JPPT | Case Report

Bradycardic Arrest in a Child with Complex Congenital Heart Disease Due to Sugammadex Administration

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The neuromuscular blocking drugs rocuronium and vecuronium are often used during general anesthesia. These drugs temporarily paralyze the patient and thus both facilitate placement of an endotracheal tube and prevent any patient movement during surgery. Reversal of neuromuscular blockade is necessary at the end of surgery to avoid postoperative weakness and adverse respiratory events in the recovery room. Neostigmine, the traditional reversal agent, may not completely restore muscle strength. Sugammadex is a reversal agent that is more effective and quicker acting than neostigmine. In adults, sugammadex administration has rarely been associated with bradycardia and cardiac arrest. In healthy children, the bradycardia that occurs after sugammadex administration is benign and does not require intervention. There is 1 case report of a 10- to 15-second bradycardic arrest after sugammadex administration to a 10-year-old child with heart disease. The present case report describes an 8-month-old child with complex congenital heart disease who experienced a 10-minute bradycardic arrest after the administration of sugammadex. Pediatric anesthesiologists should be aware that sugammadex administration to children with heart disease may cause hemodynamically significant bradycardia.

ABBREVIATIONS BP, blood pressure; BTT, Blalock-Thomas-Taussig; CPR, cardiopulmonary resuscitation; CVICU, cardiovascular intensive care unit; FiO_2, fraction of inspired oxygen; FDA, US Food and Drug Administration; HR, heart rate; IV, intravenous; O_2 sat, oxygen saturation; TAPVR, total anomalous pulmonary venous return.

KEYWORDS cardiac arrest; congenital heart disease; sugammadex

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Introduction

Neuromuscular blockade during general anesthesia facilitates endotracheal intubation and optimizes surgical conditions. Rocuronium and vecuronium are paralytic agents that prevent acetylcholine from binding to nicotinic acetylcholine receptors of the neuromuscular junction of skeletal muscle.[1] Neostigmine and sugammadex are reversal agents that limit the effects of these neuromuscular blocking agents. Neostigmine is an acetylcholinesterase inhibitor that increases the concentration of acetylcholine at the nicotinic acetylcholine receptors of the neuromuscular junction.[1] Acetylcholine, however, also binds to muscarinic acetylcholine receptors of the parasympathetic system. Therefore, neostigmine can cause bradycardia, bronchoconstriction, nausea, vomiting, and excessive oral secretions. To minimize these side effects, a muscarinic anticholinergic agent (either glycopyrrolate or atropine) must be coadministered with neostigmine.[1] Patients that have received rocuronium or vecuronium intraoperatively often have residual neuromuscular blockade and weakness after neostigmine administration.[2] Compared with patients without weakness in the postoperative period, patients with weakness are more likely to experience serious adverse respiratory events, such as hypoxia, airway obstruction, and death.[2]

Sugammadex is a modified cyclodextrin that encapsulates and irreversibly binds rocuronium and vecuronium.[1] Compared with neostigmine, sugammadex administration results in both faster and more effective reversal of neuromuscular blockade.[1–3] Not only is sugammadex associated with less postoperative weakness than neostigmine, sugammadex is associated with less bradycardia and less postoperative nausea and vomiting than neostigmine.[3] A recent survey found that 52% of pediatric anesthesiologists use sugammadex.[4] Sugammadex, however, also has side effects. There are case reports of sugammadex causing bradycardia, asystole, and cardiac arrest in adults.[5–7] Although bradycardia after sugammadex administration occurs in healthy children, this bradycardia is benign and does not require that any interventions be taken.[8] There is only 1 previous case report of hemodynamically significant bradycardia after sugammadex administration in a child that had coexisting disease: a 10-year old child with a transplanted heart had a 10- to 15-second bradycardic arrest after the administration of sugammadex.[9] The present case describes an 8-month-old child with

complex congenital heart disease who had a 10-minute bradycardic arrest following the administration of sugammadex.

