Sugammadex induced bradycardia and hypotension
A case report and literature review

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Abstract
Rationale: There is evidence that sugammadex can facilitate extubation post-surgery and attenuate postoperative pulmonary complications resulting from postoperative residual neuromuscular blockade. However, it may induce adverse effects, including bronchospasm, laryngospasm, bradycardia, hypotension, and cardiac arrest. Here, we present a case of sugammadex-induced bradycardia and hypotension.

Patient concerns: An 82-year-old female received video-assisted thoracic surgery decortication and wedge resection of the lung for empyema. Post-surgery, she developed bradycardia, hypotension, hypoxia, and weakness.

Diagnoses: The patient was suspected to have sugammadex-induced bradycardia, hypotension, hypoxia and weakness.

Interventions: The patient received immediate treatment with atropine (0.5 mg) for bradycardia. Glycopyrrolate (0.1 mg) and neostigmine (1 mg) were administered to improve the train-of-four (TOF) ratio.

Outcomes: Following initial management, we observed improvement in the hemodynamics of the patient. She was discharged without any sequelae.

Lessons: Sugammadex-induced bradycardia or cardiac arrest are rare; however, anesthesiologists must consider the possibility of the occurrence of such events and initiate appropriate management measures. Immediate treatment with atropine and inotropic or vasopressors is warranted if the patient presents with bradycardia.

Abbreviations: bpm = beats per minute, NMTM = neuromuscular transmission monitors, TOF = train-of-four.

Keywords: bradycardia, cardiac arrest, hypotension, sugammadex

1. Introduction

Neuromuscular blocking agents are often employed to facilitate intubation, mechanical ventilation, and favorable surgical conditions. However, postoperative pulmonary complications, such as pulmonary hemorrhage, difficulty breathing, reintubation, and prolongation of the patient’s length of stay could be attributed to postoperative residual neuromuscular blockade.[1,2]

Reversal agents are used to speed up recovery time from neuromuscular blockade and prevent postoperative residual neuromuscular blockade.[3] In contrast to acetylcholinesterase inhibitors, sugammadex has been demonstrated to shorten extubation time, resulting in improved operating room turnover in clinical anesthesia settings and attenuation of postoperative pulmonary complications.[4,5] However, sugammadex has been associated with several adverse effects, including bronchospasm,[6] pulmonary edema,[6] desaturation, hypotension, laryngospasm,[7] bradycardia, and cardiac arrest.[8–16] Here, we present a case of sugammadex-induced bradycardia, hypotension, and hypoxia in a patient following video-assisted thoracic surgery decortication and wedge resection of the lung. In addition, we analyzed adult cases of bradycardia or hypotension following sugammadex administration between January 2014 and January 2021 with a detailed literature review as well.

2. Case presentation

The patient was an 82-year-old woman (146 cm, 44 kg) diagnosed with hypertensive heart disease with no known history of allergy. Upon being diagnosed with empyema, she was scheduled for video-assisted thoracic surgery decortication and wedge resection of the lung. Pre-procedural electrocardiography
revealed a normal sinus rhythm. Cardiac echocardiography showed a left ventricular ejection fraction of 71% and impaired left ventricular relaxation. Abnormal laboratory data demonstrated a white blood cell count of 15,500/μL and C-reactive protein level of 220.7 mg/L. Vital signs were unremarkable except for oxygen saturation being around 90% to 95% on room air.

