ANESTHETIC MANAGEMENT OF AORTIC VALVE REPLACEMENT IN A MYASTHENIA GRAVIS PATIENT, THE ERA OF A NEW REVERSAL

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A 66 year old man diagnosed with myasthenia gravis (Type IIA) three months prior to hospital admission maintained on pyridostigmine 180mg and prednisone 40 mg orally daily, presented with dyspnea and chest pain. Severe aortic stenosis (surface valve area:0.96 cm2) was found on echocardiography and he was scheduled for aortic valve replacement.

Balanced technique of general anesthesia was performed using thiopental, sufentanil and rocuronium for anesthesia induction. A Datex Ohmeda M-NMT Module was attached and we aimed to produce deep neuromuscular blockade with rocuronium. Patient required 0.3mg/kg bolus and 0.1mg/kg/hr for maintenance for 4 hours. At the end of the procedure sugammadex 4mg/kg was given. Complete recovery of neuromuscular blockade was observed as evidenced by full recovery of the twitch response and the TOF (T4/T1> 90%) following 210 seconds from the sugammadex dose. After fulfillment of the criteria of extubation (maximal inspiratory pressure of -20 cmH2O and tidal volume of more than 10mL/kg), the trachea was extubated at one hour after the end of surgery in the surgical cardiac intensive care unit.

Postoperative course was uneventful. Patient was discharged home on day four postoperatively.

In conclusion, this case report shows that the combination of rocuronium and sugammadex for neuromuscular blockade and its reversal, in a myasthenic patient on pyridostigmine, undergoing open heart surgery under cardiopulmonary bypass, is safe and efficient without untoward effects.

Introduction

Myasthenia Gravis (MG) is an autoimmune disease characterized by the release of antibodies against acetylcholine receptors at the neuromuscular junction1. Therefore, careful perioperative management is required because of the unpredictable susceptibility to analgesia and muscle relaxants1,2. To date, however, there have been very few reports which describe perioperative management in patients with myasthenia gravis undergoing cardiac surgery3-7. In this report, we describe the successful perioperative management of a patient with myasthenia gravis who underwent aortic valve replacement under cardiopulmonary bypass.

References

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Case Report

A 66 year old man with severe ocular and limb muscle weakness along with mild oropharyngeal muscle weakness of three months duration. Edrophonium test was performed that showed an improvement in strength consistent with MG. Repetitive nerve stimulation was also done that showed evidence of muscle fatigue consistent with MG. A positive blood test for elevated concentration the acetylcholine receptor antibody test was strongly indicative of MG. Patient was diagnosed to have MG (ClassIIA) and was maintained on pyridostigmine 60mg orally three times daily and prednisone 40 mg once daily. He was also suffering from shortness of breath with ordinary physical activity that improved with rest (New York Heart Association class 2). Electrocardiogram revealed sinus rhythm. A chest x-ray showed a cardiothoracic ratio of 50% with no abnormal shadow. Cardiac echocardiography demonstrated normal left ventricular function with an ejection fraction of 65% and a cardiac index of 3.56 L/min/m2. Left atrium was severely dilated with severe aortic stenosis (The aortic valve surface area equal 0.96 cm2) so he was referred to our hospital for aortic valve replacement surgery.

