International Journal of
BioScience and Applications

ISSN : 2619-8363
Volume 2, Number 2, September 2020
https://doi.org/10.22662/IJBSA.2020.2.2.009

A Case Report of Reversal with Sugammadx in a Myasthenic Patient

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Abstract

Background/Objectives: Myasthenia gravis (MG) is an autoimmune disease caused by the development of antibodies against the nicotinic acetylcholine receptor. **Methods/Statistical analysis:** MG causes weakness and fatigue of the respiratory muscles, so that there is hypersensitivity against non-depolarizing muscle relaxants. In general acetylcholinesterase inhibitors are administered to reverse the muscle blockade, but the use of neuromuscular blocking agents in myasthenic patients is usually delayed due to the drugs that already inhibit cholinesterase, resulting in a delay in spontaneous respiration. Sugammadex eliminates the effects of steroid non-depolarizing muscle relaxants, such as rocuronium and vecuronium, by selectively encapsulating their molecules. Case: We present a case of reversal of neuromuscular blocking agent and return to spontaneous respiration with sugammadex in a myasthenic patient. **Findings**: We also evaluated the degree of spontaneous respiration by comparing pulmonary function tests before and after surgery in a MG patient. **Improvements/Applications:** Sugammadex is a good option of fast reversal of neuromuscular blocking agent and return to spontaneous respiration in a myasthenic patient.

Index Terms

Myasthenia gravis, Sugammadex, Nicotinic acetylcholine receptor, Acetylcholinesterase inhibitors, Cholinesterase, Neuromuscular blocking

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• Manuscript received July 1, 2020.
• Revised August 10, 2020 ; Accepted September 2, 2020.
• Date of publication September 30, 2020.

I. Introduction

Myasthenia gravis (MG) is an autoimmune disease caused by the development of antibodies against the nicotinic acetylcholine receptor [1]. The symptoms of MG are muscle fatigue and variable weakness. The muscular weakness may cause aspiration pneumonia, dysarthria, or even swallowing difficulty. During anesthesia, neuromuscular blocking agents(NMBAs) are administered for immobile surgical field [2]. NMBAs blocks targets the neuromuscular junction, and offers skeletal muscle relaxation for the operation. They also lead to respiratory arrest as well. This effect is reversed with acetylcholinesterase inhibitors. The increase of acetylcholine by the acetylcholinesterase inhibitors promotes a rapid return of spontaneous respiration.

In normal condition the adequate dosage of NMBAs are administered, but the dose cannot be determined optimally in certain condition such as MG. If there is a thymoma present, myasthenic symptom can be presented. Thymoma is most often a benign tumor of the thymus which produces acetylcholine receptor autoantibodies and can sometimes even produce autoantibodies. Those patients usually take anticholinesterase inhibitor for symptom relieving effect. Thus, the recovery from NMBAs through the administration of further acetylcholinesterase inhibitors might be delayed after surgery. It may lead the residual neuromuscular blockade and postoperative respiratory failure. Also, insufficient muscle strength may result in hypoventilation, oxygen desaturation, development of hypercapnia, aspirations, and postoperative bronchopneumonia in the postoperative period [3].

Sugammadex is a rapid steroidal reversal agent from the neuromuscular blocking effect from NMBAs. Unlike the mechanism of acetylcholinesterase inhibitors, sugammadex binds directly to NMBAs, quickly reversing the neuromuscular blocking effect of the NMBAs and facilitating spontaneous respiration [4]. Efficiency and reliability of sugammadex has been repeatedly proven in clinical field. Here, we report a case of MG patient who received general anesthesia for spinal surgery. The patient has recovered from the effects of NMBA rapidly by using sugammadex. We also evaluated the degree of spontaneous respiration by comparing pulmonary function tests before and after surgery in the MG patient.

II. Case Report

A 58-year-old female was admitted for scheduled posterolateral internal fixation due to Lumbar spinal stenosis L3-S1. She had been diagnosed with MG and had undergone thymectomy 10 years ago, but the symptoms such as diplopia, dysphagia and difficulty to lift heavy things were returned after thymectomy. Also, she had DM and hypertension. At the time of operation, medications included prednisolone, pyridostigmin 60 mg, azathioprine, ACE inhibitor and metformin. Detailed explanation of the respiratory risks of MG undergoing general anesthesia and information about sugammadex was offered with informed consent.

Preoperative laboratory tests were within normal range including hemoglobin 11.9 mg/dl and Prothrombin Time International Normalized Ratio (INR) 1.01. Also, electrolyte, liver function test, chest PA, electrocardiography (ECG) and echochardiogram presented non-specific. Preoperative pulmonary function test (PFT) presented FEV1 1.78 L (99%) and FVC 1.87 L (89%).

