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Sugammadex: A potential cause of unexpected re-operation after closed reduction of subcondylar mandibular fracture

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Abstract: A 58-year-old man without any significant medical history was scheduled for closed reduction of a subcondylar mandibular fracture after trauma. The fracture was treated under general anesthesia by closed reduction with intermaxillary fixation with rubber bands. The surgical procedure was completed in 45 minutes, and the surgeon confirmed the complete reduction of the subcondyle by the portable radiography scanning. Three minutes after sugammadex was administered for reversal of the neuromuscular blockade, the patient became agitated and began moving and attempting opening his mouth while still intubated. The patient's agitation during the recovery period was suspected to have resulted in failure of the closed reduction. Repeat radiography confirmed that the previous reduction had failed, indicating that the fracture now required open fixation. The patient was returned to the operating room, where he underwent successful open reduction and fixation. Neuromuscular blockade can lead to inaccurate assessment of anesthetic depth. Inadequate depth of anesthesia, as revealed by administration of sugammadex to reverse the neuromuscular blockade, can lead to patient agitation, thus increasing the likelihood of indication for re-operation to repair a previous closed fracture reduction. Therefore, unless depth of anesthesia is monitored concurrently, administration of sugammadex poses a potential risk factor for unmasking inadequate anesthetic depth.
Keywords: Neuromuscular blockade reversal, sugammadex, adverse effects, Mandibular Condyle, surgery, Mandibular Fractures, Internal Fracture Fixation, reoperation.

INTRODUCTION

Sugammadex is a modified γ-cyclodextrin, and is the first clinically used selective relaxant-binding agent. Its mechanism of action involves encapsulating neuromuscular blocking agents leading to their inactivation, thereby effectively and rapidly reversing the neuromuscular blockade [1]. This novel mechanism of action differs completely from that of acetylcholinesterase inhibitors. The formation of a complex of sugammadex with rocuronium or vecuronium occurs at any depth of neuromuscular blockade, and results in a more rapid pharmacologic reversal when compared with acetylcholinesterase inhibitors. Recommended doses of sugammadex depend on the degree of neuromuscular blockade present, and can usually antagonize the neuromuscular blockade within a few minutes [1].

Based on phase II and III clinical trials, the adverse effects of sugammadex are non-specific and include hypotension, movement, coughing, dry mouth, and nausea [2,3]. The potential for immediate patient movement after administration of sugammadex was identified in clinical trials and discussed in reviews [4,5]. These reports suggest that if the depth of anesthesia is not monitored, sugammadex administration at the end of surgery could cause a patient to show agitated movements due to an inadequate anesthetic depth that was concealed by the neuromuscular blockade.

This case report describes an unintended re-operation of a patient due to sudden spontaneous forceful movement of a closed reduction site after administration of sugammadex. The aim of this report is to identify and discuss the potential risk of sugammadex for unmasking an inadequate anesthesia in the absence of appropriate monitoring of anesthetic depth, as well as considering that appropriate analgesic administration is also important in minimizing patient agitation during recovery.

CASE REPORT

A 58-year-old man (height 164 cm, weight 63 kg) without any significant medical history was scheduled for closed reduction of a subcondylar mandibular fracture after trauma. Anesthesia was induced with propofol (2 mg/kg) and rocuronium (0.6 mg/kg) intravenously. The patient was placed under standard monitoring (EKG, arterial oxygen saturation and non-invasive blood pressure). Bispectral index (BIS) monitoring was not applied due to the location of the surgical field. After intubation via the nasotracheal route, anesthesia was maintained with sevoflurane (1-

2%) and intravenous continuous infusion of remifentanil (0.1 ~ 0.15 µg/kg/min). An additional 10 mg of rocuronium (0.16 mg/kg) was administered once during the procedure; the procedure was completed 30 minutes later. The fracture was treated by closed reduction with intermaxillary fixation with rubber bands. After 45 minutes of total general anesthesia time, the procedure was completed and the surgeon confirmed complete reduction of the subcondyle by the portable radiographic scan [Fig 1-A]. Subsequently, the anesthesiologist administered sugammadex 200 mg intravenously to antagonize the rocuronium-induced neuromuscular blockade. Within a few minutes of administration of sugammadex, the patient suddenly developed tachycardia, and showed uncontrolled coughing and agitated movements such as flailing of the arms and forcefully opening his mouth that created snapping sounds due to the rubber bands used for fixation. As the patient showed no apparent abnormalities at the surgical site at that time, the patient was delivered to the postoperative care unit after extubation, and fentanyl citrate 1.3 µg/kg was administered intravenously for postoperative analgesia. The surgeon ordered a repeat radiographic scan to confirm the surgical outcome and found that the mandibular reduction had failed, and that it now required surgical fixation [Fig 1-B]. Re-operation started at seventy minutes after discontinuation of the previous anesthetic event, and anesthesia was induced with propofol (2 mg/kg) and cisatracurium (0.25 mg/kg) intravenously. At the end of surgery, pyridostigmine was used to reverse the cisatracurium. The patient successfully underwent open reduction and fixation surgery, and recovered from anesthesia without any further complications [Fig 1-C].

