Emergency Sugammadex Reversal in an 850-G Premature Infant: A Case Report

Proshad N. Efune, MD; Gijo Alex, MD; and Sonia D. Mehta, MD

Sugammadex is a novel reversal agent for the neuromuscular blocking agents rocuronium and vecuronium; it has been shown to rapidly and completely reverse neuromuscular blockade for rocuronium and vecuronium, even when the blockade is profound. We present the case of a 2-week-old, 850-g infant born at 25 weeks' gestation, who presented to the operating room for exploratory laparotomy and repair of ileal atresia. Anesthesia was induced and neuromuscular blockade with 1.2 mg/kg of rocuronium was administered. The neonate experienced rapid oxyhemoglobin desaturation and progressively became very difficult to mask ventilate. Direct laryngoscopy failed to result in successful intubation of the trachea and ventilation became impossible. To reverse the effects of rocuronium, 16 mg/kg of sugammadex was administered. Immediately after, the infant resumed spontaneous ventilation and was able to maintain adequate oxyhemoglobin saturation between 90% and 95% with supplemental oxygen. To our knowledge, this is the first report of successful reversal of neuromuscular blockade, with sugammadex, in an emergent situation after failure to intubate/ventilate an extremely low birth weight infant.

ABBREVIATIONS ELBW, extremely low birth weight; ETT, endotracheal tube; IV, intravenous

KEYWORDS antidote; case report; extremely low birth weight infant; neuromuscular blocker; neuromuscular blockade reversal; rocuronium; Sugammadex

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Introduction

An extremely low birth weight (ELBW) infant is defined as one with a birth weight < 1000 g. Most ELBW infants are also the youngest of premature newborns, typically born before 27 weeks' gestational age. The ELBW infant poses many unique challenges to the pediatric anesthesiologist. These infants are at high risk for intraventricular hemorrhage, retinopathy of prematurity, necrotizing enterocolitis, and bronchopulmonary dysplasia. They are also at risk for rapid oxygen desaturation during airway manipulation due to their decreased functional residual capacity and high oxygen consumption rates. The unexpected difficult airway in this patient demographic is an emergency for which the typical difficult airway algorithm does not apply given the size constraints related to the airway adjuncts at our disposal. The smallest laryngeal mask airway is likely to be too large for an infant < 2 kg. In addition, the smallest video laryngoscope blade is likely to be too large to fit into the oropharynx of an infant this size. The ability to quickly obtain a surgical airway, even in the most experienced hands, would be very challenging. The 2 available options for pharmacologic reversal of neuromuscular blockade include neostigmine, an acetylcholinesterase inhibitor, and the newer drug sugammadex (Bridion, Merck & Co, Inc, Kenilworth, NJ) a neuromuscular drug encapsulating agent. The efficacy of neostigmine relies on the recovery of at least

some neuromuscular function before its administration, whereas sugammadex can offer immediate reversal. However, there is very little data on the use of sugammadex in premature infants. The following describes the immediate reversal of neuromuscular blockade with sugammadex in a cannot-ventilate-cannot-intubate scenario, which was potentially a lifesaving intervention.

Case Report

A 27-week postconceptual age infant 25 weeks' gestation weighing 850 g presented to the operating room for exploratory laparotomy and repair of ileal atresia. On arrival, the infant was resting comfortably in an isolette with an oxygen saturation ranging from 92% to 94% on 1 L nasal cannula. Her blood pressure and heart rate were normal for gestational age. Her pediatric airway appeared normal, but her abdomen was mildly distended with an orogastric tube in place. She also had a peripherally inserted central catheter line in her left arm and a peripheral IV in her right foot. Induction of anesthesia began with preoxygenation and pretreatment with 0.02 mg/kg of atropine. Hypnosis and neuromuscular blockade were achieved with 2 mg/kg of propofol and 1.2 mg/kg of rocuronium, respectively.