Case Report

An 8.3-kg 8-month-old female with complex congenital heart disease presented to the cardiac catheterization laboratory for measurement of hemodynamics and balloon dilation of a stenotic pulmonary vein. The patient had a single ventricle (heterotaxy, total anomalous pulmonary venous return [TAPVR], discontinuous pulmonary arteries, unbalanced complete atrioventricular septal defect, and pulmonary atresia). She had a history of Blalock-Thomas-Taussig (BTT) shunt placement, unifocalization of the pulmonary arteries, TAPVR repair, ventriculoperitoneal shunt placement, and gastrostomy tube placement. Her most recent surgery was TAPVR repair at 6 months of age. The patient did not have a history of dysrhythmias. Her preoperative medications included amoxicillin, aspirin, clobazam, erythromycin, furosemide, levetiracetam, milrinone, and omeprazole. Her medications did not include either a β-blocker or digoxin. One week prior to the current event being reported, the patient underwent general anesthesia for chest tube placement and percutaneous insertion of a central catheter. At the end of this anesthetic, intravenous (IV) sugammadex 4 mg/kg was administered and did not result in bradycardia. The patient's preoperative medications were the same for both cases. A transthoracic echocardiogram, performed the day prior to presenting to the catheterization laboratory for the present episode, showed the known single ventricle anatomy, right pulmonary vein stenosis, moderate to severe atrioventricular valve regurgitation, low normal systolic function, and a patent BTT shunt.

On arrival to the catheterization laboratory from the cardiovascular intensive care unit (CVICU), the patient was in sinus rhythm. She had an oxygen saturation (O_2 sat) of 82% on room air, a heart rate (HR) of 132/min, and a blood pressure (BP) of 89/48 mm Hg (mean, 62). The patient underwent an uncomplicated IV induction with fentanyl 3 mcg/kg, midazolam 0.1 mg/kg, and rocuronium 1.2 mg/kg. An endotracheal tube was easily placed. During the 3-hour case, the patient received sevoflurane (1.0%–1.5%), another 2 mcg/kg fentanyl, dexamethasone (0.5 mg/kg), and an infusion of dexmedetomidine (0.6 mcg/kg/hr). A bolus dose of dexmedetomidine was never administered. The pulmonary vein was successfully ballooned. At the end of the procedure, the femoral catheters were removed and hemostasis was achieved. The sevoflurane was discontinued. Sugammadex 5 mg/kg IV was then administered. The patient was extubated awake and had normal work of breathing. The rhythm was sinus. The patient had an O_2 sat of 84% on blow-by oxygen, a HR of 115/min, and a BP of 81/30 mm Hg (mean, 47).

Ten minutes after sugammadex administration the patient acutely became bradycardic (HR 46/min, rhythm sinus), hypotensive (BP 54/15 mm Hg; mean, 28), and desaturated (O_2 sat 50% on 1.0 fraction of inspired oxygen [FiO_2]). She was not apneic and did not have increased work of breathing. Cardiopulmonary resuscitation (CPR) was immediately started per Pediatric Advanced Life Support guidelines. End-tidal carbon dioxide was present with chest compressions. Escalating doses of IV epinephrine (2, 4, and then 10 mcg/kg) were administered during the 10-minute cardiac arrest. The patient's immediate postresuscitation vital signs were: O_2 sat 83% on FiO_2 1.0, HR 184/min (rhythm sinus), and BP 104/48 mm Hg (mean, 67). The dexmedetomidine infusion was discontinued. The patient was then intubated without any additional sedation or paralysis. An arterial line was placed. An emergent transthoracic echocardiogram was performed and was unchanged from the preoperative echocardiogram, other than showing that there was no right pulmonary vein stenosis. A serum tryptase was not obtained. On arrival to the CVICU, the patient was in sinus rhythm. She had a an O_2 sat of 80% on 1.0 FiO_2, a HR of 122/min, and a BP of 80/43 mm Hg (mean, 56). Her vital signs remained stable and her recovery was uneventful. She was extubated the next day and was discharged home 3 days later.

Discussion

In a prospective observational study, Alsuhebani et al[8] evaluated HR changes after sugammadex administration in 221 pediatric patients (median age, 8 years; IQR, 2–4). Bradycardia, defined as a HR less than the fifth percentile for age, occurred in 18 patients (8%). Following sugammadex administration, bradycardia occurred after a median of 2 minutes (range, 1–25). Patients with heart disease were more likely than patients without heart disease to experience bradycardia (OR, 3.8). Bradycardia was not associated with the dose of sugammadex administered (median dose, 2 mg/kg; range, 2–15.7). Bradycardia was self-limiting and was not associated with hypotension in any of these patients. The current case is remarkable because sugammadex administration led to a 10-minute bradycardic arrest in a child with heart disease.

