

Use of Sugammadex after Neostigmine Incomplete Reversal of Rocuronium-Induced Neuromuscular Blockade

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Summary: Menezes CC, Peceguini LAM, Silva ED, Simões CM – Use of Sugammadex after Neostigmine Incomplete Reversal of Rocuronium-Induced Neuromuscular Blockade.

Background and objectives: Neuromuscular blockers (NMB) have been used for more than half of a century in anesthesia and have always been a challenge for anesthesiologists. Until recently, the reversal of nondepolarizing neuromuscular blockers had only one option: the use of anticholinesterase agents. However, in some situations, such as deep neuromuscular blockade after high doses of relaxant, the use of anticholinesterase agents does not allow adequate reversal of neuromuscular blockade. Recently, sugammadex, a gamma-cyclodextrin, proved to be highly effective for reversal of NMB induced by steroidal agents.

Case report: A female patient who underwent an emergency exploratory laparotomy after rapid sequence intubation with rocuronium 1.2 mg.kg⁻¹. At the end of surgery, the patient received neostigmine reversal of NMB. However, neuromuscular junction monitoring did not show the expected recovery, presenting residual paralysis. Sugammadex 2 mg.kg⁻¹ was used and the patient had complete reversal of NMB in just 2 minutes time.

Conclusion: Adequate recovery of residual neuromuscular blockade is required for full control of the pharynx and respiratory functions in order to prevent complications. Adequate recovery can only be obtained by neuromuscular junction monitoring with TOF ratio greater than 0.9. Often, the reversal of NMB with anticholinesterase drugs may not be completely reversed. However, in the absence of objective monitoring this diagnosis is not possible. The case illustrates the diagnosis of residual NMB even after reversal with anticholinesterase agents, resolved with the administration of sugammadex, a safe alternative to reverse the NMB induced by steroidal non-depolarizing agents.

Keywords: Neuromuscular Blockade; Neostigmine; Postoperative Complications.

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INTRODUCTION

Neuromuscular blockers (NMB) have been used for more than half of a century in anesthesia, but always presenting a challenge for anesthesiologists. In 1954, a study by Beecher and Todd showed that in a universe of nearly 600,000 anesthetic procedures between 1948 and 1952, the use of muscle blocking increased by six times the risk of death during the perioperative period¹.

With the evolution of both neuromuscular blocking and neuromuscular junction monitoring, the management of muscle relaxation became safer and more efficient. However, recent studies show that residual neuromuscular blockade remains a reality today²⁻⁴.

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In clinical practice, we are often faced with situations that are beyond the normal pattern, such as the presence of residual neuromuscular blockade, even after reversal with anticholinesterase drug³. This case report illustrates a situation of residual neuromuscular blockade, even after reversal with anticholinesterase agents, which could be adequately managed with a new specific reversal agent, sugammadex.

CASE REPORT

Female patient, 65 years old, 55 kg, 1.57 m, with systemic hypertension. Hospitalized for three days due to an obstructive acute abdomen, secondary to sub-intestinal obstruction of unknown etiology, with progressive deterioration and requiring an exploratory laparotomy.

The patient was admitted to the operating room conscious and oriented, with significant abdominal distension, blood pressure 160 x 78 mm Hg, heart rate 94 bpm, SpO₂ = 94% on room air. We opted for general anesthesia with rapid sequence induction. After denitrogenation for 3 minutes, anesthesia was induced with sufentanil 0.3 µg.kg⁻¹, propofol 2.5 mg.kg⁻¹, and rocuronium 1.2 mg.kg⁻¹. Intubation was performed without complications. Anesthesia was maintained with propofol target-controlled infusion and remifentanil by continuous infusion.

The surgical procedure ended 90 minutes after induction of anesthesia. Neuromuscular junction monitoring was performed with train-of-four (TOF-GE Datex-Ohmeda) sequence, and only two responses were obtained. We administered neostigmine $50 \mu\text{g.kg}^{-1}$ and atropine $30 \mu\text{g.kg}^{-1}$, and about 3 minutes after, TOF was already at T4/T1 ratio of 0.3. After 45 minutes, there was no recovery of muscle activity ideal for a safe extubation (T4/T1 remained < 0.4). Then, sugammadex 2.0 mg.kg^{-1} was administered by iv bolus. After 2 minutes of administration, the ratio reached 0.9 and after three minutes, it was 0.95. The patient was extubated uneventfully and transferred to the anesthesia recovery unit where she remained for 2 hours with no sign of residual neuromuscular blockade.

