

# Is Neuromuscular Block Reversal-A Must-In Myasthenics Undergoing Open Heart Surgery?

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## Abstract

Myasthenia gravis is one of the most common progressive autoimmune diseases affecting the postsynaptic junction. However, hazardous cardiac surgery can be performed on patients with autoimmune disorders like myasthenia gravis. Herein, we describe successful anesthetic management and safe, in-time extubation of a patient with myasthenia gravis type I undergoing coronary artery bypass grafting surgery by total intravenous anesthesia and moderately effective muscle relaxation with anesthesia depth and neuromuscular transmission monitoring.

## Introduction

Myasthenia Gravis (MG) is an autoimmune neuromuscular disease leading anesthesiologists to be fairly familiar with. The anesthesiologists should know not only the interaction of drugs used by the patient with the anesthetic drugs used during the operation, but also postoperative mechanical ventilation management in these patients. Careful strategies regarding the use of muscle relaxants are required [1]. On-pump cardiac surgery owing to the alterations in pharmacokinetics and pharmacodynamics of neuromuscular blocking drugs and hypothermia decreases muscle strength even more [2].

In this report, we describe a case of successful intra and post operative anesthetic management of a MG Type I patient who didn't require prolonged mechanical ventilation following hypothermic cardiopulmonary bypass (CPB) surgery. We also wanted to emphasize that well-controlled comorbidity didn't change the process of perioperative anesthesia management, in clinically experienced hands.

## Case Report

A 60-year-old male patient (69 kg, 174 cm) complaining of chest pain and shortness of breath presented to the cardiology department of our hospital. At initial evaluation, electrocardiographic abnormalities were absent and troponin levels were within normal limits. Regarding his past medical history, the patient suffered from ptosis and diplopia in the right eye 2.5 months prior to admission. On further investigation, his anti-acetylcholine receptor (anti-AchR) was measured as 5.49 nmol.L<sup>-1</sup> and anti-muscle-specific tyrosine kinase (anti-MusK) was negative. On CT, no thymoma was detected. He was diagnosed with ocular onset seropositive MG Type I (Myasthenia Gravis Foundation of American Classification I). He was on a combination treatment including pyridostigmine 60 mg and prednisolone 16 mg per day. On physical examination, he had neither ocular weakness nor bulbar involvement. Although in 50% to 80% of these patients, the

disease develops into generalized form, it takes almost 2 years after beginning of ocular symptoms [3,4]. As our patient was diagnosed as MG Type I only 2.5 months ago; it is not easy to command about the patient's progress. Thus, we didn't perform additional electromyography before surgery. The respiratory function tests, electrocardiogram, chest X-Ray, and carotid ultrasound were normal. Transthoracic echocardiography demonstrated hypo kinetic left ventricular function with an ejection fraction of 40% and 2<sup>nd</sup> degree regurgitation of mitral and tricuspid valves. The coronary angiogram revealed severe triple vessel disease and he was scheduled for coronary artery bypass surgery. Preoperatively, he took intravenous immunoglobulin (Genivig 5% 100 mL Human Immunoglobulin; Sichuan Yuanda Pharmaceutical Co. Sichuan, China) infusion of 0.4 mg.kg<sup>-1</sup> day<sup>-1</sup> for 3 days' long. His other past medical history was unremarkable. In order to improve respiratory functions, respiratory physiotherapy was planned during this period.

On the morning of surgery, he was given his routine anti-myasthenia medications. In the operating room, standard monitoring was applied (5 leads electrocardiography, non-invasive blood pressure, SpO<sub>2</sub>). Intravenous and radial artery catheters were inserted before anesthesia induction. In addition, a urinary catheter, esophageal temperature probe, and Bispectral Index Score (BIS) monitorization were applied.

For monitoring of Neuromuscular Block (NMB) acceleromyometric method using a TOF Guard apparatus (Organ on, Holland) was applied. Following preoxygenation, intravenously, 10 µg.kg<sup>-1</sup> fentanyl with 1.5 mg.kg<sup>-1</sup> propofol were used for anesthesia induction, and 0.6 mg.kg<sup>-1</sup> rocuronium was administered for endotracheal intubation. After 1 min 40 seconds, T1 was measured as 0% according to the normal calibration value without the need for an additional dose. The patient was intubated without any difficulties. A quad-lumen central venous catheter was placed. Anesthesia was maintained with 50% to 50% O<sub>2</sub>-air and Total Intravenous Anesthesia (TIVA) with propofol titrated at a variable rate of 3-8 mg.kg<sup>-1</sup>.hr<sup>-1</sup> and remifentanyl 0.08-0.25 mcg.kg<sup>-1</sup>.min<sup>-1</sup> infusion according to hemodynamic response and BIS values to keep the depth of anesthesia between 40 to 60. A median sternotomy was made, heparin was given and a standard CPB with moderate systemic hypothermia (28°C to 30°C of nasopharynx temperature) was instituted. 70 minutes of cross-clamping with antegrade hypothermic Custodiol cardioplegia and 145 minutes of CPB were performed. Arterial blood gases (ABG) were within normal ranges. Propofol and remifentanyl infusions were continued during the CPB period maintaining the mean perfusion pressure above 60 mmHg. Anti-AChR antibody levels measured immediately after aortic cross-clamping and its removal were 1.55 nmol.L<sup>-1</sup> and 1.78 nmol.L<sup>-1</sup>, respectively. An additional dose of 10 mg rocuronium was administered during weaning from CPB at 36°C with a vasodilator and minimal vasopressor support. There were no diaphragmatic or other muscle movements throughout the procedure. At the end of the operation, the

