

SUGAMMADEX ASSOCIATED PERSISTENT BRADYCARDIA

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DOI: 10.5455/ijmsph.2013.251220131

Received Date: 28.11.2013

Accepted Date: 25.02.2014

ABSTRACT

Sugammadex is a safe selective relaxant binding agent, composed of modified cyclodextrin molecules. It especially has a selectivity for neuromuscular blocking agents (NMBAs) of steroid composition, such as rocuronium and vecuronium. In this paper, we present a case where intravenous (iv) sugammadex has been applied and subsequently persistent bradycardia has developed. A 56-year-old male patient (weight 77 kg, height 163 cm) was scheduled for ureterorenoscopy because of a stone in the upper part of ureter. Preoperative examination showed possible difficult intubation (mallampati 3). There are no known heart diseases and no history of any drug use. The electrocardiography was in normal sinus rhythm, and the blood biochemistry was normal. (WBC: 8.47 K/mm³; Hb: 14.3 g/dL; Na: 135 mEq/L; K: 3.9 mEq/L; BUN: 41 mg/dL; Creatin: 0.69 mg/dL). When the operation ended, we monitored neuromuscular block level with a neuromuscular monitoring device (TOF- Watch S). At the end of the operation, 200 mg sugammadex (Bridion 200 mg/2 mL, MSD) was administered to the patient through iv injection. Approximately 2 minutes following the administration, the patient developed sinusoidal bradycardia (pulse 35 beats/min). We believe that cardiac side effects may be observed following sugammadex administration and that atropine-resistant bradycardia may also develop.

Key Words: Sugammadex; Bradycardia; Case Report

Introduction

Sugammadex is a safe selective relaxant binding agent, composed of modified cyclodextrin molecules.^[1,2] It especially has a selectivity for neuromuscular blocking agents (NMBAs) of steroid composition, such as rocuronium and vecuronium.^[1] Serious side effects, such as anaphylactic shock and atrial fibrillation, of sugammadex, which appears to be an almost ideal reversal agent have been reported in the literature.^[3-5] However, we have not encountered any documented side effects of sugammadex associated with bradycardia. In this paper, we present a case where intravenous (IV) sugammadex has been applied and subsequently persistent bradycardia has developed.

Case Report

A 56-year-old male patient (weight 77 kg, height 163 cm, ASA II) was scheduled for ureterorenoscopy because of a stone in the upper part of ureter. Preoperative examination showed possible difficult intubation (mallampati 3). There are no known heart diseases and no history of any drug use. The preoperative examination of a 56-year-old male patient, 163 cm tall, and weighing 77 kg, on whom an ureterorenoscopy operation was planned for a stone above the ureter, was assessed as normal. The electrocardiography was in normal sinus rhythm, and the blood biochemistry was normal (WBC: 8.47 K/mm³; Hb: 14.3 g/dL; Na: 135 mEq/L; K: 3.9 mEq/L; BUN: 41 mg/dL; Creatin: 0.69 mg/dL). The patient was taken to the operating room, and standard monitoring [heart rate (HR);

peripheral oxygen saturation (SpO₂); non-invasive blood pressure (NIBP)] was made. Preoperative hemodynamic values; TA: 128/ 86 mmHg, HR: 83 beat/dk, SPO₂: 97%. During anaesthesia induction, propofol at 2 mgkg⁻¹, rocuronium at 0.6 mgkg⁻¹, and fentanyl at 1 mcgkg⁻¹ were administered through IV injection. After adequate muscle relaxation had been achieved, endotracheal intubation was applied. Anaesthesia was continued with 2% sevoflurane in a 50% air/O₂ combination at a rate of 3 L /min. The respiration frequency was regulated so that the patient's respiration end tidal CO₂ was between 34 and 38 mmHg. The vital findings remained stable throughout the operation, which was completed in approximately 30 minutes, which was less than the estimated time. When the operation ended, we monitored neuromuscular block level with a neuromuscular monitoring device (TOF- Watch S). At the end of the operation, 200 mg sugammadex (Bridion 200 mg/2 mL, MSD) was administered to the patient through iv injection. Approximately 2 minutes following the administration, the patient developed sinusoidal bradycardia (pulse 35 beats/min). The measurements of the patient observed at that time were: TA 124/81 mmHg, SpO₂ 99%, airway pressure 20 cmH₂O, and end tidal CO₂ 42 mmHg. The patient was quickly given 0.5 mg IV. Atropine, and the HR increased to 55 beats/min, then decreased to 30–35 beats/min again; atropine administration was continued. At the end of approximately 3 minutes, the total dose of the continued atropine reached 2 mg. The patient's bradycardia had recovered (HR 63 beats/min), and when the adequate spontaneous

respiration was reached the patient was extubated and moved to the postoperative care unit. When the vital findings of the patient remained stable for 1 hour, the patient was discharged to the service.

