Anesthetic management of a patient with Myasthenia Gravis for abdominal surgery.

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ABSTRACT

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This case report focuses on the anesthetic management of a patient with Myasthenia Gravis who underwent left-sided colectomy, due to the presence of a tumor on the left colic (splenic) flexure. Myasthenia gravis is a chronic autoimmune neuromuscular disease which is characterized by different degrees of weakness of skeletal muscles. The anesthetic management and treatment of every patient with myasthenia gravis should be performed carefully, due to the fact that many perioperative complications may occur. In our case anesthetic technique included the combination of general anesthesia, with the use of neuromuscular agent and thoracic epidural blockade with the use of a catheter, which permitted intermittent boluses doses and continuous infusion of local anesthetics and opioids. Neuromuscular blockade was reversed with the use of sugammadex. Patient's perioperative management was effective and uneventful.

INTRODUCTION

Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disease. It's main characteristic is the weakness and fatigue of skeletal muscles. It is the most frequent disorder of the neuromuscular junction. While it was thought that women were more affected than men, it is now known that males are more affected than females. It can occur at any age but is more common in people aged over 50. The prevalence of myasthenia gravis is 0.25 to 2 per 100000 population and its incidence is estimated at 3 to 10 per 100000 population[1,2].

Patients often experience diplopia (double vision) as the first symptom of myasthenia gravis and / or monolateral or bilateral eyelid

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dropping (ptosis) due to weakness of medial rectus, superior rectus andlevator palpebrae superioris complexrespectively[3]. Myasthenia Gravis usually develops gradually and patients experience more symptoms, including chewing, swallowing and talking disorders and progressively respiratory muscles weakness. One of the most representative characteristic of myasthenia gravis is the "hanging jaw sign", which is related with weakness of face muscles. The symptoms of myasthenia gravis worsen throughout the day.

The Myasthenia Gravis Foundation of America Clinical Classification divides Myasthenia Gravis into 5 main classes (Class I – only ocular muscle weakness to Class V – generalized muscle weakness and need for intubation) and several subclasses[4,5].

Myathenia Gravis is associated with the formation of autoimmune antibodies which destroy and block the function of acetylcholine receptors. Therefore, the neuromuscular stimulation is disrupted. 85% of patients with myasthenia gravis also present thymus disorders such as inflammation or thymoma[1].

Myasthenia Gravis is a challenging disease for neurologists to diagnose, as the symptoms are hard to distinguish from other neurological disorders (e.g. stroke). Tensilon test, intramuscular administration of neostigmine and electromyography may be useful in diagnosing myasthenia gravis. Some of the patients presenting with myasthenia gravis have certain antibodies which, when detected, can be useful in diagnosing the disease, such as antibodies against the acetylcholine receptor (AChR) and muscle-specific receptor tyrosine kinase (MuSK)[1,2].

In patients with myasthenia gravis, the use of specific drugs that block the neuromuscular junction is strictly prohibited. Aminoglycosides, d-penicillamine, antiarrhythmic drugs, beta blockers, muscle relaxants, barbiturates, benzodiazepines, contraceptive, neuroleptic and antiepileptic drugs (except for carbamazepine) are relatively contraindicated in myasthenia gravis[1].

Treatment of myasthenia gravis includes cholinesterase inhibitors, thymectomy, corticosteroids, immunosuppressant drugs, plasma exchange and intravenous immuneglobins (IVIG)[2].

Surgical procedures, along with other triggering factors such as respiratory infections, may cause a myasthenic crisis. Myathenic crisis presents with generalized muscle weakness and inability of the patient to breath, which inevitably results in intubation and transfer of the patient to the ICU[1].

The surgical and anesthetic management of every patient who presents myasthenia gravis should be performed carefully, due to many severe perioperative complications that may occur, including cholinergic crisis and death.

The use of neuromuscular blocking agents is susceptible and is probably the main challenge of the anesthetic management of a myasthenic patient, since the neuromuscular junction in these patients is more sensitive to these drugs. The most acceptable anesthetic approach in myasthenic patients is to completely avoid the use of neuromuscular blocking drugs. Most anesthesiologists prefer to use inhalational induction of anesthesia with volatile anesthetics, which provide neuromuscular blockade in a small degree. However, in abdominal surgeries the use of neuromuscular blocking agents is compulsory in order to optimize surgical conditions. The use of sugammadex, a γ-cyclodextrin with a high affinity to rocuronium and other amino-steroidal neuromuscular blocking drugs that allows the rapid and complete reversal of especially rocuronium-induced neuromuscular blockade, may help the anesthetic management of these patients[6].

