

The use of rocuronium 20 minutes after sugammadex administration – a case report

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Abstract

Sugammadex has proven to be highly effective for the reversal of moderate or deep neuro-muscular blockade induced by rocuronium or vecuronium. We present a case where optimal conditions for tracheal intubation were attained using rocuronium (0.5 mg kg^{-1}) 20 minutes (min) after sugammadex had been given. A 59-yr-old female patient, ASA II was scheduled for elective total thyroidectomy. Anesthesia included propofol, fentanyl and rocuronium with sugammadex for neuromuscular blockade reversal, and sevoflurane/air for maintenance. 20 minutes after reversal of neuromuscular blockade with sugammadex the patient returned to operating room for evacuation of cervical hematoma and second general anesthesia was induced with the usage of rocuronium (0.5 mg kg^{-1}) and propofol 2 mg kg^{-1} . Good intubation conditions were obtained after approximately 2 minutes and tracheal intubation was performed uneventfully without any observed desaturation below 96%. Patient returned to post anesthesia care unit after the second procedure, well and fully recovered, and had hospital discharge after 3 days.

Our case shows that a short time of twenty minutes between use of sugammadex and rocuronium (0.5 mg kg^{-1}) did not affect intubation conditions, with normal induction doses of propofol.

Introduction

Sugammadex, a modified γ -cyclodextrin, has proven to be highly effective for the reversal of moderate or deep neuromuscular blockade induced by rocuronium or vecuronium [1]. Sugammadex has revolutionized post-operative care due to its capability to reverse neuromuscular blockade (NMB) safely, rapidly and efficiently.

Although uncommon, patients may require anesthesia and tracheal intubation in the immediate postoperative period, soon after successful reversal of rocuronium-induced NMB by sugammadex. One of the options in such situations would be to re-administer rocuronium. We present a case where optimal conditions for tracheal intubation were attained using rocuronium (0.5 mg kg^{-1}) 20 minutes (min) after sugammadex had been given. The patient granted written consent for publication of the manuscript.

Materials and methods

A 59-yr-old female patient, American Society of Anesthesiologists Physical Status II (hypothyroidism), weight 60 kg, height 160 cm and body mass index 23.4 kg m^{-2} was scheduled for elective total thyroidectomy. The only drug usually taken was sodium levothyroxine. Laboratory values were within normal limits.

Intraoperative monitors included electrocardiogram, non-invasive blood pressure, pulse oxymetry and end-tidal CO_2 . Temperature was not monitored. Following preoxygenation, general anesthesia was induced with fentanyl $150 \mu\text{g}$, propofol 150 mg and rocuronium 50 mg (0.83 mg kg^{-1}) to facilitate tracheal intubation. Anesthesia was maintained with sevoflurane and fentanyl. Neuromuscular function was monitored with NMT MechanoSensor monitor using repetitive train-of-four (TOF) stimulation of the ulnar nerve (NMT MechanoSensor®, Datex Ohmeda Division, Finland).

Surgery was uneventful and lasted 79 min. Postoperative

analgesia was started during the procedure with tramadol 100 mg and paracetamol 1 g. Postoperative nausea and vomiting prophylaxis was provided with dexamethasone 4 mg and droperidol 0.625 mg . The antibiotic prophylaxis was made with cefazolin 2 g.

At the end of the procedure and about 80 min after rocuronium was administered there were two twitches to TOF stimulation. The NMB was antagonized with sugammadex 150 mg (2.5 mg kg^{-1}) and the patient's trachea was extubated when the TOF reached the value of 1.

Almost immediately after the patient being admitted in the post anesthesia care unit (PACU), she developed an expanding neck hematoma without airway compromise and was brought back to the operating room for hematoma evacuation. A second round of general anesthesia was performed 20 min after the previous dose of sugammadex with fentanyl $100 \mu\text{g}$, propofol 100 mg and rocuronium 30 mg (0.5 mg kg^{-1}), and the same monitors were applied.

Endotracheal intubation was performed approximately 2 minutes and 30 seconds (sec) after rocuronium. Despite the fact that a TOF of 0.6 was still registered, optimal conditions for intubation were encountered and intubation was performed without difficulty. Rocuronium time of administration to maximum effect (onset time) was about 7 min. The second surgery procedure took 34 minutes to be completed. About 40 min after the second dose of rocuronium, TOF was 0.1 and sugammadex 200 mg (3.3 mg kg^{-1}) was again administered. Extubation was carried out after consciousness and regular, spontaneous respirations resumed.

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The patient's remaining hospital course was uneventful and the patient was discharged.

Discussion

When sugammadex is administered it decreases rocuronium plasma concentration by promptly binding to free rocuronium molecules in the plasma. A rocuronium concentration gradient forms between plasma and neuromuscular junction allowing rocuronium to move from the neuromuscular junction to the plasma where it continues to form rocuronium-sugammadex complexes [2]. Evidence advocates that these complexes remain stable over time.