Routine monitoring included electrocardiography (lead II), noninvasive blood pressure, pulse oximetry, end-tidal carbon dioxide measurement, entropy, and the use of neuromuscular transmission monitors (NMTM). General anesthesia was induced with thiopental (225 mg), rocuronium (50 mg), lidocaine (40 mg), fentanyl (75 mg), and glycopyrrolate (0.1 mg). The patient was intubated with a 32 Fr left double-lumen tube, and inspected using a fiberoptic bronchoscope. Following tracheal intubation, a right radial arterial line and central venous catheter were inserted. Anesthesia was maintained with sevoflurane (0.5–0.9), minimum alveolar concentration and propofol (20 mL/h) titrated to effect under entropy. In addition, the patient received a continuous dose of rocuronium (15–10 mg/h) under NMTM. Ventilation was adjusted to maintain an end-tidal carbon dioxide of 35 to 45 mmHg. The surgery was completed uneventfully in 2 hours and 40 minutes. At the completion of the procedure, arterial blood pressure of the patient was estimated to be 124/85 mmHg; heart rate, 65 beats per minute (bpm); SpO2, 99%; NMTM count, 4; and train-of-four (TOF) ratio, 64. The patient regained consciousness and spontaneous breathing. A dose of 200 mg sugammadex was next administered. One minute following sugammadex administration, the patient developed hypotension (67/34 mmHg), hypoxia (SpO2: 65%), with an arterial blood pressure of the patient was estimated to be 124/85 mmHg; heart rate, 65 beats per minute (bpm); SpO2, 99%; NMTM count, 4; and train-of-four (TOF) ratio, 64. The patient regained consciousness and spontaneous breathing. A dose of 200 mg sugammadex was next administered. One minute following sugammadex administration, the patient developed hypotension (67/34 mmHg), hypoxia (SpO2: 65%), with an NMTM count of 0, and TOF ratio of 0. The patient was immediately administered atropine (0.5 mg) intravenously, following which her hemodynamics improved, with a corresponding heart rate of 65 bpm, SBP of 89/50 mmHg, and SpO2 of 93%. Subsequent administration of glycopyrrolate (0.1 mg) and neostigmine (1 mg) improved the TOF ratio to 69. Arterial blood gas values were as follows: pH, 7.291; PaO2, 75 mmHg; PaCO2, 51.4 mmHg; HCO3–, 22.8 mmol/L; lactate, 1.1 mmol/L; hemoglobin, 12.6 g/dL; and hematocrit, 36.7%. The anesthesiologist replaced the double-lumen tube with a single-lumen 4-dontracheal tube, following which the patient was transferred to the intensive care unit for further care. The patient was extubated and discharged 4 and 10 days post-surgery, respectively, without any sequelae.

3. Discussion

PubMed and Cochrane Database were searched for the terms “sugammadex AND (bradycardia operating room cardiac arrest)” in January 2021. Articles between January 2014 and January 2021 were included regardless of the type of publication or journal. The full text of the articles was retrieved. The authors assessed the articles using the following set of criteria:

1. the article is written in English;
2. the study is a case report or case series;
3. the study includes a description of the dose of sugammadex used, its adverse effects, and the treatment strategy;
4. the subjects are adult patients.