Mask ventilation was initially easy. Direct laryngoscopy with a Miller 00 blade revealed no view of the glottic structures. The infant experienced rapid oxyhemoglobin desaturation and mask ventilation

was resumed. Direct laryngoscopy proved to be very difficult despite an oral airway, significant jaw thrust, and high airway pressures. She remained hypoxic and became bradycardic, which necessitated IV epinephrine (10 mcg/kg) and atropine (20 mcg/kg). The attending anesthesiologist made a second attempt at direct laryngoscopy, but again the glottic structures could not be viewed. Additional attempts, by 2 different attending anesthesiologists, also proved unsuccessful. With each attempt, the endotracheal tube (ETT) was placed through what appeared to be the vocal cords, but an end-tidal carbon dioxide waveform was not reliably seen and hypoxemia persisted. Mask ventilation between attempts continued to be very difficult. Oxygen saturation fell to 50%, and mask ventilation became impossible.

At this point, she again became bradycardic and IV epinephrine (10 mcg/kg) was administered. The smallest laryngeal mask airway was deemed too large for the infant and the smallest fiberoptic scope was too large to pass through an appropriately sized ETT. Otolaryngology was consulted; however, the team was not in house and would require 45 minutes before arrival. The general surgery team planned for emergent tracheostomy. During preparations for the tracheostomy, about 10 minutes after the intubating dose of rocuronium was administered, 16 mg/kg of sugammadex (100 mg/mL; 2 mL vial) was administered via IV push over seconds. The infant resumed spontaneous ventilation within a few seconds after sugammadex and was able to maintain normal oxygenation on 100% FiO₂ by face mask. No adverse reactions were noted during or after sugammadex administration.

The decision was made to cancel the tracheostomy as well as the laparotomy. Otolaryngology performed direct laryngoscopy and bronchoscopy, which revealed an edematous glottis and severe long segment tracheomalacia. During the direct laryngoscopy and bronchoscopy procedure, she was frequently hypoxic. The infant was eventually intubated with a 2.5-uncuffed ETT by otolaryngology. Following intubation, she proved to be difficult to oxygenate and ventilate, until the positive end-expiratory pressure was titrated to 10 cm H₂O. Following several minutes on a positive end-expiratory pressure of 10 cm H₂O, we could wean her fraction of inspired oxygen to 30% and she demonstrated adequate ventilation as evidenced by the end-tidal CO₂ concentration. The infant was not extubated and was transported to the neonatal intensive care unit upon completion of the case. She did return to the operating room the following day for her exploratory laparotomy. Muscle relaxation was required for the case and because she was already intubated, she received cisatracurium.

Discussion

Sugammadex is a novel reversal agent for the neuromuscular blocking agents rocuronium and vecuronium.

The US Food and Drug Administration approved it for use in adults in 2015, but it has yet to be approved for pediatric patients. The drug encapsulates the neuromuscular blocking agent and the complex is then excreted in the urine. Acetylcholinesterase inhibitors, on the other hand, increase the concentration of acetylcholine at the neuromuscular junction and indirectly reverse the effects on muscle relaxants. Sugammadex has been shown to rapidly and completely reverse neuromuscular blockade for rocuronium and vecuronium, even when the blockade is profound.¹

The 95% effective dose (ED₉₅) of rocuronium is lower in infants than in children and adults. The time to onset of maximum block following a dose of 0.6 mg/kg is 0.6 minutes in infants, compared with 1.3 minutes in children. Conversely, the time to recovery of 3 or 4 twitches with train of 4 monitoring is longer in infants compared with children (42 minutes versus 26 minutes following a dose of 0.6 mg/kg).² These differences in onset and duration are due to age-related changes in the volume of distribution, time for the drug to reach the effect site, and clearance. Additionally, the structure of fetal acetylcholine receptors differs from the mature receptor, with neonates having a mix of both subtypes. The difference in acetylcholine receptors, as well as the fact that neonates have lower train of 4 ratios and increased fade, contributes to a reduced margin of safety of neurotransmission in infants compared with adults. The differences in the neuromuscular junction are even more pronounced in preterm neonates compared with term neonates.² Finally, the increased permeability of the immature blood brain barrier in neonates may even lead to accumulation of rocuronium in the central nervous system, with subsequent anticholinergic signaling effects.³ All of this may lead inadvertently to profound neuromuscular blockade, with sugammadex being a particularly useful antidote when rapid reversal is needed from such a state.

