

CASE REPORT

A case where rocuronium was unable to achieve neuromuscular block immediately after sugammadex administration

Yoko Sakai, Yasuo M. Tsutsumi, Narutomo Wakamatsu, Tomohiro Soga, Katsuya Tanaka, and Shuzo Oshita

Department of Anesthesiology, Institute of Health Biosciences, the University of Tokushima Graduate School, Tokushima, Japan

Abstract : We present a case where immediate muscle relaxation was needed following sugammadex administration. A 72 year-old female underwent surgery for a cerebral artery aneurysm. Upon conclusion of the operation sugammadex (9.3 mg/kg) was administered and the patient was noted to have left hemiplegia. Rocuronium (1.2 mg/kg \times 2 doses) was given in order to gain neuromuscular block approximately 25 minutes after sugammadex had been injected. Although TOF monitoring was not utilized in this case and assessing residual muscular block was difficult, spontaneous respirations continued and breathing had to be controlled with sevoflurane and remifentanyl. Sugammadex is a potent reversal agent for rocuronium-induced neuromuscular block, however, certain situations require immediate neuromuscular blockade following sugammadex. In this case, rocuronium was unable to induce neuromuscular blockade immediately after sugammadex and that higher concentrations were necessary in addition to intravenous analgesics and inhaled anesthetics. *J. Med. Invest.* 58 : 163-165, February, 2011

Keywords : *sugammadex, rocuronium, reoperation,*

INTRODUCTION

Sugammadex is a modified γ -cyclodextrin and is a selective relaxant binding agent, which was specifically developed as a reversal agent for aminosteroid neuromuscular agents (1). Sugammadex has been shown to provide rapid and dose-dependent reversal of profound neuromuscular blockade induced by high-dose rocuronium (1.0-1.2 mg/kg) in adult surgical patients (2). Re-administration of rocuronium is not recommended soon after sugammadex administration. However, certain situations

may require immediate induction of neuromuscular blockade following sugammadex. We present a case where rocuronium was unable to induce complete muscle relaxation and spontaneous breathing was controlled by volatile and intravenous anesthesia.

CASE PRESENTATION

The patient was a 72-year old female, 150 cm, 43 kg, and American Society of Anesthesiologists Physical Status II due to hypertension. The patient underwent surgery for a right cerebral artery aneurysm and was monitored with an ECG, pulse oximetry, heart rate, mean arterial pressure, and body temperature. Remifentanyl (0.1 μ g/kg/min), propofol (50 mg), and rocuronium (50 mg) were used

Received for publication December 17, 2010 ; accepted January 12, 2011.

Address correspondence and reprint requests to Yasuo M. Tsutsumi, Department of Anesthesiology, Institute of Health Biosciences, the University of Tokushima Graduate School, Kuramoto-cho, Tokushima 770-8503, Japan and Fax : +81-88-633-7182.

for induction of anesthesia.

Anesthesia was maintained by remifentanyl (0.2-0.5 µg/kg/min), sevoflurane (1%), and rocuronium (10 mg i.v. every 90 minutes). Total operation time was 230 minutes.

After the operation, sugammadex (400 mg) was injected and spontaneous breathing returned immediately. The patient became conscious, alert, and orientated but was unable to move her left side. Approximately 25 minutes after sugammadex administration, immediate exploration of the surgical site was decided. The patient was immediately hyperventilated to eliminate spontaneous breathing, however, this was unsuccessful. As a result, the patient was then administered rocuronium (50 mg). The patient continued to have spontaneous respiration and a repeat dose of rocuronium (50 mg) was injected and sevoflurane (2%) and remifentanyl (0.5 µg/kg/min) were maintained to control breathing. The total operation time for the second procedure was 117 minutes and sugammadex (400 mg) was administered at the conclusion of the surgery. The patient again became conscious, alert, and orientated without any palsy or hemiplegia and was extubated.

The patient's remaining hospital course was uneventful and the patient was discharged.

DISCUSSION

Sugammadex has revolutionized post-operative care as it is able to reverse neuromuscular blockade safely, rapidly, and efficiently. Investigators have shown that 4.0 mg/kg dosing of sugammadex is able to work in a dose-dependent manner and that rocuronium (1.2 mg/kg) can be effectively reversed in under 20 minutes (3). However, increasing the dose of sugammadex can effectively decrease the reversal time and hasten recover to less than 2 minutes (3). In this patient, by utilizing a high dose of sugammadex the patient was able to quick recover from deep neuromuscular block, therefore, quickly identifying and addressing subsequent hemiplegia. However, certain situations such as in this case, immediate muscular relaxation may be necessary following sugammadex administration. We show that normal doses of rocuronium were unable to induce muscular relaxation and that a second dose plus sevoflurane and remifentanyl were required in order to obtain suppression of spontaneous respiration.

Previous studies have shown that terminal elimination half-life of sugammadex is around 120 minutes (4) and that sugammadex requires nearly 24 hours to be excreted (5). Although an exact time has not been established, it is expected that immediately after sugammadex there may be a lag time before rocuronium can be administered again. However, in cases where neuromuscular blockade is necessary immediately after sugammadex administration, other neuromuscular blocking agents, inhaled anesthetics and/or opioids can be utilized to control respiration.

