Journal of Anesthesia & Clinical Research
ISSN: 2155-6148

Shingu et al. J Anesthe Clinic Res 2011, 2:2
DOI: 10.4172/2155-6148.1000122

Case Report Open Access

Sugammadex is Safe and Effective for Patients with Myasthenia Gravis

Chihiro Shingu[1], Taichi Nishida[2], Satoshi Hagiwara[1]*, Keisuke Shiihara[2], Yoshimasa Oyama[2], Takakuni Abe[2], Shinya Kai[2] and Takayuki Noguchi[3]

[1]Anesthesiologist, Lector at Oita University, Faculty of Medicine, Department of Anesthesiology and Intensive Care Medicine, Japan
[2]Anesthesiologist, Staff at Oita University, Faculty of Medicine, Department of Anesthesiology and Intensive Care Medicine, Japan
[3]Anesthesiologist, Chief Professor at Oita University, Faculty of Medicine, Department of Anesthesiology and Intensive Care Medicine, Japan

Abstract

Thymoma, which can be surgically treated under general anesthesia, is associated with the pathophysiology of myasthenia gravis. Muscle weakness is a hallmark of myasthenia gravis; therefore, these patients are hypersensitive to the effects of nondepolarizing muscle relaxants. Neuromuscular blockers can cause prolonged postoperative muscle relaxation, leading to decreased respiratory function. Therefore, careful administration of muscle relaxants during the perioperative period is important. The neuromuscular antagonist, sugammadex, has been used to counteract problems associated with muscle relaxants. By encapsulating nondepolarizing muscle relaxants, sugammadex can reverse the neuromuscular blockade. Here we report three cases of myasthenia gravis. In each case, perioperative management included use of a train-of-four (TOF) monitor to minimize muscle relaxant use during surgery. Sugammadex was administered postoperatively, was safe for use in patients with myasthenia gravis, and may effectively reduce the risk of postoperative respiratory complications.

Keywords: General anesthesia; Myasthenia gravis; Neuromuscular blockade; Sugammadex

Introduction

Myasthenia gravis is an autoimmune disease for which muscle weakness is the primary symptom. Although rare, the prevalence of myasthenia gravis is increasing; approximately 20 in 100,000 people have the disease [1]. Muscle weakness is caused by the blockade of neuromuscular transmission by antibodies against nicotinic acetylcholine receptors (AChRs), which are located in the post-synaptic membrane of the neuromuscular junction.

Although its cause is unknown, myasthenia gravis may be a complication of thymoma. Symptoms of patients with myasthenia gravis often improve after thymectomy [2]. Accordingly, many patients with myasthenia gravis undergo this procedure under general anesthesia. However, the prolonged action of muscle relaxants used during surgery presents a problem. Currently, perioperative management involves using a muscle relaxation monitor to minimize muscle relaxant dosage. However, patients with myasthenia gravis have intrinsic muscle weakness, thus the prolonged effects of residual muscle relaxants can lead to conditions such as respiratory failure [3].

The recently developed neuromuscular antagonist, sugammadex, specifically encapsulates nondepolarizing neuromuscular blockers such as rocuronium and completely reverses the effects of muscle relaxants. Given that sugammadex has no parasympathetic stimulatory effects, there is no need to concurrently administer atropine [4].

Here we report on three patients with myasthenia gravis, whose postoperative progress was managed with sugammadex without complications.

Case Reports

Case 1

The patient was a 53-year-old woman who was 164 cm tall and weighed 82.6 kg (BMI 30.7). She had previously undergone spinal surgery for cervical canal stenosis (2000) and had a total hysterectomy for uterine adenomyosis (2005). Nothing unusual was noted during the surgeries. The patient also had overlap syndrome (positive for antibodies against thyroglobulin, thyroid peroxidase, glutamic acid decarboxylase, and matrix metalloproteinase-3) and was allergic to aspirin.

Beginning in 2009, the patient had the sensation of a foreign matter in her eye and photophobia. In April 2010, she experienced ptosis of the right eyelid and alopecia areata. In June 2010, the patient was admitted to our hospital; generalized myasthenia gravis type IIa was diagnosed based on ptosis, proximal muscular weakness, positive Tensilon test results, depression of the evoked electromyogram, antibodies against AChR, and thymoma. Thoracoscopic extended thymectomy was scheduled with general anesthesia. No abnormalities were found in preoperative blood tests. Tests of respiratory function showed a vital capacity (VC) of 2.8 L (104% VC) and forced expiratory volume in 1 sec (FEV1) of 2.1 L (88% FEV1). Electrocardiogram showed a normal sinus rhythm and results were within normal limits (ejection fraction [EF] 72%). No problems were observed on plain chest radiography.