On the day of surgery, blood pressure was 110/60 mmHg and heart rate was 63 beats per minute. The patient was premedicated with 5 mg diazepam orally 1 hour before operation after taking his morning dose of pyridostigmine 60mg and prednisone 40mg. Upon arrival to the operating room, patient was attached to standard monitors (5 leads electrocardiography, noninvasive blood pressure, pulse oximeter and, a neuromuscular stimulator (NMS) (Datex Ohmeda M-NMT module as part of Datex Ohmeda Aisys ventilator, Helsinki, Finland) with output 40 mA, impulse duration 200 ms, and an interval of 1 min was applied at the right ulnar nerve near the wrist and measured isotonic contractions of the adductor pollicis muscle. An intravenous and radial artery catheters were inserted. General anesthesia was induced with thiopental (1mg/kg), sufentanil (0.5 mcg/kg, intravenously), lidocaine (1 mg/kg) and rocuronium (0.3 mg/kg). The trachea was then intubated without difficulty. Anesthesia was maintained with sevoflurane (1.0-1.5%), intermittent administration of sufentanil (1 mcg/kg), intravenously and a continuous infusion of rocuronium (0.1 mg/kg/hr intravenously) with no twitch on the train of four and a single stimulus following tetanic stimulation (deep neuromuscular blockade)⁸. During cardiopulmonary bypass(CPB) the nonpulsatile perfusion flow was kept at 2.5 L/min/m2, and mean arterial pressure was maintained between 60 and 70 mmHg. The myocardium was protected with intermittent antegrade cold blood cardioplegia. Aortic valve replacement was done, CPB was terminated at a rectal temperature of 36.5⁰C uneventfully. There was no patient movement throughout the procedure. A total of 0.75 mg/kg (60 mg) rocuronium was administered during surgery. At the end of surgery and after sevoflurane was washed out, end expiratory concentration of 0.15% of its minimum alveolar concentration, sugammadex (4mg/kg) was given to reverse the deep neuromuscular blockade⁸. Complete recovery of neuromuscular blockade was observed as evidenced by full recovery of the twitch response and the TOF (T4/T1 > 90%) following 210 seconds from the sugammadex dose. After fulfillment of the criteria of extubation (maximal inspiratory pressure of -20 cmH2O and tidal volume of more than 10mL/kg), the trachea was extubated at one hour after the end of surgery in the cardiac surgical unit. Arterial blood gas on 5L O2 by face mask revealed PO2 = 167 mmHg, PCO2 = 36 mmHg, and pH = 7.47, oxygen saturation of 98%. Postoperative course was uneventful and the patient was discharged home on day 4 postoperatively.

Discussion

Any myasthenia gravis patient undergoing cardiac surgery requires proper preoperative preparation, appropriate selection and administration of anesthesia, with close monitoring because of the risk of respiratory failure in the postoperative period⁴⁻⁷.

There are different anesthetic techniques reported for myasthenia gravis patients undergoing cardiac surgery under general anesthesia that range from no use of any muscle relaxants⁴ with total intravenous anesthesia, restriction of opioids and the use of propofol³; however the presence of unwanted patient movement, diaphragmatic contractions, and difficult surgical conditions were observed⁴; to continuous monitoring of neuromuscular junction
function with the use of muscle relaxants and high dose analgesia\textsuperscript{5-7}, in order to provide the deep general anesthesia sufficient to prevent movement required to produce a quiescent operative field and postoperative sedation during and after cardiac surgery\textsuperscript{5-7}. However, inadequate restoration of muscle function, especially of respiratory and swallowing muscles, causing prolonged mechanical ventilation, gastroesophageal reflux and pulmonary infection were observed\textsuperscript{5}. Also, although currently used neuromuscular transmission blockers are considered safe, with the recovery of normal muscle function occurring after a period specific to each drug but the recovery of muscle relaxation may take more than 12 hours when vecuronium is used\textsuperscript{7}. Acetylcholine esterase inhibitors use to reverse neuromuscular blockers presents a special problem in myasthenia gravis patients\textsuperscript{9} especially for patients maintained on cholinergic drugs till the day of surgery, cholinergic crisis may occur with muscular weakness that complicates postoperative course\textsuperscript{9}.

The availability of sugammadex allowed different authors to be more courageous in the use of rocuronium and vecuronium in myasthenia gravis patients\textsuperscript{10-13}. Sugammadex has a unique cyclodextrin for steroid nucleus neuromuscular blockers (NMB) reversal. Predictable, complete, and rapid reversal at any depth of neuromuscular block induced by rocuronium in adults, allows more use of deep neuromuscular blockade, with encapsulation of rocuronium and vecuronium\textsuperscript{14,15}. It is associated with both a statistically and clinically significant shorter period of potentially unsafe recovery\textsuperscript{16}. The Length of stay in the operating room (OR) and OR discharge-ready time were decreased with sugammadex reversal of deep NMB compared with placebo\textsuperscript{17}.

