ABSTRACT

Three elderly patients received sugammadex after confirmation of train-of-four (TOF) stimulation at the end of the surgery. They presented opioid-induced respiratory depression accompanied by severe acidosis postoperatively. Even after the reversal of opioid intoxication with naloxone, the respiration did not recover, and TOF revealed recurrent paralysis. Two of three cases completely recovered after additional sugammadex administration, but remnant 1 case without sugammadex transferred to intensive care unit with intubated status. Even if the recommended dose of sugammadex is administered, there can be recurrent neuromuscular blockade by complicated reasons. Continuous quantitative neuromuscular monitoring may be needed to prevent these unusual situations.

Keywords: Neuromuscular monitoring, Opioid-induced respiratory depression, Recurarization, Respiratory Acidosis, Sugammadex.

I. INTRODUCTION

Sugammadex (Bridion, Merch Sharp & Dohme, NJ, USA) is a synthetic cyclodextrin molecule, which provides rapid reversal of neuromuscular blockade by encapsulation of rocuronium [1]. After its discovery, many anesthesiologists regarded as ideal reversal agents, because it provides rapid and complete reversal either for light or deep blockade. Anesthesiologists usually determine the dose of sugammadex according to the manufacturer’s instructions and textbook to attain adequate reversal while avoiding the side effects, especially for hypersensitivity [2], which has been known to be increased as the increment of dose. There were numerous reports which showed recurrent paralysis after the sugammadex administration due to their insufficient doses or inappropriate neuromuscular monitoring [3]-[6]. However, there may be other causes which induce or aggravate recurrent paralysis. Herein, we report 3 cases of recurrent neuromuscular blockade after sugammadex administration accompanied by opioid-induced CO₂ narcosis.

II. CASES

Patient data in the present report was approved to use by the Institutional Review Board (Registration Number: 2022-01-023). The need for informed consent was waived.

All patients induced general anesthesia with 20-30 mg of lidocaine, 1.0–1.2 mg/kg of propofol, and 0.6–0.8 mg/kg of rocuronium. During maintenance period, the patient was mechanically ventilated to maintain an end-tidal carbon dioxide between 30 and 40 mmHg and anesthesia was maintained with 1.5–2.5 vol % of sevoflurane and 0.05–0.15 mcg/kg/min remifentanil with target BIS between 40–55. When the suture begins, 30mcg of fentanyl bolus was administered, and patient-controlled analgesia device (PCA) started. Rocuronium was intermittently administered or continuously administered with infusion rate of 10 mg/h and ceased 30 minutes before the end of the surgery. After confirmation of 2-3 twitches in response to train-of-four (TOF) stimulation by neuromuscular monitoring device (MiniStim MS-IV A, Life-Tech inc., TX, USA),
sugammadex 100–110 mg (2–2.5 mg/kg) was administered. Tracheal extubation was done followed by the confirmation of full 4 twitches of TOF counts, obey on verbal command, and spontaneous self-respiration.

III. CASE 1

A 78-year-old man (148cm, 40kg) with the history of chronic kidney disease stage 3, interstitial lung disease and atrial fibrillation underwent closed reduction surgery of right femur.

After post-anesthesia care unit (PACU) arrival, the patient tended to sleep, but showed good spontaneous breathing and response to obey such as grab one’s hand. Because the patient showed tendency to sleep, PCA was clamped 10 min after the PACU admission. 20 minutes after PACU arrival, the patient showed weak respiration and SpO2 of the patient suddenly decreased to 88%. The anesthesiologist decided to assist the patient’s breathing with manual mask bagging. Soon after, SpO2 of patient was maintained above 98 %, however, self-respiration was still weak and showed drowsy mentality. After confirmation of bilateral pin-point pupil, anesthesiologist decided to administer 0.05 mg of naloxone, and 0.1 mg of second dose was followed after 5 minutes. After then, the patient slowly woke up and showed better respiration, however, on the arterial blood gas analysis (ABGA) exam, severe respiratory acidosis was found (Table I). Immediately, anesthesiologist decided to re-intubate. 20 minutes after the intubation, the patient recovered consciousness but still showed weak self-respiration. Because the respiratory effort was weak even after 1 h of close observation, the anesthesiologist and the surgeon eventually decided to transfer the patient to intensive care unit (ICU) to examine the possibility of other cause. 120 minutes after PACU arrival, the patient was transferred to ICU in intubated state, and there were no specific abnormalities on neurologic exam (brain CT and physical exams). Extubation was done on 1st postoperative day, and the patient discharged without further complications on the 10th postoperative day.

IV. CASE 2

A 77-year-old woman (150 cm, 54 kg) with diabetes mellitus, hypertension, chronic kidney disease stage 4 and history of unstable angina underwent L3-L5 level spinal fusion surgery (total 355 min).

