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CLINICAL INFORMATION

Severe bradycardia and asystole associated with sugammadex: case report



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KEYWORDS

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Abstract

Background and objectives: Sugammadex is a modified gamma-cyclodextrin, the first selective agent for reversal of neuromuscular blockade induced by steroidal non-depolarizing muscle relaxants, with greater affinity for rocuronium. In this article we present a case of severe bradycardia and asystole following sugammadex administration.

Case report: A 54-year-old male patient, ASA II, with a history of hypertension, dyslipidemia and obesity, who underwent an emergency umbilical herniorrhaphy under balanced general anesthesia. Intraoperative muscle relaxation was maintained with rocuronium. At the end of the surgery, the patient maintained a neuromuscular block with two TOF responses, and sugammadex (200 mg) was administered. About thirty seconds after its administration, the patient developed marked bradycardia (HR 30 bpm) followed by asystole.

Conclusions: Documented bradycardia and asystole were attributed to the administration of sugammadex. This case shows that, although rare, cardiac arrest is a possible adverse effect of this drug, and that the knowledge of this situation can be determinant for the patient's evolution.

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PALAVRAS-CHAVE

Sugammadex;
Bradicardia grave;
Assistolia

Bradicardia grave e assistolia associadas ao sugammadex: relato de caso

Resumo

Justificativa e objetivos: O sugammadex é uma gama ciclodextrina modificada, o primeiro agente seletivo para reversão do bloqueio neuromuscular induzido pelos relaxantes musculares não despolarizantes do tipo esteroide, com maior afinidade para o rocurônio. Neste artigo apresentamos um caso de bradicardia grave e assistolia após administração de sugammadex.

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Relato do caso: Doente do sexo masculino, 54 anos, ASA II, com antecedentes pessoais de hipertensão, dislipidemia e obesidade, submetido à herniorrafia umbilical em regime de urgência sob anestesia geral balanceada. O relaxamento muscular intraoperatório foi mantido com rocurônio. No fim da cirurgia o doente mantinha bloqueio neuromuscular com duas respostas no TOF, pelo que foi administrado sugammadex 200 mg. Cerca de trinta segundos após a sua administração, o doente desenvolveu bradicardia acentuada (FC 30 bpm) seguida de período de assistolia.

Conclusões: A bradicardia e a assistolia documentadas foram atribuídas à administração do sugammadex. Este caso evidencia que, apesar de rara, a parada cardíaca é um efeito adverso possível desse fármaco e que o conhecimento dessa situação pode ser determinante para a evolução do doente.

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Introduction

Sugammadex, a modified gamma-cyclodextrin, is the first selective agent for reversal of neuromuscular block (NMB), including deep NMB, induced by non-depolarizing steroidal muscle relaxants, with greater affinity for rocuronium. Through the plasmatic encapsulation of these muscle relaxants, sugammadex inhibits its binding to acetylcholine receptors at the neuromuscular junction, thus rapidly reversing NMB.

The reversal dosage depends on block depth. For moderate block: (two TOF responses) 2 mg.kg^{-1} ; for deep block: ($\geq 1-2$ post-tetanus counts) 4 mg.kg^{-1} ; and for immediate rescue reversal: 16 mg.kg^{-1} .

Sugammadex was first introduced on the market in 2008 in Europe.¹ It is a well-tolerated drug with a demonstrated efficacy and safety profile in several clinical trials,² with rare serious adverse cardiac events.

In this article we present a case of severe bradycardia and asystole after sugammadex administration.