Theoretical calculations of the dose of rocuronium required to provide adequate neuromuscular block immediately after sugammadex (8 mg/kg) is estimated at 2.25 mg/kg (6) and is affected by the duration between the second rocuronium dose and sugammadex (7). Furthermore, rocuronium (1.2 mg/kg) was able to induce neuromuscular blockade in healthy patients following sugammadex (4 mg/kg), although, onset of blockade was slower if rocuronium was injected <25 minutes after sugammadex (8). The patient in this case originally received rocuronium (1.2 mg/kg) on induction and then received 10 mg every 90 minutes to maintain blockade. Sugammadex (9.3 mg/kg) was administered at the conclusion of the procedure and the patient was then administered rocuronium (1.2 mg/kg × 2 doses) approximately 25 minutes later. By utilizing the pharmacokinetic data for sugammadex, the dosage of rocuronium should have been sufficient to reverse sugammadex, however, it is difficult to predict the rate at which rocuronium was degrading in this patient. As a result, unbound sugammadex was likely able to inhibit the additional rocuronium and prevent neuromuscular blockade. In this case, train of four (TOF) monitoring was not used. TOF monitoring would have assessed neuromuscular block.

The concentration of rocuronium and the duration between the second rocuronium dose and sugammadex are the major factors in achieving adequate neuromuscular block. Animal studies have shown that non-steroidal agents such as suxamethonium or cistracurium given immediately after the use of sugammadex can produce variable degrees of neuromuscular block (9). Suxamethonium is unaffected by sugammadex and therefore would be an appropriate drug when muscle relaxation is required (9,10). However, the required dosage of suxamethonium is not currently known after sugammadex. Other muscle relaxants like mivacrium and

atracurium are also non-steroidal but are currently not available in Japan.

In conclusion, when immediate surgery is necessary following sugammadex administration, higher doses of rocuronium are necessary in order to induce neuromuscular blockade. Also, it is important to use the smallest possible dose of sugammadex to avoid difficult situation such a re-intubation or re-surgery. Options might be limited when high dose of sugammadex is administered. As in this case, deep anesthesia via intravenous analgesics and inhaled anesthetics can be utilized, but hypotension and bradycardia must be monitored closely.

REFERENCES

1. Mirakhur RK : Sugammadex in clinical practice. *Anaesthesia* 64 : 45-54, 2009
2. Pühringer FK, Rex C, Sielenkämper AW, Claudius C, Larsen PB, Prins ME, Eikermann M, Khuenl-Brady KS : Reversal of profound, high-dose rocuronium-induced neuromuscular blockade by sugammadex at two different time points : an international, multicenter, randomized, dose-finding, safety assessor-blinded, phase II trial. *Anesthesiology* 109 : 188-197, 2008
3. de Boer HD, Driessen JJ, Marcus MAE, Kerckamp H, Heeringa M, Klimek M : Reversal of rocuronium-induced (1.2 mg/kg) profound neuromuscular block by sugammadex. *Anesthesiology* 107 : 239-244, 2007
4. Gijzenbergh F, Ramael S, Houwing N, van Iersel T : First human exposure of Org 25969 : a novel agent to reverse the action of rocuronium bromide. *Anesthesiology* 103 : 695-703, 2005
5. Sorgenfrei IF, Norrild K, Larsen PB, Stensballe J, Ostergaard D, Prins ME, Viby-Mogenson J : Reversal of rocuronium-induced neuromuscular block by the selective relaxant binding agent sugammadex : a dose-finding and safety study. *Anesthesiology* 104 : 667-674, 2006
6. de Boer HD, Driessen JJ, van Egmond J, Booi LH : Non-steroidal neuromuscular blocking agents to re-establish paralysis after reversal of rocuronium-induced neuromuscular block with sugammadex. *Can J Anaesth* 55 : 124-125, 2008
7. Ploeger BA, Smeets J, Strougo A, Drenth HJ, Ruigt G, Houwing N, Danhof M : Pharmacokinetic-pharmacodynamic model for the reversal of neuromuscular blockade by sugammadex. *Anesthesiology* 110 : 95-105, 2009
8. Cammu G, de Kam PJ, van den Heuvel M, Suy K, Morias K, Foubert L, Grobara P, Peeters P : Repeat dosing of rocuronium 1.2 mg kg⁻¹ after reversal of neuromuscular block by sugammadex 4.0 mg kg⁻¹ in anaesthetized healthy volunteers : a modelling-based pilot study. *Br J Anaesth* 105 : 487-492, 2010
9. Bom A, Hope F : Neuromuscular block induced by rocuronium and reversed by the encapsulating agent Org25969 can be re-established using the non-steroidal neuromuscular blockers succinylcholine and cis-atracurium. *Eur J Anaesthesiol* 22 (Suppl 34) : 120, 2005
10. Caldwell JE, Miller RD : Clinical implications of sugammadex. *Anaesthesia* 64 (Suppl 1) : 66-72, 2009