After arriving at the operating room, ECG, blood pressure, pulse oximetry and a

peripheral nerve stimulator (TOF watch®, Organon Ltd., Dublin, Ireland) were monitored. Initial vital sign was blood pressure 130/64 mmHg, heart rate 65/minute, respiratory rate 20/minute, Oxygen saturation 94%. After preoxygenation for 3 minutes with 100% O2, anesthesia was induced by 1% propofol 100 mg and remifentanil (Ultiva®, GlaxoSmithKline, Parma, Italy). Remifentanil was infused using effect-site target-controlled infusion pump (Orchestra® Base Primea, Fresenius Vial, Brézins, France) with Minto model. Initially, patients were induced with remifentanil 4 ng/ml of the effect-site concentration and 3 vol% of sevoflurane with FiO2 0.5 (O2+ Air). After patients lost consciousness, 1.0 mg/kg of rocuronium were administered. The patient were manually ventilated via a face mask with air in oxygen, and the anesthesiologist tried to keep fixed tidal volume 8-10 ml/kg under spirometric monitoring. Orotracheal intubation was performed at 3 min after loss of consciousness when train-of-four count was 0 (4 stimuli at 2 Hz, 50 mA), and effect-site concentration of remifentanil was steady-state levels at 3-3.5 ng/ml. Intubation was done with Armored tube #7.0, and fixed at 21cm from the incisor. After endotracheal intubation, controlled mechanical ventilation was maintained with a TV 8 ml/kg (based on ideal body weight) and an inspiratory to expiratory ratio 1:2 with 5cmH_2O PEEP. The ventilatory frequency was set to maintain an end-tidal PCO_2 range of 38-42 mmHg. After induction esophageal temperature was monitored. Arterial line was secured for continuous BP monitoring and cardiac index. Central line was secured with 8 Fr. double lumen at the right subclavian vein and central venous pressure was monitored through out the operation. The patient was actively warmed to keep the body temperature 36.0 – 36.5 ℃ by using a forced air warming unit and a fluid line warmer. The patient's muscular relaxation, blood pressure, heart rate, peripheral oxygen saturation, and temperature were recorded throughout the operation (Table 1), (Table 2).

Table 1. Record throughout the operation 1.

	LOC	Rocuronium	Intubation	End of OP
Time	58s	114s (1' 54'')	270 s (4' 30'')	4h 15 min
TOF	100%	80%	0	68%
PR	58	56	62	76
BP	129/57	95/58	83/49	129/58
Temp	-	-	-	35.8
BIS	51	45	46	62

Table 2. Record throughout the operation 2.

	Sugammadex injection	TOF ratio 0.9	Obey
Time	180 s (3' 0'')	109 s (1' 49'')	320 s (6' 20'')
TOF	76%	90%	100%
PR	74	92	94
BP	119/57	141/63	165/85
Temp	35.8	35.8	-
BIS	69	82	92

During the operation, general anesthesia was maintained with sevoflurane 0.8-1.0

Mac (1.7-2.0 vol%) and remifentanil 0.01-0.20 μg/kg/min according to the values of BIS 40-60. The duration of the operation was 4 hours and 15 minutes. The amount of fluid was about 3900 ml crystalloid and 500 ml colloid during the period of the operation. Three packs of packed RBC was transfused. Pain control was done by Patient Controlled Analgesia with a regimen of fentanyl 700 mg, ketorolac 150 mg and nefopam 100mg in volume of 60mL mixture. The operation was done without any complication.

After the operation ended, sugammadex 120 mg (2 mg/kg) was administered to recovery spontaneous respiration. When the value of the TOF increased to 0.9 (109 seconds after the sugammadex injection), the patient was extubated. Three hundred and twenty seconds after sugammadex injection, verbal command was obeyed. Then, the patient was transferred to post-anesthesia care unit.

The patient's blood pressure, peripheral oxygen saturation, and heart rate were observed for 30 minutes postoperatively, and no specific symptoms were observed in the post-anesthesia care unit. Preoperative pulmonary function test (PFT) presented FEV1 1.91 L (89%) and FVC 1.82 L (99%). The patient was discharged without an event.

Ⅲ. DISCUSSION

Myasthenia gravis patients, particularly those undergoing major surgery and/or suffering from concomitant disorders, require special individual management in preparation for surgery, appropriate selection and administration of anesthesia, and close monitoring postoperatively [5,6].

Sugammadex is an NMBA antagonist and has a different mechanism from the usual acetylcholinesterase inhibitors. It binds directly to the NMBAs and reverses their neuromuscular blocking effects. According to Jones et al., when comparing sugammadex and a combination of glycopyrrolate and neostigmine under general anesthesia with rocuronium 0.6 mg/kg, the group that used sugammadex recovered significantly faster [7].

Sugammadex allows for faster recovery than conventional reversal agents. It is therefore a particularly useful alternative for patients with MG. Rudzka-Nowak and Piechota reported that a patient with myasthenia gravis who had undergone abdominal surgery and was administered 3 mg/kg of sugammadex intravenously completely recovered spontaneous respiration within 5 minutes [8].

All the beneficial qualities of sugammadex offer the possibility for using the drug in patients who are expected to have problems with proper ventilation and gas exchange. In the case described here, sugammadex made it possible to perform a safe general anaesthesia procedure with skeletal muscle relaxants without prolonging mechanical ventilation. The medical literature contains isolated reports on the use of sugammadex (with success) in patients with MG. We performed pulmonary function test to compare the ability of spontaneous respiration. PFT is a complete evaluation of the respiratory system so that it identifies the severity of pulmonary impairment after general anesthesia. In this case, preoperative and postoperative PFT were unchanged, which means the patient with MG was reversed completely after use of NMBAs.

The authors believe that sugammadex as an agent used for muscle relaxation in delivering anesthesia to MG patients may be the gold standard. Sugammadex, used in combination with objective neuromuscular monitoring, can be applied to reverse rocuronium induced neuromuscular blockade in patients with MG.

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