A new approach to anesthesia management in myasthenia gravis: reversal of neuromuscular blockade by sugammadex

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Summary

A neuromuscular blocking drug (NMBD) induced neuromuscular blockade (NMB) in patients with myasthenia gravis usually dissipates either spontaneously or by administration of neostigmine. We administered sugammadex to a patient with myasthenia gravis to reverse a rocuronium-induced profound NMB. NMBDs predispose such patients to severe postoperative residual paralysis and respiratory complications. Sugammadex binds steroidal NMBDs and, therefore reverses a rocuronium or vecuronium-induced NMB, without interfering with cholinergic transmission. A rapid and complete recovery from profound NMB was achieved and no adverse events were observed. This case suggests that sugammadex is a safe and effective antagonist of a rocuronium induced NMB blockade in patients with myasthenia gravis.

Key words:
Myasthenia gravis. Sugammadex. Rocuronium. Neuromuscular blockade. Reversal drug.

Un nuevo enfoque en el manejo de la anestesia en la miastenia gravis: reversión de un bloqueo neuromuscular mediante sugammadex

Resumen

Un fármaco bloqueante neuromuscular (FBNM) que induce bloqueo neuromuscular (BNM) en pacientes con miastenia gravis habitualmente desaparece bien de manera espontánea o mediante la administración de neostigmina. Nosotros administramos sugammadex en un paciente con miastenia gravis para revertir un BNM profundo inducido por rocuronio. Los FBNM predisponen a algunos pacientes a graves parálisis residuales postoperatorias así como a complicaciones respiratorias. Sugammadex anula la respuesta esteroidea del FBNM, y por tanto, revierte un BNM inducido por rocuronio o vecuronio, sin interferir en la transmisión colinérgica. Se logró una rápida y completa recuperación de un profundo BNM y no se observaron efectos adversos. Este caso sugiere que sugammadex es un seguro y efectivo antagonista de rocuronio como inductor de bloqueo neuromuscular en pacientes con miastenia gravis.

Palabras clave:
Miastenia gravis. Sugammadex. Rocuronio. Bloqueo neoromuscular. Fármaco de reversión.

Myasthenia gravis is an autoimmune disorder involving the destruction of nicotinic acetylcholine receptors at the neuromuscular junction, and is characterized by weakness and exercise-induced skeletal muscle fatigue. One of the anesthesic-related complications in such patients requiring relaxation (ie. paralysis) during general anesthesia is an increased sensitivity to nondepolarizing neuromuscular blocking drugs (NMBD)[1-3]. Furthermore, the chronic use of acetylcholinestrase inhibitors such as pyridostigmine in these patients may interfer with the dose response relationships and effectiveness of NMBDs and their antagonists[4]. Therefore, NMBDs should be given with care (ie. smaller doses) in patients with myasthenia gravis. Even small doses of a NMBD can lead to profound muscle paralysis with a prolonged spontaneous recovery or indadequate reversal by neostigmine[4]. A delayed recovery may result in a dangerous postoperative residual paralysis and the need for postoperative mechanical ventilation[1-3]. It is therefore recommended to pharmacologically reverse neuromuscular blockage at the end of surgery to prevent respiratory morbidity and mortality in every patient, especially more vulnerable patients like those with myasthenia gravis[5].

Classically, reversal of NMBDs is performed by administration of acetylcholinesterase inhibitors such as neostigmine. However patients with chronic use of acetylcholinesterase inhibitors may already have an optimal inhibition of this enzyme and therefore reversal with cholinesterase inhibitors is less effective.

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Sugammadex, a new drug which reverses rocuronium or vecuronium-induced neuromuscular blockade by encapsulating the NMBD which results in a very rapid recovery from neuromuscular blockade[6,7]. Sugammadex, a modified g-cyclodextrin has been approved by the European Medicines Agency as therapy for reversal of neuromuscular blockade induced by the steroidal non-depolarizing neuromuscular blocking drugs rocuronium and vecuronium[7]. In clinical anesthesia and emergency medicine sugammadex has been available for almost one year in several European countries and is successfully used to reverse neuromuscular blockade and to eliminate postoperative residual neuromuscular blockage, or partial paralysis induced by these NMBDs.

We describe a case in which a patient received a single dose of sugammadex to reverse a rocuronium-induced profound neuromuscular blockade. The perioperative management, and the safety and efficacy of sugammadex in this myasthenia gravis patient is discussed.