remifentanyl infusion was stopped. The patient was transferred to the cardiovascular surgery Intensive Care Unit (ICU) with IV 1g paracetamol and continuous propofol infusion for sedation. The anti-AChR antibody level was 1.48 nmol.L<sup>-1</sup> at the postoperative first hour. At postoperative 8 hour, the train-of-four ratio (T4/T1) had reached 90% and T1 exceeded 95% of baseline. The patient returned to spontaneous breathing. He could lift his arms, open his eyes, and protrude his tongue for at least 5 seconds fulfilling the criteria for tracheal extubation in a myasthenic patient [5]. He was hemodynamically stable. Thus, extubation was performed. Sugammadex was not used. The next morning he received his normal MG treatment. Our patient was discharged to the ward on the third postoperative day. The patient, who had no problems during the follow-up period, was discharged from the hospital on postoperative day 8. Even after this invasive surgery, he did not show any signs of muscle weakness or myasthenic crisis.

## Discussion

The reports describing anesthetic management of patients with MG undergoing cardiac surgeries are limited. This case report discusses an uneventful course of a well-controlled MG Type I patient having coronary artery bypass grafting without prolonged postoperative mechanical ventilation.

In our cardiovascular ICU, we used to extubate the patients in the first 4 hours to 6 hours after the operation. For this patient, we decided to wait until he was conscious and reached a tidal volume of 5 ml.kg<sup>-1</sup> and a Train-of-Four (TOF) ratio > 90%. It took almost 8 hours. We didn't prefer sugammadex for reversal, because the patient was MG I and had a short history of the disease. Since we were already going to wait until the patient's hemodynamic stability was established, we didn't need shortening of the extubation time with sugammadex. Many factors may contribute to the exacerbation of MG complications postoperatively. Gritti et al. [6] emphasized that the preoperative presence of thymoma and lung diseases are important for a patient's prognosis. They reported that both the admission ratio to ICU and postoperative hospital stay significantly increased in the ones who had used neuromuscular blocking agents [6]. Most authors suggest the reversal of neuromuscular blockers with antagonists if used. They also suggest endotracheal intubation without using neuromuscular blockers [7]. In opposition to this wide spread opinion, we used rocuronium for intubation. We didn't want to cause any deleterious sympathetic and hemodynamic response due to endotracheal intubation in this patient. He had already poor cardiovascular reserve with obstructed coronary arteries. Such hemodynamic alterations could precipitate myocardial ischemia. Fortunately, new short-acting anesthetic drugs allow less aggressive hemodynamic changes and faster anesthesia recovery. Thus, for this patient, we reduced the dose of neuromuscular blocking agent by 75% and used total intravenous anesthesia.

It has been reported that preoperative bulbar and ocular symptoms

are related to poor prognosis and post operative myasthenic crisis [7]. The patient had neither of these symptoms. Although the patient's anti-ACh receptor antibody was not too high, we preferred to give intravenous immunoglobulin preoperatively by consultation with the neurologist. The concentration of anti-AChR antibodies declined slightly during CPB due to hemodilution. The postoperative value was lower than the preoperative value. In a trial, the authors reported that IVIG used in MG patients with worsening weakness was superior to placebo treatment. Although there is conflict about the efficacy of IVIG use in comparison to plasmapheresis, we preferred IVIG in this patient, as the cardiac on-pump surgery is by itself associated with volume changes, which is a disadvantage for plasmapheresis treatment. The IVIG infusion was given as a bridging therapy for preventing Myasthenic Crisis (MC) and protection against steroid-induced exacerbation. As both anesthesiologists and surgeons try to prepare the patient in the best optimized state for surgery, this regimen of treatment was applied in the view of a neurologist.

The stress of surgery and some drugs used perioperatively may worsen myasthenic weakness. Corticosteroids are commonly used immunosuppressant drug. As anesthesiologists are well-aware, steroids can produce many side effects. These include impaired wound healing, increased blood glucose, GI ulceration, osteoporosis, and increased infection risk. Patients who have been on chronic steroid therapy may need supplemental steroid doses to deal with the stress of moderate to major surgery, though this is a source of controversy.

The concentration of anti-AChR antibodies declined slightly during CPB due to hemodilution, so the postoperative value was lower than the preoperative value.

In this patient; propofol and fentanyl were used in anesthesia induction, with titrated doses of rocuronium combined with continuous neuromuscular monitoring. Anesthesia was maintained with remifentanyl and propofol infusion. No adverse events related to myasthenia were encountered perioperatively [8].

## Conclusion

It is crucial for anesthesiologists to provide good preoperative control and careful perioperative management of type I patients in MG rather than the choice of anesthetics, muscle relaxants, and reversal agents for a safe anesthetic follow-up in hypothermic cardiac surgery.

## Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. Informed consent was obtained for this publication.

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