Case report

Male patient, 54 years old (height 1.75 m, real weight 96 kg, BMI 31.3 kg.m^{-2} , adjusted weight 83 kg), physical status classified as ASA II, with diagnosis of imprisoned umbilical hernia, scheduled for emergency umbilical herniorrhaphy with a planned duration of 60 min. The patient had a personal history of controlled hypertension, dyslipidemia and obesity (BMI 31.3 kg.m^{-2}) treated as an outpatient basis with rosuvastatin 10 mg and valsartan 80 mg + hydrochlorothiazide 12.5 mg. No history of drug allergies, no changes in preoperative diagnostic exams and no predictability of difficult airway. The patient was transported to the operating room and standard ASA monitoring was initiated. Preoperative vital signs recorded: arterial blood pressure (BP) 157/93 mmHg; HR 60 bpm; SpO₂ 97%. Monitoring with bispectral index (BIS) was also performed with an anesthetic pre-induction value of 98.

A rapid sequence induction was intravenously performed with fentanyl 2 mcg.kg^{-1} , propofol 2 mg.kg^{-1} , and rocuronium 1.2 mg.kg^{-1} adjusted weight (100 mg), and the patient underwent orotracheal intubation uneventfully. Anesthetic maintenance was done with 6% desflurane, in a mixture of air and 45% O₂. Ventilatory parameters were adjusted to maintain normocapnia. Monitoring of neuromuscular blockade was maintained through acceleromyography (TOF-Watch® - SX). After anesthetic induction, cefazolin (2 g), parecoxib (40 mg), paracetamol (1 g), and metamizole (2 g) were administered. Vital signs remained stable during the procedure, which lasted less than expected (duration of surgery 25 min, duration of anesthesia 45 min). Throughout the procedure, the electrocardiographic tracing remained in sinus rhythm with narrow QRS complexes, with no apparent ST segment changes or other signs of myocardial ischemia. At the end of surgery, vital signs recorded BP 121/83 mmHg, HR 65 bpm, SpO₂ 95%, EtCO₂ 30 mmHg, and BIS 36 under 6% desflurane. Before initiating the anesthetic emergency, the patient showed two responses in TOF, sugammadex was given at a dose of 2 mg.kg^{-1} of weight⁻¹ for neuromuscular block reversal. No other drug was administered nor was there any cutaneous reaction, hypotension, allergy, or anaphylaxis after drug administration. About 30 s after this administration, the patient developed sudden severe bradycardia (FC 30 bpm), with no evidence on the electrocardiographic monitoring of blocked P waves and without enlargement of the QRS complexes. Significant bradycardia did not reverse with administration of atropine (1 mg) and progressed to asystole. Desflurane was discontinued, and switched to open system with 100% O₂. Advanced life support (ALS) maneuvers were started after asystole confirmation, with spontaneous recovery of the life signs after about 1 min. The maneuvers were suspended, and sinus heart rate was assessed with a heart rate of 63 bpm, carotid pulse was palpable and BP was 121/71 mmHg.

Anesthesia emergency progressed and when spontaneous ventilation was recovered, the patient was extubated and transferred to the Post-Anesthesia Recovery Unit, conscious, oriented, and cooperative where he remained in

surveillance until discharged to the ward. The patient was discharged from hospital 48 h after surgery with no intercurrents recorded during hospitalization.

Discussion

Sugammadex adverse effects are rare and the most commonly described are vomiting, xerostomia, tachycardia, dizziness, and hypotension.¹

Following the introduction of sugammadex on the market, reactions of anaphylaxis and anaphylactic shock with cardiovascular collapse were described, attributed in this context to hypersensitivity to the drug and not to adverse cardiac effects.³ In the present case, the absence of anaphylactic reaction (skin rash, urticaria, wheezing or increased airway pressure) at the time of the condition onset and the spontaneous reversal allowed us to exclude the hypothesis of anaphylactic shock.