After PACU arrival, the patient was in alert mentality, showed good spontaneous breathing and activity. During the 30 minutes in PACU, 3 times of fentanyl bolus (30, 30, and 40 mcg, respectively) was administered due to severe pain (NRS >6). 5 minutes after tertiary fentanyl was given, the patient showed drowsy mentality and poor cooperation. The attending anesthesiologist clamped PCA device and started to provoke response. Soon, the desaturation occurred (SpO2 <88%) and the manual mask ventilation started. ABGA examination was done (Table I). While applying mask bagging, the anesthesiologist confirmed constricted bilateral pupil and 0.05 mg of naloxone was administered. After 2 minutes, the patient opened her eyes on the verbal command and self-respiration was slightly improved, and an additional 0.05 mg of naloxone was followed. Because there was no twitch in response to 3 consecutive TOF stimulation, an additional 110 mg of sugammadex was given and the patient’s respiration dramatically improved. 90 minutes after PACU arrival, the patient transferred to general ward with keeping venturi mask with O2 35% 9L and discharged without further complications.

V. CASE 3

A 81-year-old man (158 cm, 50 kg) underwent T11-L2 Spinal fusion surgery (total 570 min). The patient had hypertension.

After PACU arrival, Initial vital sign was stable (Blood pressure, 130/74 mmHg; Heart rate, 55 beats per minute; SpO2 100%, Respiratory rate, 13 breaths/min). 5 minutes after PACU arrival, the patient complained of pain (NRS>6) and 30mcg of fentanyl was administered and additional 30mcg was readministered after additional 10 minutes via the patient’s request. After the second dose of fentanyl, the patient gradually calmed down and tended to sleep. The patient continuously tended to sleep even the medical staff kept waking him up. ABGA exam revealed severe respiratory acidosis (Table 1). As the symmetrical pin-point pupils were observed with drowsy mentality and poor self-respiration, we administered 0.1 mg of naloxone intravenously and additional 2nd dose (0.1 mg) was followed. After the 2nd dose of naloxone accompanying the manual ventilation, the patient slowly recovered the responses such as grimace, but the respiration was still weak. Because there were no twitches in response to TOF stimulation, we decided to administer the additional sugammadex. 3 minutes after an additional 100 mg of sugammadex, the patient started to breath without additional manual ventilation and recovered the full 4 twitches. The clinician decided to cease the manual mask ventilation and transferred to the general ward after confirmation of normal ABGA. He was discharged without further complications on the 14th postoperative day.

VI. DISCUSSION

Recurrence of neuromuscular blockade, commonly called “recurarization”, is frequently observed in the PACU after intraoperative non-depolarizing neuromuscular blocking agent (NMBA) administration. Neostigmine, an acetylcholinesterase inhibitor, is commonly used to reversal of NMBA, but its onset of action is relatively slow and ends quite earlier than NMBA, and thereby recurrence of neuromuscular blockade often occurs in PACU. Sugammadex overcomes this situation because it encapsulates the rocuronium via 1:1 molecular interaction. However, there are some previous reports of recurarization even after sugammadex reversal in obese patients [4], [6] and administration in the absence of neuromuscular monitoring [5]. Contrary to previously known cases of recurarization,[4]-[6] all 3 patients were not obese and received excessive sugammadex (2–2.5 mg/kg) based on the response of TOF stimulation. In this report, the dose of reversal was evaluated by the visual and tactile assessment of the response to TOF stimulation based on the known guidelines of manufacturer and previous researches [7]-[9]. Although the use of this
Qualitative monitoring has decreased the incidence of residual block compared to no monitoring group. Qualitative monitoring is insufficient to ensure acceptable recovery (TOF ratio ≥ 0.9) because manually detect fade at TOF ratios greater than 0.4 is almost impossible even for experienced observers [10], [11].

Severe respiratory acidosis induced by opioid-induced respiratory depression may be another reason for recurarization in this case. In animal studies, CO2-induced acidosis increased the potency of the rocuronium and vecuronium [12], [13]. This effect is attributed to a change of a tertiary ammonium group into a quaternary group by combining with a hydrogen ion and consequently the molecule may change into a pseudobisquaternary structure. This increases the attraction of the rocuronium molecule to the anionic cholinergic receptors. Additionally, acidosis itself changes to alter the activity of both the plasma cholinesterase and acetylcholinesterase. Taken these together, it would be reasonable to conclude that the action of unbound rocuronium, which remained in a very small amount, was strengthened by respiratory acidosis after opioid induced respiratory depression, and thereby compromise neuromuscular blockade. Acidosis and hypercarbia are known factors to affect the action of non-depolarizing NMBAs and possibly to neostigmine, but to date there are no studies investigating the effects of these metabolic problems on the effectiveness of sugammadex. Underlying diseases such as chronic renal failure and old age can delay the elimination of sugammadex. Underlying diseases such as chronic renal failure and old age can delay the elimination of sugammadex. Underlying diseases such as chronic renal failure and old age can delay the elimination of sugammadex. Underlying diseases such as chronic renal failure and old age can delay the elimination of sugammadex. Underlying diseases such as chronic renal failure and old age can delay the elimination of sugammadex.

As the sugammadex use continuously increases, anesthesiologist will encounter new scenarios and need to update new advantages and limitations of this drug. The use of perioperative quantitative neuromuscular monitoring can reduce the risk and detect incomplete recovery in unusual situations like our cases. We should be aware that residual or recurrent neuromuscular blockade may not be fully mitigated by the administration of sugammadex alone without quantitative continuous neuromuscular function monitoring.

**CONFLICT OF INTEREST**

The authors declare they do not have any conflict of interest.

**REFERENCES**


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