Although, persistence of fade on the TOF was reported despite reversal of rocuronium by 12 mg/kg of sugammadex in a myasthenic patient undergoing thymectomy\textsuperscript{18}. Rocuronium used in our case, with the dosage titrated and minimized using a neuromuscular transmission monitor intraoperatively maintaining a deep neuromuscular blockade that was reversed with sugammadex (4 mg/kg) at the end of the surgery, as was proposed by Duvaldestin et al\textsuperscript{8}. Postoperative course was uneventful. Sugammadex made it possible to perform a safe general anesthesia procedure with skeletal muscle relaxants without prolonging mechanical ventilation. Reversal of rocuronium induced neuromuscular block by sugammadex in our patient with myasthenia gravis was rapid, efficient, and without signs of postoperative residual neuromuscular block. In conclusion, this case report shows that the combination of rocuronium and sugammadex for neuromuscular block and its reversal, in a myasthenic patient on pyridostigmine, undergoing open heart surgery under cardiopulmonary bypass, is safe and efficient without untoward effects.
References

BRIDION—optimal neuromuscular blockade management and improved recovery

Predictable and complete reversal

- 98% of BRIDION patients recovered to a TOF* ratio of 0.9 from reappearance of T2 within 5 minutes
- 97% of BRIDION patients recovered to a TOF* ratio of 0.9 from 1 to 2 PTCs* within 5 minutes

Rapid reversal

- BRIDION rapidly reversed patients from reappearance of T2 in 1.4 minutes
- BRIDION rapidly reversed patients from 1 to 2 PTCs* in 2.7 minutes

BRIDION is indicated for the reversal of neuromuscular blockade induced by rocuronium or vecuronium. In children and adolescents (aged 2-17 years), BRIDION is only recommended for routine reversal of moderate rocuronium-induced neuromuscular blockade.

Important safety information

BRIDION is not recommended in patients with severe renal impairment. Studies in patients with hepatic impairment have not been conducted, and therefore, patients with severe hepatic impairment should be treated with great caution. Caution should be exercised when administering BRIDION to pregnant women as no clinical data on exposed pregnancies are available.

Neuromuscular blockade is required within 24 hours of BRIDION administration, a non-depolarizing neuromuscular blocking agent should be used instead of rocuronium or vecuronium. The most commonly reported adverse reactions were dysgeusia (dysfunctional taste) and anesthetic complications (movement, coughing, grunting, or crackling on the endotracheal tube). In patients treated with BRIDION, a few cases of awareness were reported. The relation to BRIDION was unknown. In a few individuals, allergic reactions (e.g., flushing, erythematous rash) following BRIDION were reported. Children should be prepared for the possibility of allergic reactions and the necessary precautions. A trial of patients with a history of renal impairments, bronchospasm was reported in 2 patients and a causal relationship could not be fully excluded.

Volunteer studies have demonstrated a slight (1%-2%) and transient (<30 minutes) prolongation of the pre-mid-teratogenic part of the mid-term fetal exposure time (PTM/FET) with BRIDION; however, clinical studies have demonstrated no clinically relevant effect on pre- or postoperative bleeding complications with BRIDION alone or in combination with anticoagulants. As BRIDION has demonstrated in vitro pharmacodynamic interaction with anticoagulants, caution should be exercised. In patients on anticoagulation for a pre-existing or current condition, this pharmacodynamic interaction is not clinically relevant for patients receiving routine postoperative prophylactic anticoagulation.

Although similar interactions have not been conducted, no drug interactions were observed in clinical trials. Preclinical data suggest that clinically significant drug interactions are unlikely with the possible exceptions of beroreime, folic acid, and hormonal contraceptives.

* TOF - Train of Four
  * PTC - Post-Tetanic Count


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