Information such as the type of publication (case report), year of publication, description of adverse effects, treatment adminis-
| Authors               | Dose of Sugammadex | Signs and symptoms                                                                 | Management                                                                 | Outcome                              | Mechanism       |
|-----------------------|--------------------|-------------------------------------------------------------------------------------|---------------------------------------------------------------------------|---------------------------------------|-----------------|
| Obara et al[12]       | 73 y/o Male        | Hypotension; SBP unmeasurable (6 min after sugammadex)                              | Fluid resuscitation<br>Phenylephrine 0.1 mg for 2 times<br>Epinephrine 0.1 mg<br>Suspecting primary cardiac ischemia, lidocaine (100 mg over 2 min) and nicorandil (2 mg/h) were also administered to prevent further progression of cardiac ischemia and arrhythmia. | SBP 70 mmHg, sinus heart rhythm 110 bpm<br>I CU<br>Consciousness recovery 1 hr. after shock<br>The serum tryptase level 3 h. after the event was elevated to 9.6 mg/L (normal range, 1.2–5.7)<br>Skin prick test: positive reaction of sugammadex Anaphylaxis |                  |
|                      | 77 kg, 178 cm      | ECG: ST depression, polymorphic ventricular premature contraction, and then cardiac arrest<br>Unconscious<br>Flushed on entire body trunk and lower limbs                      | Re-intubation<br>CPR 10 min: epinephrine 3 mg i.v., defibrillations 2 times for VF<br>Suspecting an allergic reaction, methylprednisolone 1 g, hydroxyzine hydrochloride 50 mg, and a large volume of fluids | Re-intubation<br>SBP 70 mmHg, sinus heart rhythm 110 bpm<br>I CU<br>Consciousness recovery 1 hr. after shock<br>The serum tryptase level 3 h. after the event was elevated to 9.6 mg/L (normal range, 1.2–5.7)<br>Skin prick test: positive reaction of sugammadex Anaphylaxis |                  |
|                      | Sugammadex 200 mg   |                                                                                     |                                                                           |                                       |                 |
|                      | (2.60 mg/kg)       |                                                                                     |                                                                           |                                       |                 |
|                      | 41 y/o Male        | Hypotension<br>Bradycardia (HR: 25 bpm) (2 min after sugammadex)                    | CPR<br>Epinephrine 1 mg i.v.<br>Re-intubation<br>Ventilation with 100% O₂ |                      | Unknown         |
|                      |                      | No palpable peripheral pulses                                                         |                                                                           |                                       |                 |
|                      |                      |                                                                                     |                                                                           |                                       |                 |
|                      | 41 y/o Male        | Hypotension<br>Bradycardia (HR: 30 bpm) (1 min after sugammadex)                    | CPR<br>Epinephrine 30 mg i.v.                                               |                      | Unknown         |
|                      |                      | No palpable pulse                                                                    |                                                                           |                                       |                 |
|                      |                      |                                                                                     |                                                                           |                                       |                 |
|                      | 60 y/o Female       | Hypotension<br>Bradycardia (HR: 35 bpm) (< 1 mins after sugammadex)                | Atropine 1 mg (no effect)<br>Epinephrine 1 mg every 3 minutes for a total of 7 mg<br>Calcium chloride 1 gm until return of spontaneous circulation |                      | Unknown         |
|                      | 82 kg               | No rash or urticaria                                                                |                                                                           |                                       |                 |
|                      | BMI 28.4            | Bilateral breath sounds clear                                                       |                                                                           |                                       |                 |
|                      | Sugammadex 200 mg   | Peak airway pressure remained 18 cmH₂O; end-tidal CO₂ 38 mmHg; End-tidal CO₂ fell to 10 mm Hg |                                                                           |                                       |                 |
|                      | (2.4 mg/kg)         | Cardiol pulses (-)<br>PEA                                                           |                                                                           |                                       |                 |
|                      |                      |                                                                                     |                                                                           |                                       |                 |
|                      | 71 y/o Female       | Episode 1<br>Desaturation (2 min after sugammadex)                                  | Mask ventilation<br>CPR and defibrillation<br>Re-intubated 18 mins after resuscitation |                      | Kounis Syndrome (Anaphylaxis) |                  |
|                      | 65 kg               | VF                                                                                  |                                                                           |                                       |                 |
|                      | Sugammadex 200 mg   | No rash on the skin                                                                 |                                                                           |                                       |                 |
|                      | (3.08 mg/kg)        |                                                                                     |                                                                           |                                       |                 |
|                      |                      |                                                                                     |                                                                           |                                       |                 |

**Table 1: Literature review of reported cases of sugammadex induced bradycardia or cardiac arrest.**

**Notes:**
- TTE: transthoracic echocardiogram, electrocardiogram, chest X-ray, computed tomography chest, contrast-enhanced CT scans of chest and abdomen
- Unremarkable findings:
  - TTE: normal EF with no regional wall motion abnormalities
  - Blood tests, chest X-ray, brain CT scan, contrast-enhanced CT scans of chest and abdomen
- Transferred to a rehabilitation hospital on day 61 (continued)
Table 1 (continued).

