Case report

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Sugammadex in patients with chronic renal failure: two case reports

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Abstract

Rocuronium is a non-depolarizing aminosteroidal neuromuscular blocking agent that is widely used in general anesthesia. Its effects may be prolonged in patients with renal disease, especially renal failure, due to reduced clearance of the drug. Sugammadex, a modified γ-cyclodextrin, is known to be a highly effective reversal agent for rocuronium-induced muscle relaxation. However, the administration of sugammadex for reversal of rocuronium-induced neuromuscular block in patients with renal disease is controversial. Recently, we administered rocuronium for neuromuscular blockade during the surgery of two patients with chronic renal failure, instead of cisatracurium, a benzylisoquinoline compound. Therefore, we had to administer sugammadex to ensure maximum alleviation of residual neuromuscular blockade risk after surgery. Although the effect of rocuronium was prolonged during surgery, sugammadex quickly and completely restored the response of train-of-four stimulation postoperatively. There were no residual neuromuscular block signs or symptoms observed in these patients throughout the postoperative period. In this report, we share our experience with these cases, and discuss the effectiveness and safety of sugammadex in the context of chronic renal failure.

Keywords: Neuromuscular blockade; Neuromuscular monitoring; Renal failure; Residual neuromuscular blockade; Rocuronium; Sugammadex

Introduction

Since the number of patients with renal failure has steadily increased over the last decade, the response of these patients to neuromuscular blocking drugs remains an important concern in the field of anesthesiology (1). In these patients, the effect of neuromuscular blocking drugs is usually prolonged, and can be very harmful. Prolonged or residual neuromuscular blockade (NMB) can cause respiratory dysfunction and delayed recovery after surgery, potentially leading to severe complications such as desaturation or respiratory failure.

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There are numerous reports on the prolonged effect of rocuronium in renal failure patients. The NMB effect of rocuronium 0.6 mg/kg under propofol anesthesia was reported to be markedly prolonged in young and elderly renal failure patients compared with patients with normal renal function (2). In addition, the pharmacokinetics of rocuronium has been shown to be impaired and the duration of action (of a 0.6 mg/kg dose) increased under propofol anesthesia in renal failure patients (3). Therefore, in patients with renal failure, it is critical to ensure complete NMB reversal without prolonged or residual NMB. Sugammadex, a modified γ-cyclodextrin, quickly and completely reverses NMB by forming very tight water-soluble complexes with steroidal neuromuscular blocking drugs, in particular rocuronium and vecuronium. Although some studies have reported that sugammadex effectively and safely reverses rocuronium-induced moderate (4) or deep NMB (5,6), the use of sugammadex for rocuronium-induced NMB reversal in patients with renal disease is controversial.

Recently, we administered rocuronium for NMB during the surgery of two patients with chronic renal failure. In this report, we aim to discuss the effectiveness and safety of sugammadex in the context of chronic renal failure through these cases.

Case report

We obtained written informed consent from the patients to publish this report.

Case 1

A 59-year-old woman (height 156 cm, weight 72 kg) was admitted for total laparoscopic hysterectomy. The patient had a medical history of hypertension and chronic renal failure, and had been receiving continuous ambulatory peritoneal dialysis for 15 years. Peritoneal dialysis was planned to switch to hemodialysis therapy in the postoperative period. At preoperative evaluation, her serum creatinine level was 9.6 mg/dl and creatinine clearance was 4.5 ml/min.