Anesthesia was induced with propofol and fentanyl. A muscle relaxation monitor (TOF Watch SX™, Merck & Co., Inc., Whitehouse Station, NJ) was attached, and rocuronium (20 mg) was administered until a maximum block of T1 was achieved for a train-of-four (TOF) stimulus. Subsequently, the patient was intubated with a 35 F double-lumen tube (Broncho-Cath™) using the Airtraq™ optical laryngoscope. Epidural anesthesia (T7-8) was administered in combination with general anesthesia (oxygen, air, and sevoflurane). TOF was monitored every 5 minutes with the muscle relaxation monitor. Either T3 or T4 was exerted every 10 to 30 min, so, we administered 5 mg rocuronium

Corresponding author: Satoshi Hagiwara, Department of Anesthesiology and Intensive Care Medicine, Oita University Faculty of Medicine, 1-1 Idaigaoka-Hasamamachi, Yufu City, Oita, 879-5593; Tel: +81-97-586-5943; Fax: +81-97-586-5949; E-mail: saku@oita-u.ac.jp

Received December 26, 2010; **Accepted** February 15, 2011; **Published** February 16, 2011

Citation: Shingu C, Nishida T, Hagiwara S, Shiihara K, Oyama Y, et al. (2011) Sugammadex is Safe and Effective for Patients with Myasthenia Gravis. J Anesthe Clinic Res 2:122. doi:10.4172/2155-6148.1000122

(total 80 mg). The patient was stationary during surgery. After surgery, when TOF recovered to 0.6 and spontaneous respiration and body movements were confirmed, 2 mg/kg sugammadex (total dose 165 mg) was administered. After confirming that TOF immediately and completely recovered, awakening and extubation proceeded satisfactorily. The patient returned to the ward uneventfully. Myasthenic symptoms did not recur. The patient improved and was discharged 22 days postoperatively.

Case 2

The patient was a 71-year-old man who was 170 cm tall and weighed 82.3 kg (BMI 28.5). Prior medical history included pneumonia (2000), duodenal ulcer, prostatic hyperplasia, hypertension, diabetes, and asthma; the patient was undergoing oral treatment for Sjogren's syndrome. Prior history of surgeries under anesthesia included partial resection of the left lung and a benign hamartoma (2005); anesthesia was uneventful during these surgeries. In June 2010, the patient had difficulty chewing and swallowing. Breathing difficulty on exertion increased; asthma and thymoma were subsequently diagnosed. In July of the same year, ptosis, fatigability of the upper body, and diplopia appeared with diurnal variations. The patient was positive for AChR antibody and Tensilon tests, and showed deterioration in electrophysiological exams. Generalized myasthenia gravis type IIa was diagnosed, and thoracoscopic extended thymectomy under general anesthesia was scheduled.

Results of preoperative blood tests were normal. Testing of respiratory function showed that %VC was 3.1L (90% VC) and FEV1 was 1.5L (60% FEV1), confirming obstructive respiratory disorder. Electrocardiography revealed sinus rhythm, left ventricular hypertrophy, moderate ST reduction, and QTc extension. Echocardiography revealed left ventricular dilatation, EF of 68%, and aortic, mitral, and pulmonary regurgitation. Sporadic calcification of both pulmonary fields was observed by plain chest radiograph.

Anesthesia was induced with propofol and fentanyl. A muscle relaxation monitor (TOF Watch™; Nihon Kohden Corporation, Tokyo, Japan) was attached, and 20 mg rocuronium was administered to achieve a maximum block of T1 for a TOF stimulus. The patient was intubated with a double-lumen tube (37 Fr Broncho-Cath™). Epidural anesthesia (T6-7) was administered in combination with general anesthesia (oxygen, air, sevoflurane). TOF was monitored every 5 minutes using the muscle relaxation monitor. Either T3 or T4 was exerted every 30 to 60 min, so 5 or 10 mg rocuronium was administered as needed (total dose, 60 mg). The patient was stationary during surgery. When spontaneous respiration was confirmed and TOF recovered to 0.9 or above, 2 mg/kg sugammadex (total 160 mg) was administered. The patient was extubated upon confirming immediate and complete recovery of TOF, and returned to the ward uneventfully. Myasthenic symptoms did not recur. The patient improved and was discharged 16 days postoperatively.

Case 3

The patient was a 21-year-old woman who was 160.3 cm tall and weighed 59.7 kg (BMI 23.3). Prior medical history included epileptic seizures, although the symptoms had subsided. A mediastinal tumor was detected in April 2009. The patient underwent an extended thymectomy in August 2009 at another hospital without complications. Two weeks postoperatively, the patient experienced myasthenic symptoms (bulbar palsy, swallowing disturbances); myasthenia gravis type IIb was diagnosed. Anti-AChR levels increased despite continued oral steroid treatment. In July 2010, a growing tumor mass immediately above the right diaphragm was detected by computed tomography, which was diagnosed as ectopic thymoma. Thoracoscopic tumor excision under general anesthesia was scheduled. There were no significant test findings. Results of respiratory tests were within normal range (VC was 2.7 L (88% VC) and FEV1 was 2.7 L (85% FEV1)). Electrocardiogram and echocardiogram were normal. The plain chest radiograph showed bilateral diaphragm elevation.