CASE REPORT

A 62 year old white male patient was scheduled for left-sided colectomy due to a tumor located in the left splenic flexure. The patient's height was 175 cm and weight 72 kg (BMI=23.5). He had been treated for myasthenia gravis (Osserman class II) since 2014. His first symptoms of myasthenia gravis were swallowing and talking disorder, the "hanging – jaw sign". He also did not presented any alterations of the thymus gland. The muscle-specific receptor tyrosine kinase (MuSK) antibodies were found negative, however, antibodies against the acetylcholine receptor (AChR) were found positive, which added in the confirmation of the diagnosis. His treatment included 50mg azathioprine per day, 10mg prednisolone (every other day), combined with 60mg pyridostigmine. Additionally, the patient received immunoglobulins intravenously (IVIG) one week before surgery. It must be noted that the patient had not experienced any myasthenic crisis after the diagnosis and since then the disease was in complete remission.

His medical history included also benign hypertrophy of the prostate gland for which he was receiving treatement (10mg alfuzosin). There was no history of other systemic diseases, smoking or alcohol consumption. He reported that he underwent laparoscopic cholocystectomy 8 years ago, with no perioperative complications. Physical examination showed a mild generalized muscle weakness. No respiratory problems were reported, while ECG, laboratory and screening tests were normal. The patient was considered to be in the optimum condition prior to surgery, with no absolute contraindications to the operation.

The patient was scheduled for surgery under general endotracheal anesthesia (ASA class III). He did not receive any premedication, as ben-

zodiazepines are contraindicated in myasthenic patients[1].

Upon arrival at the operation room standard monitoring that consisted of ECG 3-lead continuous recording, noninvasive blood pressure measurement, pulse oximetry and Bispectral index monitoring in order to assess the depth of anesthesia was connected to the patient. Venous access with an 18G catheter and invasive blood pressure measurement were also established and 20 mL/kg/hr Ringer's Lactated solution was administered prior to anesthesia induction. An epidural block was performed in the sitting position via median approach at the thoracic level (T10-T11) with the use of a catheter that would allow intermittent bolus doses and continuous infusion of local anesthetics and opioids at the epidural space. Patient received a total dose of 5ml lidocaine epidurally, which produced anaesthesia of T_{4-12}segments.

Anesthesia induction was obtained with fentanyl 2γ/Kg, lidocaine 1 mg/kg, propofol at 2,5 mg/kg and rocuronium 0,6 mg/kg. Endotracheal intubation was done without difficulty using 8mm cuffed endotracheal tube by direct laryngoscopy after 90 seconds. With laryngoscopy, the laryngeal view score by Cormack and Lehane was two. Five minutes after, 5ml of Ropivacaine 7,5% were administered through the epidural catheter. Additionally, 2ml of Ropivacaine 7,5% were also administered ten and twenty five minutes after the anesthesia induction. General anesthesia was maintained with the use of Desflurane 6% in order to achieve a MAC of 1.0 and continuous infusion of remifentanyl (100μg/h) was delivered. Doses of anesthetic agents were modified according to the clinical assessment of the depth of anesthesia. Thirty minutes before the end of surgery, a 24-hour continuous epidural infusion of Ropivacaine 0,2% and Morphine 4mg was initiated.. Other drugs administered to the patient throughout surgery were 500 mg methylprednisolone, 2 gr cefoxitine, 50 mg ranitidine and 4 mg ondansetrone mg.

During anesthesia, the patient's mechanical ventilation parameters were the following: Tidal Volume 7,5ml/Kg, Respiratory Rate 12 breaths and FiO_2 0.45 and PEEP 5 cmH_2O. The operation lasted two and a half hours. The patient was operated in the supine position through the entire procedure and remained hemodynamically stable during surgery. The patient's vital signs during surgery are shown in table 1.

Emergence from anesthesia was initiated at the time of placement of the final skin sutures. A peripheral nerve stimulator was used and Train of Four (TOF) test was performed in order to assess the depth of neuromuscular blockade. By visual assessment four responses to TOF stimulation were observed in the adductor pollicis muscle. Sugammadex was then administered (2mg/Kg) for neuromuscular blockade

reversal. Seven minutes later, the patient breathed regularly and opened his eyes to verbal command. The tidal volume measured by a spirometer and level of consciousness was adequate and the patient was extubated.

Table 1. Patient's vital signs during surgery

PARAMETERS	HR (bpm)	MAP (mm Hg)	BIS (%)
Anesthesia induction	75	90	96
Start of surgery	72	77	45
15 min after surgery	75	67	45
30 min after surgery	85	68	51
45 min after surgery	60	73	44
60 min after surgery	63	62	40
75 min after surgery	60	59	40
90 min after surgery	58	66	45
105 min after surgery	55	67	46
120 min after surgery	65	65	58
End of surgery	80	85	58
Extubation	86	103	93

HR:heart rate, MAP: mean arterial pressure, BIS: bispectral index.