Anesthesia was induced with propofol 120 mg and then an anesthesiologist, who has been accustomed to using rocuronium in ordinary anesthesia practices, habitually administered rocuronium 50 mg, instead of cisatracurium, to facilitate tracheal intubation. Anesthesia was adjusted with desflurane 3–5 vol% and 50% nitrous oxide in oxygen to maintain bispectral index (BIS) values of 40–60. Fifty-five minutes after anesthesia induction, another anesthesiologist realized that rocuronium had been administered to the patient and could potentially prolong the duration of NMB. Therefore, we immediately attempted to reverse rocuronium-induced NMB using sugammadex to minimize residual NMB. We applied train-of-four (TOF) stimulation monitoring using acceleromyography (TOF-Watch SX®, Organon Ltd., Dublin, Ireland) in the adductor pollicis muscle. At the start of TOF monitoring, the TOF count was 0, and 15 min after initiating TOF monitoring (70 min after anesthesia induction) it was 1. Seventy-two minutes after anesthesia induction the TOF count was 2, and rocuronium 5 mg was additionally administered to relax abdominal muscles, at the surgeon's request. The TOF count remained at 1 for 24 min after the first additional dose. Since the TOF count recovered to 4, after approximately 30 min from the first additional dose, a second rocuronium 10 mg dose was administered. The TOF count remained at 1 until the peritoneum was closed. Following surgical completion, 150 min after anesthesia induction, the TOF count was 2, indicating moderate NMB (7). Therefore, sugammadex 140 mg (2 mg/kg) was administered according to the dosage guidelines for moderate NMB (4) and, simultaneously, administration of all anesthetics was stopped. The TOF count was 4

after 30 sec from sugammadex administration, and self-respiration recovered after 50 sec. The TOF ratio reached 90% after 1 min and 15 sec, BIS was 80 after 3 min and 36 sec, and the patient was extubated after 7 min and 10 sec. To assess quality of recovery from NMB upon arrival in the recovery room, we measured 15 signs and symptoms of muscle weakness: general weakness; eye opening, hand grip, protrude tongue and head lift during 5 sec; track object eyes; double and blurry vision; ability to speak, smile, swallow, cough, and breathe deeply; and facial weakness and numbness (8). The patient had no symptoms of residual NMB except mild general weakness, and fully performed in all tests except the ability to cough (mild limitation). The patient completely satisfied every category of the tests performed at 1, 6, and 24 h postoperatively, and underwent hemodialysis within 24 h postoperatively. No significant adverse events were observed during a 7-day postoperative period when the patient was discharged.

Case 2

A 58-year-old woman (height 153 cm, weight 40 kg) was scheduled to undergo hip fracture surgery. She required careful preoperative evaluation due to underlying diseases. She had been suffering from hypertension and chronic renal failure for 25 years and bronchiectasis for 16 years. She was a hepatitis B carrier; however, her liver function was within the normal range. The patient had been receiving hemodialysis for 24 years; her serum creatinine level was 5.9 mg/dl and creatinine clearance was 7.1 ml/min. Her pulmonary function test showed a forced expiratory volume in 1 second (FEV1) of 1.04 L (44%), a forced vital capacity (FVC) of 1.35 L (47%), and the FEV1/FVC ratio of 77%; indicating moderate obstruction pattern.

Considering the estimated surgical time of > 2 hours, we decided to perform general anesthesia. Additionally, considering the patient's pulmonary condition, even a small quantity of residual NMB could have led to severe complications. Therefore, we planned to use rocuronium combined with sugammadex to minimize residual NMB. Before anesthesia induction, TOF stimulation monitoring (TOF-Watch SX®) was applied. Anesthesia was induced with propofol 80 mg and rocuronium 30 mg, and was maintained with desflurane 4–5 vol%, remifentanil 0.02–0.05 μg/kg/min, and 50% air in oxygen. The surgery lasted for 150 min and additional muscle relaxants were not required. The TOF count was 1 after 50 min from rocuronium administration and increased to 3 postoperatively. Therefore, sugammadex 80 mg (2 mg/kg) was administered and the TOF count reached 4 (TOF ratio 81%) after 50 sec. Since the patient moved uncontrollably, TOF monitoring was no longer possible and the patient was then extubated.

In the recovery room, 15 signs and symptoms of muscle weakness were measured in the same manner as in Case 1. The patient showed minimal general weakness and mild limitation in the ability to cough, that fully recovered in 3 min. These tests were repeatedly checked 1, 6, and 24 h postoperatively, and all results indicated normal muscle function without any complications. The patient underwent hemodialysis within 24 h postoperatively, and was discharged after 3 weeks without any adverse events.