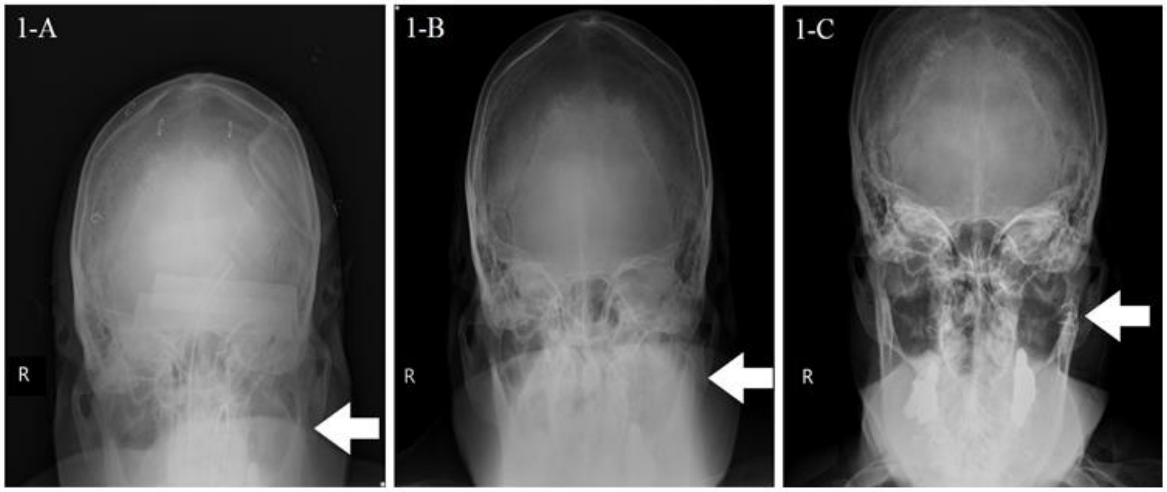

Fig 1: Simple skull radiograph with modified Towne's projection

The left mandibular subcondyle was well fixed after closed reduction (1-A, white filled arrow). After administration of sugammadex, the patient suddenly showed agitated movements and struggled to open his mouth that had just been reduced and fixed. At the post-anesthesia care unit, dislocation of the fixed mandibular subcondyle was detected (1-B, white filled arrow). The patient was re-operated for open fixation using plate and wire fixation (1-C, white filled arrow).

DISCUSSION

Intraoperative anesthetic depth monitoring is essential for effective use of anesthetic agents and prevention of intraoperative patient awareness. Anesthesiologists usually rely on physiologic signs and anesthetic dosing strategies to assess awareness and anesthetic depth under general anesthesia. Physiologic signs of changes in heart rate, arterial blood pressure, and absence of movement are the measurements most commonly used to track anesthetic depth during the maintenance phase of general anesthesia. Real-time analysis of unprocessed electroencephalogram (EEG) and spectrogram (density spectral array) is an objective and highly informative approach to evaluate the degree of consciousness in patients receiving general anesthesia. However, despite the utility of these techniques, these are not routinely used to monitor patients under general anesthesia.

Sugammadex is a modified γ-cyclodextrin and the first clinically used selective relaxant-binding agent. The mechanism of action of this class of drugs involves encapsulation of neuromuscular blocking agents such as rocuronium or vecuronium, thereby rapidly rendering them incapable of binding to nicotinic acetylcholine receptors and effectively inactivating them. After a dose of 4.0 mg/kg of sugammadex, the mean recovery time to a TOF ratio of 0.9 was 1.1 minutes and 1.5 minutes after rocuronium and vecuronium, respectively [6]. In a separate study, patients who received 1.2 mg/kg of rocuronium followed 3 minutes later by 16 mg/kg of sugammadex show faster recovery than one who received 1.0 mg/kg of succinylcholine followed spontaneous recovery [7].

Sugammadex produces rapid and effective neuromuscular blockade reversal but can induce adverse effects such as coughing and movement. The most clinically relevant common adverse effects of sugammadex (incidence of 2%) are due to the rapid recovery of muscle function during balanced anesthesia, which could unmask an anesthetic plane that is too light. In such cases, patients may attempt to cough, move, grimace, or suckle on the endotracheal tube [2] after reversal by sugammadex, especially in the presence of surgical stimuli.

Unexpected movement after administration of sugammadex was observed in several studies, likely due to rapid restoration of motor function and lighter anesthetic levels [8]. Administering sugammadex after weaning anesthetic depth toward the end of a procedure increases the risk of patient movement and withdrawal. Maintaining deeper levels of neuromuscular blockade until the conclusion of surgery may mask light anesthetic depth and awareness that would have otherwise been identified by patient movement. This highlights the importance of intraoperative anesthetic depth monitoring.

