2001. *Neofax: 2001,* 14th ed. Raleigh, North Carolina: Acorn, 88–89.

typically focus on the resultant tachycardia and masking of bradycardic signs of hypoxia. However, hypoxia can be monitored with concurrent pulse oximetry and minimized with brief intubation attempts.

Sedatives and/or Analgesics

Sedatives (Table 2) and/or analgesics (Table 3) are administered primarily to sedate the neonate. Intubation is an unpleasant procedure, especially when performed on an awake and struggling infant. Sedation can make intubation much easier. Sedatives should be administered to "put the child to sleep" before chemical paralytics are administered. Beyond their sedative effects, sedatives can decrease ICP, minimize spikes in blood pressure, and significantly decrease the stress of the intubation experience for the patient and staff members.[6] Analgesics such as morphine or fentanyl are commonly administered as sedative agents, although their primary properties are analgesic in origin.

Neuromuscular Blockers

Neuromuscular blocking agents (Table 4), or chemical paralytics, are categorized as depolarizing or nondepolarizing and also as short-, medium-, or long-acting. Neuromuscular blockers simply do as their name implies: block transmission of the nerve impulse at the neuromuscular junction, the space between the nerve and striated muscles. Acetylcholine (ACH), a neurotransmitter, is found at the neuromuscular junction. The receptor sites for ACH are shaped like squares. When a square-shaped molecule (ACH) or a square-shaped depolarizing blocker (succinylcholine) binds with the receptor site, cells depolarize and muscles contract. This happens because the sodium-potassium pump is activated, so that potassium floods out of the cell and sodium enters the cell. Whether via ACH or succinylcholine, the striated muscles contract, relax, and are then blocked for the duration of the drug's action. When nondepolarizing blockers (vecuronium, pancuronium) are used, the action is slightly different. Nondepolarizing blockers are circle shaped, not square shaped, as are the ACH receptor sites. These blockers do not fit into the spaces, but do block anything else from getting into them. In this way, these medications "block" the ability of muscles to contract, but without the depolarizing effects and muscular contractions. To use muscle relaxants in either of these categories properly and humanely, it is important to

TABLE 2 ■ Sedatives[11–13]

Drug/Action	Dose	Onset	Duration	Considerations
Midazolam (Versed) Sedation, amnesia, anti-anxiety	IV: 0.1–0.2 mg/kg/dose over 5 minutes	IV: 3–5 minutes	IV: 2–6 hours up to 22 hours for very low birth weight infants	May be given IM Nonirritating to veins Reversed with flumazenil *Significantly decreases cerebral blood flow in preterm infants—not recommended by Cochrane Review.* Monitoring required for respiratory and central nervous system status and blood pressure
Amidate (Etomidate) Sedation	IV: 0.2–0.4 mg/kg/dose over 30 seconds	IV: <1 minute	IV: 5–10 minutes	Extremely short onset/duration Very hemodynamically stable Reversed with time
Diprivan (Propofol) Sedation	IV: 2 mg/kg/dose over 30 seconds	IV: <1 minute	IV: 5–10 minutes	Rapid recovery period Looks like milk Reversed with time

TABLE 3 ■ Analgesics

Drug/Action	Dose	Onset	Peak	Duration	Considerations
Morphine Opioid, narcotic-analgesic	IV: 0.05–0.2 mg/kg/dose over 5 minutes	IV: <1 minute	IV: 15–30 minutes	IV: 2–4 hours	Analgesia and sedation Reversed with naloxone
Sublimaze (Fentanyl) Opioid, narcotic-analgesic	IV: 1–4 µg/kg/dose over 1–2 minutes 100 times more potent than morphine	IV: <1 minute	IV: 2–4 minutes	IV: 30–60 minutes	Chest wall rigidity possibly minimized by slow administration and lower doses. May be used for sedation as well as for analgesia Skeletal muscle rigidity prevented by use of concurrent neuromuscular blocking agents Reversed with naloxone. The most hemodynamically stable opioid

Adapted from: Young T, and Mangum B. 2001. *Neofax: 2001,* 14th ed. Raleigh, North Carolina: Acorn, 120–121, 128–129; and Cote C, Lugo R, and Ward R. 2001. Pharmacokinetics and pharmacology of drugs in children. In *A Practice of Anesthesia for Infants and Children,* Cote C, et al., eds. Philadelphia: WB Saunders, 146–149.

remember that these medications block only the striated or voluntary muscles and do not affect the level of consciousness, pain, or awareness.[4] These agents, therefore, should be used in conjunction with sedative and/or analgesic agents.

