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Hypotension and Bradycardia with Sugammadex Administration

Samantha Nicholson, BSN, RN, CCRN

Affiliation:
Texas Christian University

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Biographical data:
Samantha Nicholson is a Registered Nurse pursuing her DNP in Nurse Anesthesia at Texas Christian University

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Abstract

The Food and Drug Administration (FDA) approved sugammadex for use as a reversal agent for nondepolarizing muscle relaxants.[1] Sugammadex binds free molecules of muscle relaxant, specifically rocuronium and vecuronium, resulting in a rapid offset of neuromuscular blockade.[2] When compared to the use of neostigmine and glycopyrrolate for reversal, sugammadex has shown to be faster and able to provide reversal for deeper blockades.[2] However, this new drug is not without risks. Several case reports have been published describing profound hypotension and bradycardia after administration of sugammadex, with some cases progressing to asystole and death.[1,3,4,5,6,7] This case report describes a patient who experienced a significant drop in cardiac output after being reversed with sugammadex.

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Introduction

- In 2015 the Food and Drug Administration (FDA) approved sugammadex (Bridion) for use as a reversal agent for nondepolarizing muscle relaxants.[1]
- Since it's release in 2015 several cases of severe hypotension and bradycardia associated with sugammadex administration have been reported. [1-7]
- Although the mechanism of these cardiac events is unknown, it is important to investigate all potential causes as sugammadex is gaining popularity for the reversal of nondepolarizing muscular blockade.

Case Report

Preanesthetic evaluation

- 63-year-old Caucasian female who underwent general anesthesia for a laparoscopic cholecystectomy
- Past medical history of current cigarette use, hypertension, hyperlipidemia, gastroesophageal reflux disease (GERD), anxiety, depression and chronic pain
- Labs day of surgery were within normal limits
- 100 mg of Atenolol at 0430 to remain current on her beta-blocker therapy
- Preoperative vital signs: HR 69, BP103/75 mmHg, SpO_2 96%, RR 16, temperature 36.3°C

Intraoperative Management

- Standard monitors were applied, patient was preoxygenated with facemask prior to intubation
- The patient received 30 mg of rocuronium at the beginning of the procedure for relaxation
- The patient was maintained with sevoflurane and intermittent boluses of fentanyl and hydromorphone for pain control
- Patient had displayed slight hypotension prior to incision that resolved with intermittent boluses of 100 mcg of neosynephrine
- Patient was given 8mg of dexamethasone after induction and 4mg of ondansetron during the procedure for PONV prophylaxis
- At the end of the procedure sevoflurane was discontinued and the patient was given 200mg of sugammadex (2.6 mg/kg) to reverse a train of four (TOF) of 2/4 with fade
- After the administration of sugammadex heart rate dropped as low as 44 bpm and her blood pressure decreased as low as 48/33 mmHg
- The patient was treated with 0.2 mg of glycopyrrolate and 20 mg of ephedrine. The patient's heart rate returned to 77 bpm and blood pressure increased to 109/77 mmHg.

Postoperative Care

- After blood pressure and heart rate stabilized, patient was extubated successfully without any signs of residual paralysis. Patient was transported safely to the PACU and vital signs remained stable.

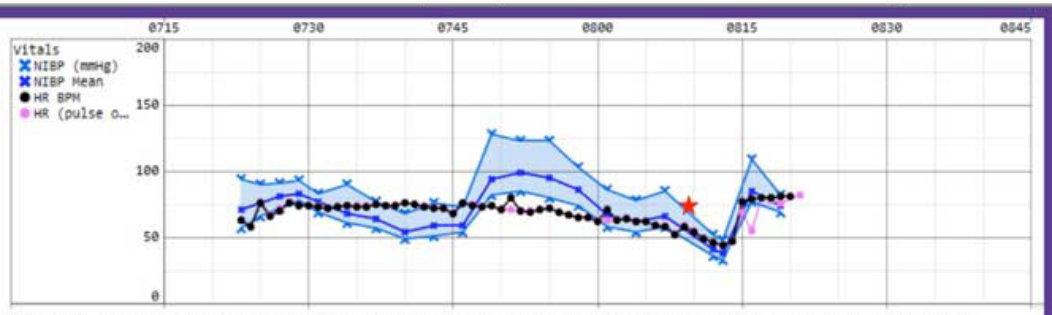

Figure 1. Anesthesia timeline displaying episode of hypotension and bradycardia post sugammadex administration. The red star indicates approximate time of sugammadex administration.

