Perioperative Management of Myasthenia Gravis Patient for off Pump Coronary Artery Bypass Surgery and Thymectomy

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ABSTRACT

Myasthenia gravis (MG) is an autoimmune disorder characterized by antibody-mediated immunologic reaction striking the acetylcholine receptors. The anesthesia concerns for patients with MG include the disease state, drug interactions, and the anesthetic medications particularly the neuromuscular blocking agents (NMBAs). The anesthesia management in these patients is meticulous and requires appropriate execution of knowledge. Besides, such patient for off-pump coronary artery bypass surgery is quite uncommon; hence, we report this case.

Keywords: Anesthesia, myasthenia gravis, myasthenic crisis, off pump coronary artery bypass surgery, thymectomy

INTRODUCTION

Myasthenia gravis (MG) is a disease with enormous implications for the safe conduct of anesthesia and perioperative management. Anesthesiologists should be familiar with the myasthenic disease and the interaction between the anesthetic and nonanesthetic drugs along with the susceptibility to postoperative mechanical ventilation issues in these patients. The execution of strategies regarding usage of muscle relaxants should be precise. They may need prolonged mechanical ventilation owing to the residual muscular blockade or even worsening of myasthenic disease itself.1 Thymectomy is a surgical procedure commonly undergone by these patients.2 and the case reports of MG patients for thymectomy state that the procedure ameliorated both hyperthyroidism and MG.3 We could not find the case report of MG patient for off-pump coronary artery bypass surgery (OPCAB) to the best of our knowledge, although cases of on-pump CABG in a patient with MG4 have been published.

CASE HISTORY

A 67-year-old male patient with a known case of MG was posted for OPCAB with thymectomy. He had diabetes mellitus and hypertension since 10 years and was on treatment for the same. He was not diagnosed of thymoma. Although significant ptosis was present, he was in a stable state of disease and was on tablet pyridostigmine 60 mg thrice a day (tds), tablet azathioprine 50 mg twice a day for MG. His past history was significant as he was diagnosed of MG 10 years back and before 4 years, he had an episode of myasthenic crisis with bulbar dysfunction presented as poor swallowing and cough. Treatment with intravenous immunoglobulins (IVIgG) was given then. Now, he had non-ST elevation myocardial infarction (NSTEMI) for which OPCAB was planned.

His investigations were within normal limits including the pulmonary function test (PFT). Antibody titer was not done as per Neurologist’s opinion. Angiography revealed...
normal left main coronary artery, left anterior descending artery midpart 90% eccentric lesion, and right coronary artery dominant with proximal to midpart 90% long tubular lesion. Echocardiography showed concentric left ventricular hypertrophy, hypertensive heart disease, no regional wall motion abnormalities, good biventricular function with ejection fraction of 55% and grade I diastolic dysfunction.

Preoperative management was carried out meticulously. Patient was posted as first case and the morning dose of pyridostigmine was not given so as to avoid larger induction doses of neuromuscular blocking agent (NMBA), atracurium. Preinduction arterial blood gases (ABG), serum electrolytes, and blood sugar levels were normal.

Anesthesia management
Our patient weighed 82 kg. Drugs given were Inj Midazolam 1 mg intravenous (iv), Inj Fentanyl 150 mcg + 50 mcg iv, Inj Etomidate 8 mg iv [0.1 mg/kg], and Inj Atracurium 35 mg iv [<0.5 mg/kg] at 9:35 am. Isoflurane inhalation was started simultaneously, intubated with appropriate size endotracheal tube, and ventilated. Since neuromuscular monitoring was not available slight respiratory efforts were recognized as indication for further dose of neuromuscular blocker. Inj Atracurium 10 mg iv was given at 10:45 am, repeated 5 mg iv at 1:10 pm, and again 5 mg iv was given at 1:50 pm. Inj Fentanyl 50 micrograms was given only once intraoperatively. Inhalational agent isoflurane was given throughout the procedure. Inj Nitroglycerine and Inj Noradrenaline were required in minimal doses. Inj potassium was given as per required and Inj magnesium was avoided. Blood sugar levels were tightly controlled. ABG done and corrected as per required. Fluids, blood loss, and urine output all were meticulously managed.

Postoperative management
The patient remained hemodynamically stable and the immediate postoperative ABG was within normal limits. Neuromuscular blockade was reversed with Inj Neostigmine 3.75 mg [<0.05 mg/kg] and Inj Glycopyrrolate 0.5 mg given intravenously. Patient was extubated in 6 h after shifting to intensive care unit. On postoperative day 1 tablet pyridostigmine was started 60 mg tds and on day 2 Inj Cordarone 300 mg bolus iv received for atrial fibrillation which then settled.

