CLINICAL VIGNETTE

Sugammadex for Reversal of Deep Neuromuscular Blockade in a Neonate

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Introduction

Sugammadex is a novel agent used for the reversal of neuromuscular blockade (NMB) induced by aminosteroid nondepolarizing neuromuscular blocking agents, specifically rocuronium and vecuronium. It was approved by the FDA for use in the United States in 2015, however according to the manufacturer's package insert the safety and effectiveness of sugammadex have not been established in patients 17 years of age or younger. Only a few studies and case reports that have shown sugammadex to be safe and effective in the pediatric population.[1-3] There is even less data in neonates. We present a 3-week-old neonate who had a profound NMB at the conclusion of surgery, which was safely and effectively reversed with sugammadex.

Case Report

A 3-week-old boy with pyloric stenosis presented for pyloromyotomy. He was delivered at 37 weeks by caesarean section and did not require neonatal intensive care at birth or in the immediate postdelivery period. Initially, the neonate had mild intermittent episodes of reflux and vomiting, but the mother and pediatrician believed these to be physiologic and trialed a different feeding formula. After this switch, the mother noted persistent vomiting after each feed. By the time of presentation, these episodes involved projectile vomiting with the distance averaging three to four feet. Ultrasound showed hypertrophic pyloric stenosis and the patient was scheduled for a laparoscopic pyloromyotomy.

He was admitted the day prior to surgery and his chemistry panel was notable for mild hyperkalemia and an anion gap acidosis. He had no other medical problems and weighed 3.9 kg with height of 51 cm. Overnight, the patient was resuscitated with intravenous fluids and a nasogastric tube was inserted and placed on low continuous suction. By the following morning, the anion gap and potassium levels had normalized, and the patient appeared euvolemic on exam.

In the operating room, standard American Society of Anesthesiologists (ASA) monitors were placed and the nasogastric tube was suctioned with the patient in supine, left and right lateral decubitus, and prone positions to decrease the risk of aspiration on induction. After preoxygenation, the neonate underwent a rapid sequence induction with cricoid pressure using propofol 3mg/kg (12 mg) and rocuronium 1.2mg/kg (5 mg). He was intubated on the first attempt without any issues and the surgery commenced. Anesthesia was maintained with nitrous oxide and sevoflurane in oxygen. During the case, he received cefazolin 30 mg/kg (120 mg), rectal acetaminophen 30 mg/kg (120 mg), and a total of 50 mL of normal saline. There were no adverse events and surgery was completed without complications or hemodynamic instability, with the patient maintaining appropriate oxygen saturation throughout. Total surgery time was 41 minutes and estimated blood loss was 2 mL.

At the end of the case, 64 minutes after the administration of rocuronium, the patient still had profound NMB with zero out of four twitches on the nerve stimulator and a post tetanic count of zero. After 30 additional minutes had passed, the patient only had a post tetanic count of 1. Given the deep NMB neostigmine was not indicated, and the decision was made to administer sugammadex 4 mg/kg (16 mg). Within 1 minute of receiving sugammadex, the neonate began to breath spontaneously and within 2 minutes, he had a train of four ratio greater than 90 percent on a quantitative nerve stimulator. Once he met all extubation criteria, the neonate was extubated and taken to the recovery room awake, with a patent airway, and moving all extremities. No bradycardia or hemodynamic changes, allergic reactions, or respiratory events were observed. The patient had an uneventful recovery and was discharged home on postoperative day #1 without any issues.

Discussion

Sugammadex is a selective antagonist that encapsulates aminosteroidal muscle relaxants and can reverse the deep NMB seen with rocuronium and vecuronium. It offers several advantages over the commonly used acetylcholinesterase inhibitor neostigmine, which nonspecifically acts on acetylcholine receptors and can cause bradycardia, bronchospasm, nausea, and increased secretions[3]. Sugammadex does not require simultaneous administration of an anticholinergic that may cause its own adverse effects. Because of its selectivity, sugammadex can reverse deep NMBs and offer a more complete reversal than neostigmine. This is especially important in the pediatric population, where residual NMB may not be tolerated in immature lungs and muscles.

Sugammadex was approved by the FDA in 2015 for use in adults, however data has been insufficient for approval in children.[4] Few studies and case reports have reported the effects of sugammadex in the pediatric population, with minimal data

specifically on neonates. In 2014, Alonso et al. published one of the first studies to look at 23 neonates receiving sugammadex. They reported fast and complete NMB reversal with sugammadex, without adverse events or hemodynamic changes.[2] Since this report, information regarding neonates have mostly come from pediatric studies with sparse neonatal representation. A systemic review in 2017 of 580 children, including 8 infants, noted that the sugammadex group had a significantly shorter time to reverse NMB than the control group and less bradycardia than the neostigmine group.[3] A later retrospective study by Gaver et al. included 18 neonates which similarly saw a significant decrease in reversal time that was most notable in the neonatal group.[5] In 2019, Franz et al. looked at 331 sugammadex administrations to patients less than 2 years old (including 53 infants) and saw no significant difference between sugammadex and neostigmine in terms of efficacy and adverse events.[6] Overall, most accounts of sugammadex use in neonates have been well tolerated without major adverse events.

However, there is limited data on the dose-response of sugammadex in the unique neonatal population characterized by pharmacokinetic variability, immature systems, and undeveloped muscles. The recommended sugammadex dose for deep NMB reversal in adults is 4 mg/kg, however there is no suggested dose for neonates.[7] In the study by Alonso et al., neonates received 4 mg/kg of sugammadex and achieved complete reversal without issues.[2] Simonini et al. looked at 423 children aged 3-12 years and saw no significant difference in adverse effects between those receiving 2 and 4 mg/kg.[8] Matsui et al. reported 75 children who received either 1, 2, or 4 mg/kg of sugammadex, and observed incomplete reversal in the 1 mg/kg group, while the 2 and 4 mg/kg groups had complete and rapid reversal without issue.[9] These reports propose that 4 mg/kg of sugammadex is well tolerated by children for NMB reversal, however this remains to be tested in neonates.

Pediatric studies have also been underpowered, retrospective, or heterogenous to draw conclusions. However available evidence suggests sugammadex is well tolerated in neonates. Our case report of a 3-week-old neonate who received sugammadex 4 mg/kg is one of few reports that demonstrates the medication's beneficial effects in neonates. Similar to the pediatric studies previously discussed, sugammadex achieved a rapid and complete reversal of a deep NMB without any adverse events such as bradycardia or anaphylaxis with this dose. However, given the paucity of data, caution should be used when administering sugammadex to the neonatal population. Additional focused studies are needed to better characterize the safety and efficacy of sugammadex use in neonates.

Conclusion

Neonatal administration of sugammadex 4 mg/kg for deep NMB block was safely tolerated and achieved a rapid and complete NMB reversal.

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