Discussion

The NMB effect of rocuronium may be prolonged in patients with renal failure due to reduced clearance (9). Clearance of rocuronium can be reduced by 39% in end-stage renal disease patients compared with healthy patients (3). Morales Martín et al. (10) presented a case of extremely prolonged NMB following a 0.9 mg/kg dose of rocuronium in a woman undergoing allogenic kidney transplantation. Kim et al. (11) also reported a

markedly prolonged neuromuscular effect of 0.6 mg/kg rocuronium under desflurane anesthesia in patients with renal failure compared with patients with normal renal function. The 25%, 75%, and 95% twitch recovery times, recovery of TOF ratio to 70% (TOF 70), and the recovery index were prolonged in patients with renal failure compared with those with normal renal function (e.g., TOF 70: 123.1 ± 49.1 min vs. 68.7 ± 15.5 min, respectively). Similarly, in Case 2 of the present report, the NMB effect of initially administered rocuronium was markedly prolonged; TOF monitoring failed to reach even TOF count 4. When considering the prolonged NMB effect of rocuronium in renal failure patients, it is difficult to establish which of the following two NMB strategies is most appropriate: cisatracurium combined with anticholinesterase or rocuronium combined with sugammadex.

Previously, before the development of sugammadex, muscle relaxants, such as atracurium or cisatracurium that are not metabolically affected by renal function, were recommended for patients with end-stage renal disease in order to prevent prolonged NMB. Currently, in many countries, sugammadex is recommended for use in the reversal of rocuronium- or vecuronium-induced moderate or deep NMB in adult (including elderly) patients. In relatively healthy patients, sugammadex provides rapid reversal of rocuronium- or vecuronium-induced NMB and is generally well tolerated (12). However, since sugammadex and the sugammadex-rocuronium complex are cleared renally, clearance may be delayed in cases of chronic renal failure.

Lobaz et al. (13) demonstrated that sugammadex rapidly reversed persistent rocuronium NMB with recurarization in a patient with severe renal failure without adverse sequela. Some clinical trials have also reported that sugammadex effectively and safely reverses rocuronium-induced moderate (4) or deep NMB (5,6). Staals et al. (4) investigated the efficacy and safety of sugammadex for reversal of rocuronium-induced NMB in patients with end-stage renal failure (creatinine clearance < 30 ml/min) and normal renal function (creatinine clearance > 80 ml/min). They found that sugammadex 2 mg/kg administered at the state of moderate NMB rapidly and effectively reversed NMB induced by rocuronium in renal failure and healthy patients; mean (standard deviation) time to recovery of the TOF ratio to 0.9 was 2.0 (0.72) min in renal patients. This is comparable to the present cases.

We aimed to investigate whether recurarization occurred during the postoperative 24 h at least, by checking 15 signs and symptoms of muscle weakness in the present cases (8). We confirmed normal clinical test results during the postoperative 24 h, indicating acceptable patient safety. In addition, these patients underwent hemodialysis within 24 h postoperatively; this may be useful for preventing recurarization considering a previous report on the effectiveness of hemodialysis at removing sugammadex and the sugammadex-rocuronium complex in patients with severe renal impairment (14).

In conclusion, we found that rocuronium-induced NMB was prolonged in renal failure patients and that administration of sugammadex 2 mg/kg, based on TOF monitoring of moderate NMB, rapidly and safely reversed NMB without recurarization or complications. If clinical tests on the 15 signs and symptoms of muscle weakness, and hemodialysis during the postoperative 24 h, are carefully conducted alongside intraoperative TOF monitoring in renal failure patients, the NMB strategy of rocuronium combined with sugammadex can be effectively and safely applied. However, considering the lack of

experiences to support recommended use of sugammadex for reversing deep NMB in this population (5,6), further studies are required.

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Conflicts of Interest: None

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