Discussion

Since 1950, acetylcholinesterase inhibitors have been used to reverse the effects of NMBAs. Acetylcholinesterase inhibitors, however, have been reported to have undesired effects, such as bradycardia, bronchospasm, hypersalivation, residual curarization, and extension of the block when used in overdose.^[6] In recent years sugammadex, which is a selective relaxant binding agent and has been frequently used in reversing the block caused by non-depolarizing neuromuscular blocking agents. It has been successfully used in reversing steroid agents, primarily rocuronium.^[7] Also we used rocuronium bromure as a neuromuscular blocker agent. Sugammadex, contrary to anticholinesterases, has been noted as not influencing cholinergic conduction nor having muscarinic side effects.^[8] In a study of thirty patients, five different doses of sugammadex (0.5, 1, 2, 4, 6 mg/ kg) following rocuronium had a side effect ratio of 17%.^[9] These side effects were: dry mouth, nausea, vomiting, pyrexia, rigors, agitation polyuria, urinary retention, dyspnoea, and respiratory failure. In our case we did not observe any kind of side effect rather than bradycardia. Persistent bradycardia was not observed among these side effects; however, atrial fibrillation (at a dose of 0.5 mg/kg) was observed in one patient and was attributed to a probable sugammadex association.^[9]

Osaka et al.^[5] reported that a Wenckebach-type atrioventricular block developed in a 21-year-old female patient who underwent an operation for nevus pigmentosus on the face and arm, and that this was induced by sugammadex. In this case, the preoperative anaesthesia examination was normal, 200 mg sugammadex was applied prior to tracheal extubation, and the Wenckebach-type atrioventricular block was observed.^[5] As mentioned in our case, the author did not define a relationship between sugammadex and the cardiac side effect. But, it was argued that sugammadex caused atrioventricular block due to the absence of another possible reason. Also there are other side effects another from cardiac origin (bradycardia, arrhythmia, hypotension, QT dispersion) attributable to sugammadex without possible explanations such as nausea, vomiting, pyrexia, rigors, urinary retention, dyspnoea, and respiratory failure. The heart rhythm of the patient, without any intervention, returned to normal within a short time. In our case, the 200 mg sugammadex that was

applied prior to tracheal extubation led to bradycardia without any obvious arrhythmia, such as atrial fibrillation or atrioventricular block. Although the rhythm rate returned to normal within a short time with atropine administrations, a persistent drop was observed.

We have not encountered any published reports on atropine-resistant bradycardia following sugammadex administration. Different doses of sugammadex (4 mg/kg or 32 mg/kg) were used individually or together with rocuronium and did not influence the corrected QT interval in the ECG, although palpitation and ventricular tachycardia developed at a sugammadex dose of 32 mg/kg.^[2] In another study, Kokki et al.^[10] reported a serious hypotension case following the use of sugammadex. Within 10 minutes after administering 50 mg of sugammadex to the patient, whose intraoperative arterial blood pressure remained normal, the patient had a TA of 50/30 mmHg.^[10] In this case, hypotension was not observed during intra and postoperative period.

There are studies available in the literature, report that sugammadex applications in different doses prolong the QT interval.^[11,12] Pühringer FK et al. reported asystole after the sugammadex (4 mg/kg) in their phase 2 multicentre study, conducted on 176 patients. In one of those patients, during endoscopic sinus surgery to reverse the effect of rocuronium; Sugammadex 4 mg / kg was given and after that, atropine responsive asystole had been observed. That patient had got no electrocardiographic abnormality before the operation. The authors have stated that, the condition could be related with trigeminocardiac reflex.^[12] Groudine SB et al. reported mild bradycardia 2 min after the administration of 8.0 mg/kg sugammadex. The Patient's heart rate has declined from 62 to 42 beat/dk. That have been treated with 0.4 mg of glycopyrrolate. Heart rate had increased to 65 bpm after glycopyrrolate.^[13] In our case, heart rate fell from 82 to 35 beat/dk. Heart rate reached of 63 beat/min with 2 mg. Atropine.

In our case, sugammadex caused bradycardia is quite difficult to prove and explain the mechanism. However; patient did not have any heart disease, no drug use and blood biochemistry was normal. Bradycardia right after the sugammadex application is attributed to the sugammadex, because any other possible reasons are eliminated.

Conclusion

In conclusion, it was reported that, mild bradycardia, QT dispersion and arrhythmia were defined after the use of

sugammadex. However, it should be kept in mind, atropine resistant bradycardia can also develop after the use of sugammadex.

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Cite this article as: Bilgi M, Demirhan A, Akkaya A, Tekelioglu UY, Kocoglu H. Sugammadex associated persistent bradycardia. *Int J Med Sci Public Health* 2014;3:372-374.

Source of Support: Nil

Conflict of interest: None declared