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Case Report

Case of a Severe Sugammadex-Induced Bradycardia in the Young

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Abstract

Neuromuscular blocking agents (NMBAs) are a critical component of general anesthesia used to ease endotracheal intubation, mechanical ventilation, and surgical access.

Residual paralyzing effects are among the most dangerous occurrence in the post-operative wards, leading to dyspnea, acute respiratory insufficiency and death.

Sugammadex is the first selective reversal drug for steroidal NMBAs; it has been shown to give full and rapid recovery of muscle strength, thus minimizing the occurrence of residual curarization. Although rare, adverse drug reactions (ADRs) to Sugammadex have been documented, the most threatening being severe bradycardia and asystole, occurred almost exclusively in elderly patients. We present the case of a 23 y.o. trauma patient admitted to the hospital with a fracture of the middle third of the clavicle, that underwent surgery under general anesthesia. When Sugammadex was administered, the almost immediate drop in blood pressure and severe bradycardia seriously threatened the patient's life, but the ADRs were promptly treated and resolved with a bolus of Atropine.

In our opinion, all evidence points at Sugammadex as the most probable cause of the severe bradycardia and subsequent arterial pressure drop, events that could have been catastrophic, especially if they had occurred in an elderly end fragile patient. This highlights the necessity of increased pharmacovigilance and further studies to examine Sugammadex safety, and possibly demand an update in the Sugammadex data sheet regarding the speed of the drug's recommended administration.

INTRODUCTION

Neuromuscular blocking agents (NMBAs) are a critical component of general anesthesia used to ease endotracheal intubation, mechanical ventilation, and surgical access. However, it may lead to potential residual paralyzing effects in the postoperative period including the risk of postoperative respiratory complications. For this reason, neuromuscular monitoring in an intra-operative and post-operative setting is strongly advocated. Acetylcholinesterase inhibitors can reverse the muscle block, but their short half-life may lead to residual curarization in the ward, especially when intermediate or long-acting NMBAs have been administered. Sugammadex is the first selective reversal drug for steroidal NMBAs; it has been shown to give full and rapid recovery of muscle strength, thus minimizing the occurrence of residual curarization. Sugammadex is a compound derived from γ-cyclodextrin capable of nullifying the action of rocuronium and vecuronium, through a selective antagonism [1]. It forms a complex with the neuromuscular blocking agents rocuronium or vecuronium in plasma and thereby reduces the amount of NMBAs available to bind to nicotinic receptors in the neuromuscular junction. This results in the reversal of neuromuscular blockade. The use of Sugammadex has been increasing exponentially [2], mainly since it has been reported to be more effective and safer than other drugs, such as Neostigmine, with lower incidence of common adverse drug reactions (ADRs) such as postoperative nausea and vomiting, dry mouth, tachycardia, and dizziness. However rare, the incidence of serious adverse events such as bradycardia, hypotension and asystole are reported in literature, mainly regarding elderly patients.

CASE PRESENTATION

We present the case of a young male aged 23 years admitted to the hospital with a fracture of the middle third of the clavicle, occurred after being involved in a motorcycle accident, he was treated with surgery under general anesthesia His vitals, general physical evaluation, as well as systemic evaluation including preoperative electrocardiogram (ECG), chest X-ray and laboratory tests were normal. Medical history was unremarkable. The patient is a smoker with a 25-pack-year history, admits to recreational drug use including cocaine and marijuana and has a body mass index of 33,2 kg/m^2. The patient went into surgery

after premedication with 2 mg Midazolam intravenously (i.v.) and antibiotic prophylaxis with 2g of Cefazoline i.v. Since initial post-fracture pain may not respond to opioids, a clavipectoral fascial plane block was performed injecting 15ml of ropivacaine 0,375% into the fascia of the medial and lateral thirds, towards the clavicle fracture, providing intra-operative and post-operative analgesia.3 ECG, noninvasive blood pressure (NIBP), end-tidal carbon dioxide ($EtCO_2$) and oxygen saturation (SpO_2) were monitored throughout the surgery. The patient's initial vital signs were: NIBP 120/70 mmHg, SpO_2 98% and heart rate 85 beats/min. General anesthesia was induced with 140 mg Propofol and 50 mg Rocuronium and tracheal intubation was performed without accident 2 minutes after Rocuronium administration. General anesthesia was maintained with 2% (v/v) Sevoflurane and 0.3 mg Fentanyl. An additional 10 mg Rocuronium bolus was administered twice during surgery to maintain muscle relaxation, making the total amount of Rocuronium 70 mg, the intraoperative course was uneventful. After surgery ended, we measured the residual neuromuscular blockade with TOFcuff®, the Sevoflurane administration was stopped and a vial of 200 mg Sugammadex was administered to the patient; few seconds later the ECG showed severe bradycardia with the heart rate dropping below 40 beats/min and immediately after below 25beats/min, a severe systolic blood pressure drop occurred, with a registered NIBP below 50 mmHg. The bradycardia was promptly treated with 1,5 mg Atropine i.v., which restored the normal heart rate and, subsequently, the systolic blood pressure.

DISCUSSION

Given the scarce but reported cases in literature [4], the temporal relationship and biological plausibility, we suggest Sugammadex being the most probable cause of the peri-cardiac arrest, especially considering that no alternative causes that could have caused the ADR were detected [5,6]. The Sugammadex data sheet clearly states that some cases of marked bradycardia, most of them escalating to cardiac arrest, have been observed within minutes after the administration of Sugammadex. We feel confident in overruling the hypothesis of an anaphylaxis shock almost causing a cardiac arrest since our patient responded to a single dose of Atropine without a relapse in hemodynamic instability. For this reason, in our opinion, the ADR would most likely be the result of a direct cardiovascular effect rather than a secondary vasogenic shock caused by the anaphylaxis.

CONCLUSIONS

The molecular and physiological mechanisms involved in the adverse drug reaction are still to be identified, further research should be put in place to better understand its nature and origin. It would be interesting to define a degree of the patient's susceptibility to Sugammadex-induced bradycardia, in order to prevent such a dangerous event. Moreover, physicians should be advised to subminister Sugammadex slowly, rather than with a bolus, to minimize the occurrence of the abovementioned cardiac effect. In conclusion, although Sugammadex provides an important tool of prevention of postoperative residual neuromuscular blockade, anesthesiologists should keep in mind that it should be considered as a causative agent of cardiac arrest after administration, even at the lowest recommended doses. Furthermore, is essential to be aware that this occurrence is not only limited to elderly patients, but our experience shows that it can occur in young and otherwise healthy patients as well.

Above all, it should be imperative to always check the patience's residual curarization with devices such as TOFcuff, and only use Sugammadex when strictly necessary, in order to minimize ADR occurrence.

Reversal agents' administration need to be guided by monitoring and, most importantly, their use should not exempt from verifying the complete recovery of the neuromuscular block afterwards.

DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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