Anesthesia was induced with propofol and fentanyl. A muscle relaxation monitor was connected, and 10 mg rocuronium was administered to achieve a maximum block of T1 for a TOF stimulus. The patient was intubated with a 35 Fr double-lumen tube (Broncho-Cath™). Epidural anesthesia (T7–8) was administered in combination with general anesthesia (oxygen, air, sevoflurane). TOF was monitored every 5 minutes using the muscle relaxation monitor. TOF was increased at the beginning of surgery. Rocuronium (5 or 10 mg) was administered (total dose 25 mg) when TOF ≥ 0.5. The patient was stationary during surgery. When spontaneous respiration was confirmed and TOF reached 0.86 or above postoperatively, 2 mg/kg (120 mg) sugammadex was administered. The patient was awakened and extubated upon confirming immediate and complete recovery of TOF. The patient returned to the ward uneventfully. Myasthenic symptoms did not recur. The patient improved and was discharged 11 days postoperatively.

Discussion

In the present cases, we used a muscle relaxation monitor perioperatively in thymectomy cases complicated by myasthenia gravis. We managed anesthesia safely by antagonizing muscle relaxation with sugammadex postoperatively.

Myasthenia gravis is an autoimmune disease in which antibodies against AChRs, which are located in the post-synaptic membrane of the neuromuscular junction, block neuromuscular transmission. Weakness of skeletal muscles is the chief complaint of myasthenia gravis [1]. Although rare, the incidence of the disease appears to be increasing [1]. Thymoma is associated with the pathophysiology of myasthenia gravis. Although the precise cause remains unclear, it is treated by thymectomy. During general anesthesia, the normal amount of nondepolarizing neuromuscular blocker has prolonged effects in patients with myasthenia gravis. This can result in a postoperative decline in respiratory function [5]. Because muscle relaxants are commonly required for intubation and surgical procedures, a muscle relaxation monitor is recommended during the perioperative period [3]. In the present cases, we used a muscle relaxation monitor perioperatively to minimize muscle relaxant use. However, we could not completely eliminate its residual effects immediately after surgery. Accordingly, caution is needed in the perioperative use of muscle relaxants in patients with myasthenia gravis.

The anticholinesterase agent neostigmine is often used as an antagonist for nondepolarizing muscle relaxants. Neostigmine inhibits acetylcholinesterase at the neuromuscular junction, thereby increasing acetylcholine levels. As such, neostigmine has been used to antagonize the effects of nondepolarizing neuromuscular blockers [6]. Furthermore, its duration of action is shorter than that of muscle relaxants, which allows for residual neuromuscular blocker effects that can be difficult to detect. Neostigmine, through parasympathetic stimulation, is also associated with adverse effects such as pupillary constriction, bradycardia, bronchospasms, increased airway/salivary secretion, and facilitation of intestinal peristalsis. Accordingly, the adverse effects must be controlled with atropine [6]. This has led to the

restricted use of neostigmine [6]. Antagonists of muscle relaxants with novel mechanisms of action have recently been developed for clinical use [4]. Sugammadex is one such antagonist that forms strong bonds to enclose a substance in a process known as clathration. Sugammadex encapsulates nondepolarizing neuromuscular blockers, thereby blocking their effects. Its duration of action is short, and it even reverses deep muscle relaxation [4]. Furthermore, unlike neostigmine, there are few contraindications with sugammadex. Here, we successfully used sugammadex postoperatively as an antagonist of muscle relaxants in patients with myasthenia gravis. This suggests that sugammadex use immediately after surgery can prevent complications such as postoperative respiratory failure in these patients.

In the present cases, we administered sugammadex after partial recovery from the effects of the neuromuscular blocker. However, sugammadex can reverse the deep neuromuscular blockade and it was safe and completely recovered from neuromuscular blockade [7]. Thus, we administered sugammadex immediately after surgery. However, since sugammadex may accumulate, an anesthesiologist must closely follow the effects of the neuromuscular blocker using a TOF monitor in patients with myasthenia gravis. In the present cases, we used a muscle relaxation monitor perioperatively to minimize the dose of muscle relaxant administered to patients, and used sugammadex to safely and completely antagonize residual postoperative muscle relaxant effects. Similar management in patients with muscle weakness may decrease complications during the perioperative period.

References

1. Phillips LH 2nd (2003)The epidemiology of myasthenia gravis. Ann NY Acad Sci 998: 407-412.
2. Juel VC, Massey JM (2007) Myasthenia gravis. Orphanet J Rare Dis 6; 2: 44.
3. Dillon FX (2004) Anesthesia issues in the perioperative management of myasthenia gravis. Semin Neurol 24: 83-94.
4. Kovac AL (2009) Sugammadex: the first selective binding reversal agent for neuromuscular block. J Clin Anesth 21: 444-53.
5. Juel VC (2004) Myasthenia gravis: management of myasthenic crisis and perioperative care. Semin Neurol 24: 75-81.
6. Morita T, Kurosaki D, Tsukagoshi H, Shimada H, Sato H, et al. (1997) Factors affecting neostigmine reversal of vecuronium block during sevoflurane anaesthesia. Anaesthesia 52: 538-543
7. Rex C, Bergner UA, Pühringer FK (2010) Sugammadex: a selective relaxant-binding agent providing rapid reversal. Curr Opin Anaesthesiol 23: 461-465.