Few case reports and studies have described the use of sugammadex in neonates to reverse neuromuscular blockade.³⁻⁶ The Table summarizes the available literature in this population. No studies have described the use of sugammadex in an ELBW premature neonate. Likewise, no information has been published on its use for reversal of neuromuscular block in a neonate in a cannot-intubate-cannot-ventilate situation. In our patient, the use of 16 mg/kg of sugammadex was likely a lifesaving intervention. The 16 mg/kg dose is recommended to reverse neuromuscular blockade within 3 minutes of administration of 1.2 mg/kg of rocuronium. Because otolaryngology was not in house at the time of the crisis to perform a rigid bronchoscopy and intubation, an emergent tracheostomy would have been required by the pediatric surgeon if sugammadex were not administered. Because of the size of the infant, it is unclear if a tracheostomy would have been effective or feasible. Marked bradycardia and bradycardia with car-

Table. Summary of Available Literature on Use of Sugammadex in Neonates

Reference	Patient Information	Sugammadex Dosing	Onset of Reversal
Langley ³	Case report of a 2-day-old term neonate	16 mg/kg, administered 4 hr after cessation of a rocuronium infusion (average 0.79 mg/kg/hr for 4 hr)	90 sec
Carlos ⁴	Case report of a 3-day-old neonate; gestational age unavailable	4 mg/kg, administered 75 min after 0.9 mg/kg rocuronium. Neuromuscular monitoring showed 1 posttetanic count at the time of administration.	90 sec until train of 4 ratio of 0.9
Ozmete ⁵	Case report of an 11-day-old term neonate	3 mg/kg upon completion of procedure (duration of procedure not stated). Neonate received 0.6 mg/kg of rocuronium at the start of procedure.	Unavailable
Alonso ⁶	Case series of 23 neonates up to 7 days old	4 mg/kg upon completion of surgery following median total dose of 1.6–1.7 mg/kg of rocuronium. Neuromuscular monitoring showed “profound block” at the time of administration in all patients.	Median 1.2–1.3 min until train of 4 ratio 0.9

diac arrest have been reported with sugammadex, usually within minutes after administration. Importantly, our patient did not experience any hemodynamic changes during and after reversal of neuromuscular blockade.

In 2015, the Association of Pediatric Anaesthetists of Great Britain and Ireland developed a pediatric guideline for the management of the unanticipated difficult airway. The guideline’s authors suggested it could be given in a cannot-intubate-cannot-ventilate scenario if readily available, but that it should not be given to a child who is rapidly deteriorating with an oxyhemoglobin saturation < 80% and/or the heart rate falling. In this scenario, the consensus group felt the priority is establishment of a surgical airway and that the administration of sugammadex does not guarantee return of spontaneous ventilation and may actually interfere with rescue techniques. In particular, the guideline’s authors felt that sugammadex is unlikely to result in a return of spontaneous ventilation where there is an anatomical cause of upper airway obstruction, such as edema following repeated laryngoscopies.⁷ In our case of an ELBW preterm infant, it seemed unlikely that typical rescue techniques such as a laryngeal mask airway or rapid attainment of a surgical airway would have been successful, so we determined that sugammadex was warranted in this case.

Conclusion

To our knowledge, this is the first report of successful reversal of neuromuscular blockade in an unanticipated cannot intubate/cannot ventilate situation in an ELBW infant. Although sugammadex is not currently approved by the US Food and Drug Administration for pediatric use due to a lack of safety and efficacy data, it can be a very valuable tool in ELBW infants in whom standard adjuncts to difficult airway management are unsuitable due to size constraints. For immediate reversal of a large dose of rocuronium (i.e., 1.2 mg/kg), it is reasonable to give a single dose of sugammadex 16 mg/kg

IV over seconds to infants and children. The expected response with resumption of spontaneous ventilation should be less than a minute. It is imperative to closely monitor the patient for hemodynamic changes such as severe bradycardia due to sugammadex during and after administration, with the immediate availability of an agent such as atropine for management.

Article Information

Affiliations. Department of Anesthesiology and Pain Management (PNE, GA), University of Texas Southwestern Medical Center, Children’s Health, Dallas, TX; Department of Anesthesiology (SDM), University of Florida College of Medicine, Gainesville, FL.

Correspondence. Sonia D. Mehta, MD;
sdeshmukh@anest.ufl.edu

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Ethical Approval and Informed Consent. Given the nature of this study, the institution review board/ethics committee did not require HIPAA Waiver of Authorization, Waiver of Assent, and Waiver of Parental Permission under Expedited criterion.

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