Afterwards the patient was transferred to the recovery room with oxygen through a facial mask. There he complained for postoperative nausea and vomiting and received 8 mg dexamethasone. The patient's respiratory function, hemodynamic status and pain scores were continuously evaluated. The patient stayed in the recovery room for one hour before being transferred to the general surgery department.

In the postoperative period no respiratory or hemodynamic complications were detected and the patient did not receive additional analgesics. The epidural catheter was removed two days after surgery and finally the patient was discharged from hospital six days later.

DISCUSSION

Anesthetic management of patients with myasthenia gravis who undergo surgery is challenging for the anesthesiologist, due to the great risk of intraoperative and postoperative complications, including cholinergic crisis and severe postoperative respiratory failure. The lack of formal perioperative recommendations adds to the difficulties in taking good anesthetic the care of these patients[7].

Preoperatively, the anesthesiologist should focus on bulbar and respiratory symptoms, on the evaluation of the muscles affected and also on a neurological assessment that should be should be obtained. Preoperative pulmonary function tests may be necessary as a reference to determine the optimal conditions for extubation postoperatively as well as the need for postoperative mechanical ventilation[8]. Prior history of exacerbations or myasthenic crisis should also be considered. Additionally, in

preoperative visit the anesthesiologist should also be informed about the medication prescribed to the patient, including cholinesterase inhibitors or medication for another autoimmune disease (such as hypothyroidism)[8].

The myasthenic patients are typically sensitive to nondepolarizing neuromuscular blockers and there is always the risk of the residual neuromuscular blockade. Although the use of neuromuscular blocking agents is still controversial in myasthenic patients, intermediate and short-acting nondepolarizing agents can be used with careful monitoring of neuromuscular transmission[8]. Therefore many anesthesiologists titrate the doses of non-depolarizing muscle relaxants, whereas others prefer to use inhalational techniques with a volatile anesthetic agent because it is known that inhaled anesthetics may cause muscle relaxation in normal patients and this effect may be profound[8].

Sugammadex is a neuromuscular reversal drug, which reverse neuromuscular blockade with the aminosteroid non-depolarizing muscle relaxants rocuronium and vecuronium. The use of sugammadex, allows the rapid and complete reversal of especially rocuronium-induced neuromuscular blockade and may help the anesthetic management of myasthenic patients[7,8]. It is well known that sugammadex shortens the time of extubation and optimizes the respiratory drive of the patients. Six case reports in patients with myasthenia gravis documented the successful use of sugammadex[9]. However there are still not enough data of the use of sugammadex for the reversal of neuromuscular blockade to these patients. Therefore the anesthesiologist should keep in mind that even with the use of the suggested dose of sugammadex, there may be a possibility of residual muscle blockade. A neurostimulator and Train of Four (TOF) test must be used to assess the neuromuscular blockade of these patients[10-12].

This case report focuses on a patient who presents a mild form of myasthenia gravis (Osserman Class II) which had affected only the muscles of the eye. Sensitivity to nondepolarizing agents has been described in patients with minimal disease (i.e., ocular symptoms, like our patient), in those in apparent remission, or those with subclinical undiagnosed myasthenia[8]. Other studies have shown that, even if the symptoms of myasthenia gravis appear to isolated muscles of the patient, other muscles may also be affected subclinically, therefore the reversal of neuromuscular blockade should be obligatory[3]. That is the reason why although we had a visual assessment four responses to TOF stimulation, the neuromuscular blockade of our patient was reversed with sugammadex.

Several general anesthetic techniques have been proposed, although none has been proven to be superior to the others in patients with myasthenia gravis. Another anesthetic option

for myasthenic patients undergoing surgery is regional anesthesia, (epidural, spinal anesthesia or other forms of nerve blockade). When anesthesiologists prefer regional anesthesia over general anesthesia, the need for benzodiazepines, opioids and neuromuscular blocking agents (NMBA) may be avoided. Especially, epidural anesthesia offers a better postoperative pain control and respiratory function, and can minimize the need for NMBA during surgery[8]. However the combination of general-epidural anesthesia, as presented in our case report, could be an alternative for myasthenic patients for whom neuromuscular blockade is mandatory during surgery, as it reduces the need for neuromuscular blocking agents and opioids and provides optimal surgical conditions[13].

In conclusion we have effectively used the combined anesthetic technique of general and epidural anesthesia in a myasthenic patient who underwent abdominal surgery. We also used sugammadex in order to reverse rocuronium-induced neuromuscular blockade. Sugammadex, used in combination with objective neuromuscular monitoring, can be applied to reverse neuromuscular blockade in patients with myasthenia gravis.

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