There are multiple options available to manage NMB when surgical reintervention is needed after sugammadex administration: the use of succinylcholine; the use of a benzylisoquinoline muscle relaxant (atracurium, cisatracurium, or mivacurium); or a second use of rocuronium [3]. Despite the continuing debate, it is still not clear which one is the best option [4,5]. When the option, after administering sugammadex (up to 4 mg kg⁻¹) is to use rocuronium the recommendations are as follows: 0.6 mg kg⁻¹ and 1.2 mg kg⁻¹, 4 hours and 5 min, respectively, after using sugammadex [6].

In our case, the subsequent dose of rocuronium 0.5 mg kg⁻¹ was given 20 min after a dose of sugammadex, and it produced an effect with a slower onset time (approximately 7 min) that would be expected under usual circumstances. Likewise, other authors reported cases where doses of rocuronium after sugammadex lower than the recommended ones produced slower NMB onset time. Fabregat-Lopez *et al.* reported a case where rocuronium-induced NMB (0.53 mg kg⁻¹) was achieved 143 min after sugammadex (4.2 mg kg⁻¹) had been given [4]. However, the effect produced was less intense (86% T1 block) and had a slower onset time than would normally be expected, upon which another 10 mg of rocuronium were added. On the other hand, Matsuki *et al.* reported a case where rocuronium 1 mg kg⁻¹ administered 19 min later after sugammadex 2.75 mg kg⁻¹, in a patient under sevoflurane anesthesia, was unable to induce muscular relaxation and an additional 30 mg were required [7].

Cammu *et al.* designed a study to evaluate the onset times and the clinical duration of NMB induced by 1.2 mg kg⁻¹ rocuronium administered at variable times after 4.0 mg kg⁻¹ sugammadex had been given. This study was performed in healthy volunteers under propofol anesthesia [8]. Rapid re-onset of NMB occurred after repeat dosing of rocuronium as early as 5 min after sugammadex. Therefore, it is possible to induce a complete NMB by increasing the second rocuronium dose even immediately after sugammadex administration. They found an inverse relationship between the onset time and the time interval between sugammadex and repeat dosing of rocuronium. Cammu *et al.* also observed that the shorter the interval between a sugammadex and rocuronium, the shorter would be the NMB duration [8]. This can be explained by the presence of significant amounts of free sugammadex that remains available to reverse the second dose of rocuronium.

The clinical duration (duration from the initial administration to spontaneous recovery to 25% of control twitch height) with 0.6 mg kg⁻¹ rocuronium bromide is 30 to 40 min [9]. In the presented case the clinical duration was within the range of what was expected for the repeat dosing of rocuronium (about 30 min), as were the observations of Matsuki *et al.* [7]. These authors reported the re-appearance of T1 64 min after re-administration of rocuronium 1 mg kg⁻¹ being administered 19 min later after sugammadex. They attributed the lack

of consistency of their observations with the results of Cammu *et al.* [8] to the anesthetic technique, namely the sevoflurane. Inhaled anesthetics enhance the neuromuscular blocking effects of nondepolarizing neuromuscular blockers. Sevoflurane may also have prolonged the duration of action of the second dose of rocuronium in our case.

Nonetheless, the onset time and duration of action of a second dose of rocuronium following the administration of sugammadex are unpredictable due to the dose of rocuronium, the previous dose of sugammadex and the duration of time between the administrations of these two drugs, among others [10]. This might indicate that in this setting depolarizing NMB agents and benzylisoquinoline muscle relaxants would be more appropriate choices. Bom *et al.* reported, in an animal study, a small delay in the onset time but a normal speed of recovery when succinylcholine was administered 3 minutes after reversing the rocuronium-induced NMB with sugammadex [11]. The same study reported a normal speed of onset and recovery when cis-atracurium was used instead of a depolarizing NMB agent, in the same circumstances. Unfortunately, studies involving the use of depolarizing and benzylisoquinoline neuromuscular blockers following the administration of sugammadex are limited and additional studies on the changes of the pharmacokinetics of these drugs are required.

If the option is to re-administer rocuronium the dose chosen should also have into account the patient and the clinical context in place. If the patient doesn't have a significant risk of regurgitation and the surgical procedure doesn't qualify as an emergent one, a smaller dose of rocuronium than the one recommended could be given at the time of the induction of anesthesia and if necessary adjusted posteriorly.

One of the clear indications for the use of muscle relaxants in anesthesia practice is to facilitate laryngoscopy and tracheal intubation, though this can be accomplished without NMB agents. Barclay *et al.* assessed three factors when evaluating conditions for tracheal intubation: ease of jaw opening and laryngoscopy, position of the vocal cords and their movement and degree of straining after tracheal intubation and cuff inflation [12]. Tracheal intubation was considered optimal when jaw opening and laryngoscopy was not difficult, vocal cords were not closed and if straining occurred after tracheal intubation and cuff inflation would not involve the abdominal muscles. In this case, optimal tracheal intubation conditions were considered to exist even though the TOF was about 0.6 since all of the requirements above were verified.

Conclusion

1) A short time of twenty minutes between use of sugammadex and rocuronium may not affect intubation conditions, with normal induction propofol doses.

2) Neuromuscular monitoring is, in every case, mandatory to adequately assess the NMB of the individual patient and doses of rocuronium and sugammadex should be tailored to the clinical context.

3) More studies to analyze the pharmacokinetic and pharmacodynamic profile of repeated administration of rocuronium and sugammadex are in need.

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