American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2022; 23: e937128
DOI: 10.12659/AJCR.937128

Received: 2022.05.03
Accepted: 2022.08.25
Available online: 2022.09.09
Published: 2022.10.14

Case Report: Successful Reversal of Residual Block with Sugammadex in a Patient Not Known to Have Myasthenia Gravis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Financial support: None declared
Conflict of interest: None declared

Patient: Female, 40-year-old
Final Diagnosis: Myasthenia gravis
Symptoms: Prolonged neuromuscular blockade • strabismus • weakness
Medication: —
Clinical Procedure: —
Specialty: Anesthesiology

Objective: Unusual clinical course

Background: Incomplete recovery from residual neuromuscular block agent (NMBA) after anesthesia is a serious adverse event in the post-anesthesia care unit. Acetylcholinesterase neostigmine is usually used to reverse residual neuromuscular blockade and facilitate spontaneous breathing and endotracheal extubation.

Case Report: A 40-year-old woman received general anesthesia for strabismus correction surgery. At the end of surgery, repeated doses of neostigmine up to 85 μg/kg failed to reverse the residual neuromuscular blockade (train-of-four [TOF] ratio below 21%). Sugammadex (200 mg) provided immediate reversal, with the TOF ratio up to 100%. The patient regained spontaneous breathing, and the endotracheal tube was removed. After surgery, myasthenia gravis was diagnosed.

Conclusions: When unexpected prolonged neuromuscular blockade presents, the TOF ratio should be used to detect its depth and guide a reasonable dose of reversal agents. Anticholinesterase has a ceiling effect; once acetylcholinesterase activity is fully inhibited, administration of additional anticholinesterase can result in no further recovery. Furthermore, excessive acetylcholine can cause muscle weakness. In contrast, sugammadex is a selective reversal agent for steroidal NMBA, which works by encapsulation via tight water-soluble complexes with amino steroids (eg, rocuronium) rather than increasing acetylcholine at the neuromuscular junction. In this case, the recovery from moderate neuromuscular blockade by sugammadex was more effective and rapid than that by neostigmine. When refractory and prolonged residual neuromuscular blockade presents after repeated doses of anticholinesterase, sugammadex should be considered as an effective reversal agent. Particularly in cases of myasthenia gravis, sugammadex is superior to neostigmine for reversing rocuronium-induced NMBA in patients undergoing surgery.

Keywords: Myasthenia Gravis • Neostigmine • Neuromuscular Monitoring • Postanesthesia Nursing • Sugammadex

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/937128

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Background

Incomplete recovery from neuromuscular block agents (NMBAs) after anesthesia is a major adverse effect in the post-anesthesia care unit (PACU) despite the routine use of anticholinesterase reversal agents. The incidence of muscle weakness is still significantly high in patients with train-of-four (TOF) <0.9. The use of anticholinesterases, via an indirect mechanism, to reverse residual neuromuscular block at the end of surgery has become a routine anesthesia practice. Although most patients do recover from NMBAs with the use of anticholinesterase reversal agents, the risk of increased residual block, recurarization, is still an issue in the PACU [1]. We report a case of delayed recovery from NMBAs after repeated anticholinesterase administration, and the complete recovery obtained immediately by sugammadex.

Case Report

A 40-year-old woman (height 160 cm; weight 70 kg; BMI 27.3 kg/m^2; American Society of Anesthesiologists physical status II) was scheduled for ambulatory strabismus surgery under the diagnosis of left eye exotropia. She had a history of hysterectomy years ago and otherwise denied having any systemic disease and taking routine medication. She had no known allergies to drugs or food. There were no specific findings in the routine preoperative examinations. The patient received a diagnosis of myasthenia gravis after surgery.

On arrival to the operating room, the patient's ECG and vital signs were normal, and her body temperature was 35.9°C. General anesthesia was induced with intravenous atropine 0.5 mg, lidocaine 50 mg, fentanyl 150 mcg, propofol 150 mg, and rocuronium 30 mg. The train-of-four (TOF) ratio showed 100% at the beginning of induction and a TOF of 1/4 before tracheal intubation. The maintenance of anesthesia was provided with 1 minimum alveolar concentration of sevoflurane. She had a normal core temperature at all times (35.7-35.9°C). The patient's hemodynamics were stable during the whole surgery.