The only short-acting neuromuscular blocker currently in use is succinylcholine. Succinylcholine is unmatched for speed of onset and duration of action. In the majority of neonatal patients, it is quite safe and will result in chemical paralysis for only 4–8 minutes. This is encouraging in the case of an unexpectedly difficult intubation because the infant will regain spontaneous respirations within this short period of time. Succinylcholine can also increase ICP (minimized with concurrent sedation), however, and can precipitate life-threatening hyperkalemia. This electrolyte imbalance is most common in patients with neuromuscular diseases (especially muscular dystrophy), burns, and crush injuries. Because succinylcholine can cause bradycardia in infants and children, it should be administered only following atropine.[7] Potential complications related to succinylcholine have resulted in efforts to create newer, nondepolarizing medications with an onset as fast and a duration as short as succinylcholine. The medium- and long-acting paralytics range from 15 to 60 minutes in duration, quite a long time if the ETT cannot be placed. Nondepolarizing blockers (such as vecuronium, pancuronium, cisatracrarium, and rocuronium) work by blocking the ACH site and preventing striated muscular contractions from occurring. These blockers block but do not mimic the actions of ACH and do not significantly increase potassium.[7]

When given in conjunction with atropine and sedation, neuromuscular blockers can optimize intubating conditions by causing the airway musculature and the infant to relax. These medications *must* be administered with concurrent

TABLE 4 ■ Neuromuscular Blocking Agents

Drug/Action	Dose	Onset	Duration	Indications and Cautions
Succinylcholine (Anectine)	IV: 1–2 mg/kg/dose over 10–30 seconds	IV: 30–60 seconds	IV: 4–8 minutes	RSI Extreme caution needed in patients with neuromuscular diseases, hyperkalemia, increased ICP Monitor for bradycardia Pretreatment with atropine minimizes bradycardia
Vecuronium (Norcuron)	IV: 0.1 mg/kg/dose over 1–2 minutes	IV: 3–5 minutes	IV: 30–60 minutes	Routine longer paralysis Hemodynamically stable Little change in heart rate or blood pressure
Pancuronium (Pavulon)	IV: 0.02–0.09 mg/kg/dose over 1 minute	IV: 1 minute	IV: 40–60 minutes	Routine longer paralysis Increases heart rate and blood pressure
Cisatracurium (Nimbex)	IV: 0.1 mg/kg/dose over 1 minute	IV: 2–3 minutes	IV: 20–35 minutes	Broken down by pH and temperature Should be reserved for those with multisystem organ failure

Adapted from: Young T, and Mangum B. 2001. *Neofax: 2001,* 14th ed. Raleigh, North Carolina: Acorn, 132, 136–137; and Goudsouzian N. 2001. Muscle relaxants in children. In *A Practice of Anesthesia for Infants and Children,* Cote C, et al., eds. Philadelphia: WB Saunders, 199–202, 204–205, 207.

sedatives and/or analgesics to avoid chemical paralysis while the infant is fully awake.

REVIEW OF THE LITERATURE

Intubation is a physiologically stressful procedure. The literature has frequently described increases in blood and intracranial pressures as well as hypoxia as side effects.[1] The uses of medications in neonates for humane reasons and to minimize the negative effects associated with intubation have also been described.[5]

Standard procedure at the Massachusetts General Medical Center NICU is to administer atropine, sedation, and muscle relaxants before intubation. In an emergency situation—when there is no time to medicate the patient or when oxygenation cannot be maintained with bag and mask ventilation—awake intubation is performed. The center estimates that only 10 percent of intubations in its NICU fit this category, however, with the remaining 90 percent of infants receiving premedications.[2]

Ziegler and Todres reviewed survey responses of 74 NICUs to find out if they routinely practiced sedation before intubation. All of the survey respondents denied routine use of atropine, with rationales ranging from their belief that it is "unnecessary" to concerns about masking the clinical signs of hypoxemia. Eighty-four percent of NICUs stated that they never or only rarely utilized sedatives and muscle relaxants to aid intubation attempts. If they administered the medications at all, they did so only for full-term newborns who were "difficult" to intubate. A summary of the authors' opinions, however, is that premedication involving atropine, sedation, and muscle relaxants allows for the least physiologic alterations, reduces airway trauma, and maximizes pain control in critically ill infants.[2]