Case Report

A 73 year-old female patient, weight 81 kg, was diagnosed with a malignant tumor of the left breast. Her medical history revealed seronegative myasthenia gravis with ocular signs and symptoms and mild generalized muscle weakness (class I-IIa myasthenia gravis severity classification system by Osserman and Jenkins), diagnosed at the age of 61 years[8]. Eight years earlier the patient underwent an operation for appendectomy under general anesthesia which was complicated by prolonged neuromuscular blockade (NMB) after administration of a single dose (0.6 mg/kg) of the NMBD rocuronium to facilitate endotracheal intubation. After that procedure the patient was admitted to the ICU for postoperative mechanical ventilation.

Eight years later the patient was scheduled for mastectomy and sentinel node procedure under general anesthesia. An ICU bed was available postoperatively if needed. She had a decreased forced vital capacity and decreased maximal forced inspiratory and expiratory flow as measured by preoperative pulmonary function tests. Residual volume and total lung capacity were normal. There were no signs of cardiac (or other) pathology. Evaluation of the blood values, including blood chemistry and hematology analysis showed no abnormalities. Her medication, which was oral pyridostigmine 60 mg six times a day, was continued perioperatively.

After obtaining informed consent, the patient agreed that we would study the use of sugammadex in order to determine its rocuronium-binding effectiveness in patients with MG. We agreed to administer a small dose of rocuronium, which would be allowed to recover spontaneously, followed by a second equal dose which we would reverse shortly after its administration. The patient was therefore acting as its own control. Wouldn't the second dose have a more profound effect?

Neuromuscular function measurement was performed using the TOF-Watch SX (Schering-Plough Ireland Ltd, Dublin, Ireland) monitor. The ulnar nerve was stimulated near the wrist with square wave pulses of 0.2 msec, delivered as train-of-four (TOF) pulses of 2 Hz, at intervals of 15 seconds. The contractions of the adductor pollicis muscle were quantitatively measured using acceleromyography. The data were recorded on a computer (TOFMON 1.2, Schering-Plough Ireland Ltd, Dublin, Ireland). The primary efficacy variable for reversal was defined as the time (recovery time) from the start of the administration of sugammadex, until 90% recovery of the ratio of the fourth (T4) to the first (T1) response in the pulse train. This is the standard of safe recovery as defined in the guidelines for Good Clinical Practice in neuromuscular monitoring[9].

Premedication consisted of oral paracetamol 1000 mg before anesthesia. On arrival at the operating room, an intravenous (IV) line was inserted. Standard intraoperative monitoring included ECG, non-invasive measurement of arterial blood pressure and pulse oximetry. After the patient breathed 100% oxygen, anesthesia was induced and maintained with continuous IV infusion of propofol (6-12 mg/kg/h) and remifentanil (0.10-0.25 μg/kg/min). Procedures for the setup, calibration, and stabilization of neuromuscular monitoring were performed. The patient then received an IV bolus injection of rocuronium 0.15 mg/kg (total 12.1 mg), which resulted in a profound neuromuscular block. This was followed by endotracheal intubation, and the lungs were ventilated with a mixture of oxygen and air in a ratio of 2:3. After spontaneous recovery (TOF-ratio > 90%) of this profound neuromuscular blockade in about one hour, a second dose of rocuronium 0.15 mg/kg (total 12.1 mg) was given, which again lead to a profound neuromuscular blockade. After reaching profound neuromuscular blockade from this second dose of rocuronium (Fig 1), neuromuscular blockade was reversed by the IV administration of 4.0 mg/kg sugammadex (324 mg). The dose of sugammadex was chosen according to the dose advice in the label regarding the depth of neuromuscular blockade at the time of reversal. The recovery times of both, spontaneous recovery and recovery after reversal with sugammadex were compared.

The time to spontaneous recovery from the first profound rocuronium-induced neuromuscular blockade to a TOF of 0.9 was 36.5 min. The time from the start of the administration of sugammadex after the second dose of rocuronium to recovery of the TOF-ratio to 0.9 was 2.7 min.

No changes were observed in arterial blood pressure, heart rate or ECG after administration of the sugammadex dose.

The surgical procedure was uneventful, and at the end of the anesthesia the trachea was extubated. The recovery from anesthesia was also uneventful, and the patient was discharged to the post-operative recovery ward for further observation. There she was monitored until 120 minutes after the administration of sugammadex for signs of possi-