| Authors | Patient Information | Dose of Sugammadex | Signs and symptoms | Management | Outcome | Mechanism |
|---------|---------------------|--------------------|--------------------|------------|---------|-----------|
| Teng et al. Medicine (2021) 100:30 | 71 y/o Female | | Episode 2 | • Blood pressure drop suddenly | • Noradrenaline i.v. drip | Spontaneous circulatory failure after 13 min of resuscitation | Kounis Syndrome |
| | 65 kg Sugammadex 130 mg (2 mg/kg) | | | • Bradyarrhythmia (HR < 60 bpm) | | ECG: diffuse ST depression | Anaphylaxis |
| | | | | • Bradycardia (without mention of HR) | | TTE: diffused, severely depressed left ventricular wall motion | |
| | | | | • PEA | | Coronary angiogram: multiple spasms in RCA, resolved via intraoperative administration of nitroglycerin | |
| | | | | | | Hypertension (41/25 mmHg) and alveolar hypoventilation (SpO2 93% [FO2 1.0]). | |
| | | | | | | Spontaneous breathing during the following 3 days in ICU | |
| | | | | | | Normal systolic function of both ventricles | |
| | | | | | | | | |
| Yoshida et al.[16] | 50 y/o Female | | | | | Spontaneous respiration during the following 3 days in ICU | Unknown |
| | 79.2 kg, 156 cm Sugammadex 200 mg (2.53 mg/kg) | | | | | Discharged on POD 9 | |
| | | | | | | | |
| Mirza et al.[11] | 82 y/o Male | | | | | Spontaneous respiration during the following 3 days in ICU | Unknown |
| | 68.97 kg Sugammadex 200 mg (2.9 mg/kg) | | | | | Discharged on POD 9 | |
| | | | | | | | |
| Carmen et al.[18] | 80 y/o Male | | | | | Spontaneous respiration during the following 3 days in ICU | Unknown |
| | 55 kg, 158 cm Sugammadex 200 mg (0.64 mg/kg) | | | | | Discharged on POD 9 | |
| | | | | | | | |
| Murat Bilgi et al.[9] | 56 y/o Male | | | | | Spontaneous respiration during the following 3 days in ICU | Unknown |
| | 77.9 kg, 163 cm Sugammadex 200 mg (2.6 mg/kg) | | | | | Discharged on POD 9 | |
| | | | | | | | |
| Evangelia Samara et al.[13] | 54 y/o Male | | | | | Spontaneous respiration during the following 3 days in ICU | Unknown |
| | 175 cm, 75 kg Sugammadex 200 mg (2.7 mg/kg) | | | | | Discharged on POD 9 | |
| | | | | | | | |
| Bedriti et al.[7] | 22 y/o Female | | | | | Spontaneous respiration during the following 3 days in ICU | Unknown |
| | 213 cm, 85 kg | | | | | Discharged on POD 9 | |
| | | | | | | | |

(continued)
From 2014 to December 31, 2020, a total of 282 cases of major cardiac events were reported following sugammadex/sugammadex sodium/bridion administration as per the Food and Drug Administration Adverse Event Reporting System database. These events include bradycardia (n = 160), cardiac arrest (n = 110), cardiopulmonary arrest (n = 16), hypotension (n = 83), and decreased oxygen saturation (n = 53). However, in this study, we have investigated only 11 case reports from previous literature. Therefore, the incidence of adverse effects associated with sugammadex could have been underestimated.

4. Conclusions
Although sugammadex-induced bradycardia or cardiac arrest are rare, anesthesiologists should consider the possibility of the occurrence of such events. Immediate treatment with atropine and inotropic or vasopressors is recommended in such cases. Furthermore, advanced cardiac life support is required if initial management fails to manage the adverse effects.

Author contributions
Investigation: I-Chia Teng, Yao-Tsung Lin, Zhi-Fu Wu.
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