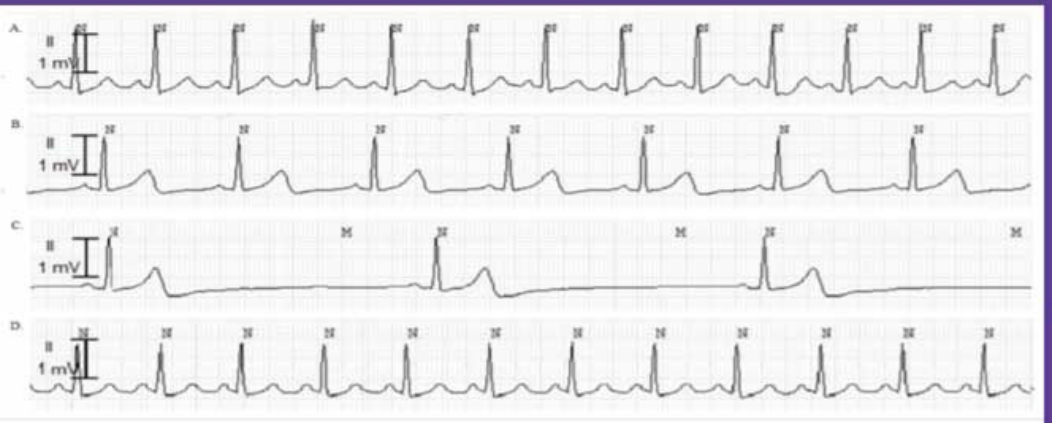

Figure 2. ECG tracing from case report of 46-year-old female patient who underwent subtotal gastrectomy and developed profound bradycardia and hypotension after administration of sugammadex.[7]

A. Before anesthesia induction, ECG showed normal sinus rhythm (HR 93 beats/min, QTc 441 ms). B. After surgery, ECG showed slight sinus bradycardia (HR 55 beats/min, QTc 491 ms). C. Three minutes after 200 mg sugammadex administration, ECG showed severe bradycardia (HR 23 beats/min, QTc 490 ms). D. One minute after 0.5 mg atropine injection, HR increased to 89 beats/min (QTc 490 ms).

Discussion

- Between 2009 and 2020, 350 serious cardiac adverse events from sugammadex were reported to the FDA, along with 49 deaths.[8]
- Of these 350 cases, 160 were reports of bradycardia, 108 were reports of cardiac arrest and 82 were reports of hypotension.[8]
- Although the mechanism of these reactions is still unknown, phase 2 trials suggested that sugammadex may cause QT prolongation, which at the time was not considered clinically significant.[3]
- The EMA states in the Summary of Product Information that, "In rare instances, marked bradycardia has been observed within minutes after the administration of sugammadex for reversal of neuromuscular blockade. Bradycardia may occasionally lead to cardiac arrest. Patients should be closely monitored for hemodynamic changes during and after reversal of neuromuscular blockade. Treatment with anti-cholinergic agents such as atropine should be administered if clinically significant bradycardia is observed."[9]
- This patient was immediately treated with 0.2mg of glycopyrrolate because it was drawn up and readily available. Once the hypotension developed, the patient was given 20mg of ephedrine. After the ephedrine was administered the patient's heart rate and blood pressure increased with no further issues.
- Moving forward atropine would be the better choice over glycopyrrolate as it is more efficacious in treating bradyarrhythmias.
- Pretreatment with glycopyrrolate may be indicated with sugammadex administration if the patient is already bradycardic prior to reversal, especially if larger doses of sugammadex are required.

Case Critique

- The rapid decline in cardiac output described in this case report is similar to other case reports of sugammadex reactions, however other factors in this case cannot be ruled out as potential causes for the event.
- The patient's baseline blood pressure was slightly hypotensive, and she had taken her beta-blocker the morning of surgery, causing her to be more prone to bradycardia and hypotension.
- She had required several boluses of 50-100 mcg of phenylephrine after induction of anesthesia to maintain a blood pressure within 20% of her baseline. Her blood pressure remained stable after incision. Her hypotension at the conclusion of the procedure may have been partially due to lack of surgical stimulation.
- Prior to receiving sugammadex, she received 4 mg of ondansetron, which has a black box warning for QT prolongation. The combination of these two drugs may have worked together to potentiate the decrease in cardiac output.
- The patient had been on long-term antidepressant therapy with duloxetine, a serotonin-norepinephrine reuptake inhibitor which may have caused her to become catecholamine depleted. This factor could also have potentiated her decrease in cardiac output.

Conclusion

- Further investigation is required to understand the mechanism behind these cardiovascular events associated with sugammadex.
- Sugammadex should always be administered slowly with ECG and hemodynamic monitoring.
- Emergency drugs do not need to be drawn up but should be readily available.

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