The surgery took approximately 50 min. No extra NMBAs were given after anesthesia induction. We proceeded with the emergence of the patient at the end of the surgery. The patient recovered spontaneous respiration soon after we stopped sevoflurane, and neostigmine 3 mg plus glycopyrrolate 0.6 mg was given to reverse the residual neuromuscular blockade (**Table 1**). The tidal volume was persistently below 200 mL. At this time, the patient could only slightly move her limbs with muscle power of 2/4, but could not open her eyes. She was also aware and responded by nodding. Four TOF counts were presented, with a TOF ratio of 16%. After 15 min, following the first dose of neostigmine and glycopyrrolate, a second dose of neostigmine 2 mg and glycopyrrolate 0.4 mg was administered, still with only minimal response, with a TOF ratio of 25%. The third dose of neostigmine 1 mg and glycopyrrolate 0.2 mg made mild clinical improvement at 30 min after the first dose. Persistent no change on the neuromuscular monitor was observed, with a TOF ratio of 25%.

Table 1. The timeline of reverse agent administration in the emergence phase. Reverse agent dosage was 0.2 mg of glycopyrrolate for every 1 mg of neostigmine.

Timeline	Reversal agent (dose)	Train-of-four ratio
0 min	Neostigmine 3 mg	16%
15 min	Neostigmine 2 mg	25%
30 min	Neostigmine 1 mg	25%
40 min	Sugammadex 200 mg	105%

The emergence phase went for 40 min, and the patient showed no significant improvement in her muscle power. Owing to the prolonged residual neuromuscular blockade, sugammadex 200 mg (2.85 mg/kg) was administered as an additional reversal of neuromuscular block (**Table 1**). Fortunately, 5 minutes later, the TOF ratio increased to 100%, and the patient regained enough muscle strength to lift her hand for more than 5 s. The patient was then extubated and sent to PACU for further observation. She was kept for 2 h in the PACU, with stable vital signs and full recovery of her muscle strength. She was then discharged from the hospital, accompanied by family.

Discussion

When a patient emerges from general anesthesia, anticholinesterase inhibits the cholinesterase function to provide a sustainable acetylcholine level at the neuromuscular junction in order to compete with the nondepolarizing muscle relaxant with nicotinic acetylcholine receptors to reverse the residual neuromuscular blockade. Once acetylcholinesterase activity is fully inhibited, the administration of any additional anticholinesterase may have no further effect [2].

Moreover, an adverse effect of neostigmine and other anticholinesterase is paradoxical anticholinesterase-associated muscle weakness. A previous study showed that neostigmine can even induce muscle weakness when administered after a patient is fully recovered from the neuromuscular blockade. In healthy volunteers given rocuronium, the administration of neostigmine after the recovery of the TOF to 1.0 induced genioglossus muscle impairment and increased upper airway collapsibility [3].

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In contrast, sugammadex is a selective reversal agent for steroidal NMBAs and works by encapsulating the free molecule to form the sugammadex-rocuronium complex to remove the nondepolarizing muscle relaxant, particularly rocuronium, from the neuromuscular junction to reduce the nicotinic acetylcholine receptor occupancy. Following rocuronium-induced moderate and deep neuromuscular block, sugammadex can achieve rapid recovery in minutes [4]. On the contrary, anticholinesterases are ineffective in reversing profound and deep neuromuscular block. Sugammadex does not appear to produce adverse effects on upper airway tone or normal breathing when given after neuromuscular recovery [5].

In a study that defined residual neuromuscular blockade as a TOF ratio <0.9, the incidence of symptoms of muscle weakness was significantly higher in the TOF <0.9 group at all times (P<0.001). It is recognized that residual neuromuscular block is a risk factor for postoperative pulmonary complications [6,7]. The incidence of residual neuromuscular block in the recovery room is lower if sugammadex, rather than neostigmine, has been used [7,8].