A retrospective study on unplanned reoperation following 3,688 primary surgical management of orthopedic trauma indicates an overall re-operation rate of 1.9% (99% CI: 1.4 to 2.6) [9], most frequently due to technical errors. Subcondylar fracture is the most common site of mandibular fracture, and is treated by either closed reduction with mandibular-maxillary fixation or open reduction and internal fixation [10].

Because of the pain associated with this type of fracture and fracture repair, inappropriate anesthetic and analgesic selection and management could result in increased risk of patient agitation and movement during the recovery phase of anesthesia. This could then result in complications that require further surgical intervention.

In this case, the patient's unexpected agitation and struggling during the emergence from anesthesia is thought to be due to inadequate analgesia and anesthetic depth. The oral cavity procedure itself , as well as the anesthetic agent selection, may have contributed to the agitation, as it is reported to be more frequent when using sevoflurane than when using other inhalational anesthetics [5,11]. Therefore, for patients undergoing oral cavity surgery under general anesthesia, the anesthesiologist must closely monitor the depth of anesthesia and determine the proper dose and appropriate administration time of analgesic agents for postoperative pain, especially if sugammadex as a neuromuscular blocking agent reversal is used.

CONCLUSION

The development of sugammadex enables rapid reversal of deep neuromuscular blockade whenever reversal is indicated. However, maintaining deeper levels of neuromuscular blockade until the end of surgery may mask light anesthetic depth and awareness that would otherwise have been identified by patient movement. Unexpected patient agitated movements during the perioperative period can result in unplanned re-operation, as reported in this case. Therefore, sugammadex administration without anesthetic depth monitoring poses risks to patients who are inadequately anesthetized.

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Author Disclosure

The author declares that there is no conflict of interest regarding the publication of this paper.

REFERENCES

1. Fuchs-Buder T, Meistelman C, Raft J. Sugammadex: clinical development and practical use. Korean journal of anesthesiology. 2013 Dec 1;65(6):495-500.
2. Sparr HJ, Vermeyen KM, Beaufort AM, Rietbergen H, Proost JH, Saldien V, Velik-Salchner C, Wierda JM. Early reversal of profound rocuronium-induced neuromuscular blockade by sugammadex in a randomized multicenter study: efficacy, safety, and pharmacokinetics. Anesthesiology. 2007 May;106(5):935-43.
3. Tsur A, Kalansky A. Hypersensitivity associated with sugammadex administration: a systematic review. Anaesthesia. 2014 Nov 1;69(11):1251-7.
4. de Boer HD, Driessen JJ, Marcus MA, Kerkkamp H, Heeringa M, Klimek M. Reversal of Rocuronium-induced (1.2 mg/kg) Profound Neuromuscular Block by SugammadexA Multicenter, Dose-finding and Safety Study. The Journal of the American Society of Anesthesiologists. 2007 Aug 1;107(2):239-44.
5. Sorgenfrei IF, Norrild K, Larsen PB, Stensballe J, Østergaard D, Prins ME, Viby-Mogensen J. Reversal of Rocuronium-induced Neuromuscular Block by the Selective Relaxant Binding Agent SugammadexA Dose-finding and Safety Study. The Journal of the American Society of Anesthesiologists. 2006 Apr 1;104(4):667-74.
6. Suy K, Morias K, Cammu G, Hans P, van Duijnhoven WG, Heeringa M, Demeyer I. Effective reversal of moderate rocuronium-or vecuronium-induced neuromuscular block with sugammadex, a selective relaxant binding agent. The Journal of the American Society of Anesthesiologists. 2007 Feb 1;106(2):283-8.
7. Lee C, Jahr JS, Candiotti KA, Warriner B, Zornow MH, Naguib M. Reversal of Profound

Neuromuscular Block by Sugammadex Administered Three Minutes after RocuroniumA Comparison with Spontaneous Recovery from Succinylcholine. The Journal of the American Society of Anesthesiologists. 2009 May 1;110(5):1020-5.

8. Welliver M, McDonough J, Kalynych N, Redfern R. Discovery, development, and clinical application of sugammadex sodium, a selective relaxant binding agent. Drug Des Devel Ther. 2008 Dec;2:49-59.
9. Barksfield RC, Coomber R, Woolf K, Prinja A, Wordsworth D, Lopez D, Burtt S. The epidemiology of reoperations for orthopaedic trauma. Annals of the Royal College of Surgeons of England. 2015 Jan;97(1):40.
10. Boutros SG. Closed reduction and fluoroscopically assisted percutaneous stabilization of displaced subcondylar mandible fractures. Plastic and reconstructive surgery. 2005 Sep 15;116(4):971-7.
11. Fassoulaki A, Chondrogiannis K, Staikou C. Sugammadex at both high and low doses does not affect the depth of anesthesia or hemodynamics: a randomized double blind trial. Journal of clinical monitoring and computing. 2016 Feb 19:1-6.