DISCUSSION

Rocuronium is a steroidal non-depolarizing neuromuscular blocking agent of intermediate action. It is a safe alternative to succinylcholine for rapid sequence intubation⁵. With a dose of 1.2 mg.kg^{-1} , the pharmacodynamic profile of the drug is modified by reducing the onset of action ($55 \pm 14 \text{ sec}$), but extending its duration (average of 73 min, ranging from 38 to 150 min)⁶. This might be the main reason why TOF had only two responses 90 minutes after rocuronium administration. There are also reports in literature showing that, in elderly patients and female, the time of action of NMB may increase⁷.

Besides the previously mentioned factors, the surgical time was short. Therefore, we decided to reverse muscle blockade. Initially, we decided to use neostigmine with atropine at the usual dose ($40\text{-}70 \mu\text{g.kg}^{-1}$), which has onset within 1 minute, peak action in about 10 minutes, and 20 to 30 of duration⁷. In deep blocks, neostigmine (post-tetanic count [PTC] 1 to 2 responses) does not promote complete reversal of muscle blockade and may have some adverse effects, such as bradycardia, tachycardia, bronchoconstriction, dry mouth, nausea, and vomiting⁸⁻¹⁰. Moreover, the time to obtain a TOF stimulation ratio of 0.9 with its use may be greater¹¹.

Another relevant aspect in this case is the use of neuromuscular junction monitoring. Unfortunately, this practice is not common. In recent work, it was shown that approximately 20% of anesthesiologists in Europe and 10% in North America never used neuromuscular block monitors¹².

Residual neuromuscular block (RNMB) is defined as the presence of signs and symptoms of muscle weakness during postoperative period after NMB administration. Its incidence is quite variable in literature, considering the various factors that may affect the evaluation of residual block. A recent meta-analysis provides a little more precise idea on this issue¹³.

The authors analyzed 3,375 patients in 24 studies between 1979 and 2005. They found that NMB antagonists were used in 62.1% of patients and monitoring (qualitative and quantitative) in 24.4%. It was concluded that in cases where there was reversal of the blocking agent, the incidence of RNMB was 12% (TOF < 0.7) and 41% (TOF = 0.9). Furthermore, the influence of monitors on residual block reduction was not defined. We believe, however, that its use is of paramount importance for muscle blockade management, particularly to define whether there is need for reversal and if the patient is already in safe conditions for extubation.

Currently, there is a new option to antagonize the action of rocuronium¹⁴. Sugammadex is a modified gamma-cyclodextrin with a volume of distribution of 10 to 15 L, half-life of 2 hours, and low protein binding. It has a spatial conformation with a water-soluble outer portion and lipophilic central region, which encapsulates the rocuronium molecule by non-covalent bonding and forms a new molecular complex, which does not act on the neuromuscular junction¹⁵.

When administered, sugammadex binds at a 1:1 ratio to free steroidal NMB in plasma. Therefore, plasma concentration falls dramatically and shifts the neuromuscular junction blocking agent by the concentration gradient generated.

Sugammadex dosage varies according to the depth of muscle blockade. In moderate neuromuscular block (reappearance of T2), 2 mg.kg^{-1} is used. In deep block (1-2 PTCs), 4 mg.kg^{-1} is used. In case of immediate reversal (3 minutes after administration of 1.2 mg.kg^{-1}), 16 mg.kg^{-1} is used. Several studies have shown the efficacy and speed of rocuronium reversal.

The most common adverse reactions of sugammadex are post-surgical pain, nausea, vomiting, pyrexia, back pain, headache, sore throat, cough, and constipation¹⁶⁻¹⁷. The patient showed no such changes during anesthetic recovery.

CONCLUSION

Sugammadex has shown to be a safe drug, fast acting, and effective for reversal of neuromuscular block, avoiding the associated complications. It is therefore a new alternative for the reversal of muscular blockade induced by steroidal agents, more specifically for rocuronium. We emphasize that the diagnosis and appropriate treatment were only possible thanks to the use of neuromuscular junction monitoring, which allowed, with the use of sugammadex, a safe extubation.

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