When unexpected prolonged neuromuscular block is present, the TOF can be helpful to detect the depth of neuromuscular blockade and provide guidance of the dose of reversal agent. The recommended intravenous dose of neostigmine for reversal of neuromuscular blockade is 30 to 70 µg/kg, with a maximum total dose of 70 µg/kg [8]. In the present case, neostigmine, at a dose of 85 µg/kg, did not shorten the recovery but also showed no objective evidence in recovering muscle power.

Because sugammadex is a self-pay drug, it was not used as the first choice for the prolonged and delayed recovery of muscle power, and then myasthenia gravis. We think the direct rocuronium reversal agent may be used for bypassing the indirect preserving acetlycholine anticholinesterase inhibitor for competing with the acetylcholine receptor.

The recovery from moderate neuromuscular blockade was significant, on the contrary, as a rapid recovery of the patient's muscle power was obtained by sugammadex rather than by neostigmine. Although the TOF ratio was 25% before sugammadex administration, we decided to administer 1 vial of sugammadex 200 mg (2.85 mg/kg). In the dose-finding study of Kaufhold et al [9], the median time to restore neuromuscular transmission to a TOF ratio ≥0.9 after injection of study drug was 33 to 3.3 min with saline, 1.7 to 19 min with neostigmine (70 µg/kg), and 1.5 min with sugammadex (1.25 mg/kg). The authors concluded that residual neuromuscular blockade of a TOF ratio of 0.2 could not be reversed reliably with neostigmine within 10 min [9].

After carefully tracing back the daily activity of our patient, we determined that she did have signs of weakness and fatigue in the afternoon; at this point, myasthenia gravis was highly suspected. Myasthenia gravis can be generalized, or only involved in the extraocular muscles, designated as ocular myasthenia gravis. We informed the patient about the possibility of myasthenia gravis in follow-up, and myasthenia gravis was diagnosed soon after.

A patient with myasthenia has greater sensitivity to nondepolarizing neuromuscular blockade due to the reduced number of functional acetylcholine receptors. Patients with myasthenia gravis have an unpredictable response to the administration of NMBAs, and the use of anticholinesterases for reversal is usually not effective, especially for those patients who are taking anticholinesterase medication; excessive acetylcholine could result in paradoxical muscle weakness and potentiation of a myasthenic or cholinergic crisis [10]. Reversal with sugammadex has been reported to reverse neuromuscular blockade of rocuronium in patients with myasthenia via direct encapsulation of rocuronium, in a predictable, rapid, and safe way [11,12].

Myasthenia gravis may only affect the muscles of the eyes and eyelid movement; extraocular muscles are most commonly affected, as twitch fibers in extraocular muscles develop tension faster and have a higher frequency of synaptic firing than do limb muscles. Ocular myasthenia gravis should be suspected in any variable incomitant strabismus, with or without ptosis [13].

Conclusions

When a patient comes to neuromuscular block recovery and extubation, clinical evaluation is commonly used in anesthesia practice. Utilizing qualitative neuromuscular monitoring during the emergence phase to assess the depth of block can provide more precise guidance for management and reversal agent selection. Neostigmine is not always routinely given to reverse the residual neuromuscular blockade for all patients received NMBA. Quantitative monitoring, however, should be considered as a routine practice to determine the appropriate selection and administration of reversal agent. When a refractory and prolonged residual neuromuscular blockade is present, sugammadex should be considered as an alternative muscle relaxant reversal agent. In cases of myasthenia gravis, sugammadex is obviously superior to neostigmine for reversing rocuronium-induced neuromuscular blockade in patients with myasthenia gravis at the end of surgery.

A patient with myasthenia gravis can present with extraocular muscle involvement as the only manifestation of the disease. When patients undergoing strabismus correction present a

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prolonged residual neuromuscular blockade, myasthenia gravis should be considered in the differential diagnosis. In these cases, the recovery from moderate neuromuscular blockade by sugammadex was shown to be significantly more rapid and effective than classic indirect anticholinesterase neostigmine.

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Statement

The authors certify that they obtained all appropriate patient consent forms and the case report was also review and approved by our institution Review Board (CGH-P111020).

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