Changes in cardiac conduction were also associated with sugammadex administration. Osaka et al. (2012) reported a case of Mobitz Type I atrioventricular block (AVB) after administering sugammadex in a 21-year-old patient with no associated disease undergoing cutaneous nevus resection.⁴

Saito et al. (2015) reported a case of transient grade 3 AVB after the administration of 200 mg of sugammadex in a 64-year-old patient undergoing abdominal surgery with no preoperative ECG changes or electrolytic disturbances.⁵ Unfortunately, in the present case, there is no electrocardiographic records of the intraoperative event, as the cardiac monitor used had no recording capacity. Therefore, it was not possible to identify accurately whether asystole was due to a change in the production of cardiac electrical impulses or to the anomaly of its conduction. However, the occurrence of rapidly progressive bradycardia evolving to asystole without blocked P waves or enlargement of QRS complexes suggests that the most likely explanation is the compromised genesis of electrical impulses with sinus arrest. It should be noted that the patient had no known history of sinus node dysfunction and was not previously medicated with drugs with negative chronotropic action and that none of the other drugs administered in the procedure had an inhibitory action on the sinus node. Importantly, the event occurred at a stage of the procedure in which there were no potentially stimulating maneuvers of vagal reflexes.

Bilgi et al. (2014) also reported a case of sinus dysfunction following the administration of sugammadex, with atropine-resistant bradycardia in a 56-year-old male undergoing ureterorenoscopy, without associated disease or history of toxicophilia, and without changes in preoperative assessment.⁶ Also, in this case the event occurred at a time when the patient maintained anesthetic depth compatible with general anesthesia and was not undergoing any anesthetic-surgical intervention that could be vagotonic.

More recently, Shin et al. (2017) reported a case of profound bradycardia and hypotension after administration of sugammadex, reversed with the administration of atropine (0.5 mg) in a 46-year-old patient who underwent subtotal gastrectomy due to stomach neoplasia, with no other associated disease except frequent atrial extrasystoles.⁷

King et al. (2017) reported a case of deep bradycardia immediately following the administration of sugammadex,

which reversed after a single dose of adrenaline ($2 \text{ mcg} \cdot \text{kg}^{-1}$) in a 10-year-old cardiac transplanted patient, with no history of bradycardia or arrhythmias undergoing cardiac catheterization and endomyocardial biopsy.⁸ In this case, the authors reported concomitant administration of dexmedetomidine, so they could not exclude that it had an influence on documented bradycardia. In our case, there was no temporal relation between the event and the administration of any other drug, so we assumed that it was unlikely that the medication previously administered interfered with the presented condition.

Cases of cardiac arrest related to sugammadex have been recently described in the context of coronary vasospasm. Hoshino et al. (2015) reported a case of repetitive cardiac arrest after sugammadex administration, attributed to the occurrence of coronary vasospasm.⁹

Ko et al. (2016) reported a case of dysrhythmia followed by repetitive cardiac arrest at the defibrillation rate 2 min after the administration of 130 mg of sugammadex in a 76-year-old patient with variant angina undergoing laparoscopic radical prostatectomy. The authors admitted coronary vasospasm and attributed hypomagnesemia and sugammadex as possible causes, suggesting this drug as the most probable cause given the moment of administration.¹⁰

In both cases, the authors excluded the hypothesis of anaphylaxis as the cause of vasospasm and consequent cardiac arrest.

In our case, there were no documented signs of ischemia or anaphylaxis, so we excluded these hypotheses as cause of the event, the temporal relationship between the administration of sugammadex and cardiac arrest prevailed.

Thiazide diuretics, such as hydrochlorothiazide, are an important cause of hypokalemia, which can lead to changes in cardiac conduction, arrhythmias, and cardiac arrest. In this case, the preoperative serum potassium level was $4.5 \text{ mmol} \cdot \text{L}^{-1}$. After the cardiac event, the ionogram remained unaltered, with a potassium value of $4.2 \text{ mmol} \cdot \text{L}^{-1}$ in arterial blood gases, and we excluded hypokalemia as the cause of cardiac arrest.

Conclusions

In recent years, sugammadex has been a frequent choice in anesthetic practice, and its use is presumed to continue to grow. This case shows that, although cardiac arrest is a possible adverse effect of sugammadex, patients should be closely monitored for hemodynamic changes during and after neuromuscular block reversal, and knowledge of this condition may be determinant for the evolution of the patient.

Conflicts of interest

The authors declare no conflicts of interest.

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