Friesen and colleagues compared two groups of premature infants who were undergoing intubation. Group I received atropine; Group II received atropine, sedation, and a muscle relaxant. Mean anterior fontanel pressure increased by 197 percent for 28 seconds in the Group I infants; systolic blood pressure also increased by an average of 20 percent. Infants in Group II experienced no significant change in fontanel or blood pressure. Laryngoscopy times were also less in Group II, and time to successful ETT placement was shorter.[8] Raju and colleagues found similar results, with a mean increase of 16.5 cm H_2O in the infants' ICP measurements when intubation was performed with premedication compared to a mean increase of 89.7 cm H_2O without premedication.[9]

Kelly and Finer showed that the physiologic effects associated with neonatal intubation (such as bradycardia and hypertension) represent reflexive, cardiovascular, and psychological responses. The study also showed no significant associations between birth weight, gestational age, and study age versus measured physiologic responses. Three groups of premature and full-term neonates were randomized to receive either no premedications (control), atropine, or atropine and pancuronium. Those who received only atropine before intubation did have fewer bradycardic episodes than those in the control group, but still had significant changes in ICP, oxygenation, and blood pressure. The infants who received atropine and muscle relaxants (but no sedatives) had the lowest ICP elevations of the groups. The hypertensive response to intubation was not abolished with any of these premedications, however. The authors felt that the positive physiologic outcomes were related to the vagolytic

effects of atropine, as well as to the muscle relaxant effects of pancuronium, which caused the infant not to struggle against intubation.[3]

Barrington and colleagues compared two groups of premature infants in which one group received atropine and the other received atropine and succinylcholine before intubation. They found that the infants receiving atropine and succinylcholine had significantly smaller decreases in oxygen level and less increase in ICP associated with intubation, indicating that struggling against intubation does increase ICP and hypoxia in the infant. The time to successfully place the ETT was also much shorter in infants receiving atropine and succinylcholine than in those receiving only atropine. Again, this combination of medications did not prevent hypertension associated with intubation. This study concluded that premedication with atropine and succinylcholine prior to intubation avoids significant increases in ICP in the infant and speeds up the intubation process.[10]

Barrington and Byrne instituted a policy that "all neonates, regardless of postnatal or gestational age or body weight, would receive premedication for neonatal intubation in the Neonatal ICU or on transport if an IV was in place and if the intubation was not an absolute emergency (i.e. the patient could not be kept stable using bag & mask IPPV [intermittent positive pressure ventilation])" (p. 213). Atropine, fentanyl, and succinylcholine were administered to 253 consecutive patients. Of those, 194 infants were intubated without incident. Fifty-nine required two or more attempts, but all were successfully intubated. Summarizing their experiences, the authors wrote, "It is inconceivable that we should ever go back to a practice of allowing infants to cough, gag, choke, and struggle against a laryngoscope and endotracheal tube!" (p. 215).[5]

CONCLUSION

Research suggests that the combination of atropine, a sedative/analgesic, and a neuromuscular blocker decreases the adverse effects of tracheal intubation. Future research should be done to further document the safety and neurologic outcomes associated with this combination of premedications for intubation in the neonatal population. Although some units may currently be able to provide the personnel, training, monitoring, and policies to implement this practice, additional research should be undertaken before this can become a standard of care. "Unpremedicated intubations, which are considered inhumane by the Canadian council on *animal* care, are more disturbing to the physiology of the high risk neonate and should only be considered under exceptional circumstances" (p. 216).[5]

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About the Authors

Scott DeBoer is the flight nurse educator for the University of Chicago Aeromedical Network and the owner of Peds-R-Us Medical Education.

Lisa Peterson is a member of the critical care registry team and also a staff nurse in a PICU/NICU at Children's Memorial Hospital in Chicago. She was completing her master's degree in critical care nursing at the time this article was written.

For further information, please contact:
Scott L. DeBoer, RN, MSN, CFRN
2301 Flint Court
Dyer, IN 46311
888-280-7337
E-mail: pedsrusscott@cs.com