The current patient did not have a history of bradycardia or any other dysrhythmias. She was not receiving any medications, such as a β-blocker or digoxin, that would predispose her to bradycardia. Although dexmedetomidine may be associated with bradycardia, the dexmedetomidine infusion had been started 2 hours prior to the bradycardia, the infusion rate was never changed, and no bolus doses of dexmedetomidine were ever administered. End-tidal carbon dioxide was present with chest compressions and so the bradycardic arrest was not due to laryngospasm, bronchospasm, anaphylaxis, pulmonary hypertension,

or BTT shunt occlusion. Bradycardia after sugammadex has been reported to occur up to 25 minutes after its administration.[8] While bradycardia after sugammadex administration does not require intervention in healthy children, bradycardia may not be tolerated in children with heart disease. Patients with a single ventricle are very dependent on their HR to maintain adequate ventricular filling and adequate cardiac output. The patient being reported may have been especially unlikely to tolerate the bradycardia because she also had moderate to severe atrioventricular valve regurgitation and low normal systolic function on the preoperative echocardiogram.

Arends et al,[10] in a prospective observational study, evaluated the effects of sugammadex on HR in 99 children with heart disease (median age, 3 years; IQR, 0–10). Bradycardia, defined as an HR less than the fifth percentile for age, occurred in 20 patients (20%). Bradycardia was not associated with the dose of sugammadex administered (median dose, 3.9 mg/kg; range, 0.5–7.8). Bradycardia was not associated with hypotension in any of these patients, and no interventions were required. The current case report contrasts with this study because sugammadex administration in our patient caused a 10-minute bradycardic arrest.

King et al[9] reported the first and only case of a bradycardic arrest after sugammadex administration in a child. The patient was a 10-year-old boy with a heart transplant and recent cellular rejection. The patient was in the cardiac catheterization laboratory undergoing measurement of hemodynamics and heart biopsy. He had normal biventricular function preoperatively. After the procedure, sugammadex 2 mg/kg was administered. Thirty seconds later his HR dropped from 102/min to 26/min. Cardiopulmonary resuscitation was started and epinephrine 2 mcg/kg IV was administered. The bradycardia resolved. The duration of CPR was 10 to 15 seconds. The patient was then extubated and sent to the CVICU. He was discharged home the next day. This patient responded to 1 dose of epinephrine and required only 10 to 15 seconds of CPR, in contrast to our patient, who required 3 doses of epinephrine and 10 minutes of CPR.

Carvalho et al[11] reported 2 healthy children who experienced bradycardia after sugammadex administration. The first child, who was 3 years old, became bradycardic (HR 53/min) after sugammadex 2 mg/kg IV was administered. The patient was not hypotensive. Atropine 20 mcg/kg IV was administered and the bradycardia resolved. The second child, who was 6 years old, became bradycardic (HR 55/min) after sugammadex 2 mg/kg IV was administered. The BP was mildly decreased (mean BP, ~50 mm Hg). The HR and BP recovered after atropine 20 mcg/kg IV was administered. In contrast to our patient, these 2 patients did not experience cardiac arrest or severe hypotension after sugammadex administration.

Naranjo et al[12] developed a reliable adverse drug reaction probability scale to assess the likelihood of a drug being the cause of an adverse event. Drug reactions were classified as definite, probable, possible, or doubtful. The current case being reported represents a probable adverse drug reaction (Naranjo score of 3) because there are previous reports of this reaction, the adverse event occurred after administration of the drug, and an alternative reason for the adverse event could not be found. This event has been reported to the US Food and Drug Administration (FDA). Although the FDA has approved sugammadex use in children as young as 2 years,[13] sugammadex has been used safely in patients younger than 2 years in 4 studies.[10,14] The reason for sugammadex causing bradycardia after its administration is not known.[15]

This is the second case reported in which the administration of sugammadex to a child resulted in bradycardic arrest. Children in both cases had heart disease. The child in the first report[9] had a 10- to 15-second bradycardic arrest. This present case is especially noteworthy because sugammadex administration resulted in a 10-minute bradycardic arrest. Pediatric anesthesiologists should be aware that sugammadex administration to children with heart disease may cause hemodynamically significant bradycardia. We continue to use sugammadex in pediatric patients with heart disease because it is more effective and faster acting than neostigmine.

Article Information

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Ethical Approval and Informed Consent. Written informed consent was obtained from the parent of the child for publication of this case. Our institution does not require Institutional Review Board approval be obtained for submission of a case report.

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