DISCUSSION
MG is an autoimmune disorder with antibodies against the acetylcholine receptors characterized by fatigable weakness of skeletal muscles. Weakness results from decrease in the number of functional acetylcholine receptors in postsynaptic membranes of neuromuscular junctions.[8]

The myasthenic patient poses a challenge to anesthesiologists regarding the preoperative and intraoperative management. Furthermore, the postsurgical risk of respiratory failure is also a matter of concern that needs to be dealt with.[9]

One of the fundamentals of managing the MG patient successfully is, the elective surgery should be performed during the stable phase of the disease, when the patient requires minimal immunomodulatory medication to minimize the chance of postoperative myasthenic crisis. Also, surgery should be scheduled as early as possible in the day, when the patient is strongest. Anesthesiologist needs to take into account the bulbar symptoms like dysphagia, dysarthria, nasal speech, low-intensity speech which predisposes the patient to aspiration, history of myasthenic crisis, respiratory muscle weakness, and dyspnea. These patients may have myocarditis causing cardiomyopathy, atrial fibrillation, or heart block. The MG therapy, associated diseases, and any other autoimmune diseases like thyroiditis should also be taken into consideration.

In the patients with MG, the postoperative mechanical ventilation can be predicted by several parameters like the duration of the disease >6 years, presence of any lung disease, past history of myasthenic crisis, PFT reporting the vital capacity <2.9 L and the requirement of the dosage of pyridostigmine >750 mg/day. Hence, a preoperative lung function assessment is of utmost importance.[4] Our patient had two criteria among the criteria mentioned for prediction of postoperative myasthenic crisis which were duration of MG (>6 years) and history of myasthenic crisis.

The PFT should be carried out preoperatively especially when general anesthesia with NMBA is planned to help establish a baseline protocol for ventilation and extubation and to facilitate in planning the level of postoperative care.

The anesthesiologist should be acquainted with the treatment modalities of MG such as the symptomatic treatment is with the anticholinesterase agents. The other drugs these patients might be on are as follows:

- The chronic immunomodulating drugs such as glucocorticoids and other immunosuppressants. Patients on glucocorticoids are at risk for hypothalamic-pituitary axis suppression and adrenal insufficiency in the perioperative period. Therefore they may require administration of stress-dose glucocorticoids. While for the patients who are currently taking glucocorticoids, it is advisable that they...
should take their usual daily dose of glucocorticoid or the parenteral equivalent should be prescribed to them.

- The immunotherapy drugs like azathioprine, cyclophosphamide, cyclosporine, methotrexate, mycophenolate mofetil, rituximab, and tacrolimus. The morning dose of these drugs can be held given the long duration of effect they provide.

- Also, the rapid immunomodulating treatments like the plasmapheresis and IVIgG may be required in some of the myasthenic patients. These are rapid therapies with immediate action over days, but the benefits they offer are only short-term up to weeks. Albeit, it is useful in the following situations:
  - Preoperatively before thymectomy or other surgery.
  - As a bridge to slower-acting immunotherapies.
  - During myasthenic crisis.
  - Periodically to maintain remission in patients not well controlled otherwise.
  - Lastly, the patients refractory to conventional therapy receive monoclonal antibodies.

General anesthesia considerations

- The main goal of anesthetic management is to prevent prolonged effects of drugs on respiratory and bulbar muscles and allow rapid recovery at the end of surgery.

- Use of short-acting sedatives, hypnotics, and anesthetic agents to minimize respiratory depression on emergence from anesthesia is the mainstay.

- In premedication, the smallest effective dose should be titrated while monitoring signs of bulbar weakness and respiratory compromise. Intravenous anesthetics also should be titrated to effect during induction and maintenance of anesthesia.

- Continuation of anticholinesterase agents is a matter of preference depending upon the patient’s condition. If continued till the morning of surgery, the response to both depolarizing and nondepolarizing NMBAs may be modified by these medications.

- Furthermore, the response to reversal agents may be unpredictable or insufficient. Neuromuscular effects of muscle relaxants vary greatly in these patients hence neuromuscular monitoring should be used. On the contrary, patients may even be sensitive to discontinuation and develop respiratory and bulbar weakness. Therefore, it is advisable to be cautious in this regard.

- Important aspects of depolarizing NMBAs in MG patients is that these patients are resistant to neuromuscular blockade with depolarizing NMBAs (succinylcholine) as they have decreased number of acetylcholine receptors. Because succinylcholine is metabolized by plasma cholinesterase, treatment with anticholinesterase medication (pyridostigmine) may prolong the effect of succinylcholine. Furthermore, they are at higher risk of development of phase II neuromuscular block with repeated doses of succinylcholine.

- Regarding the nondepolarizing NMBAs—MG patients are extremely sensitive to nondepolarizing NMBAs (rocuronium, vecuronium, cisatracurium). Even small doses and residual drug effect may result in respiratory distress or loss of airway protection after emergence from anesthesia. They should be administered in incremental and minimal doses titrated to effect. The neuromuscular monitoring is essential while administering general anesthesia to avoid the prolonged neuromuscular blockade in them and also for the fact that they are more sensitive to the relaxant effect of volatile anesthetics.

- Sugammadex has been used safely for the reversal of steroidal NMBAs such as vecuronium and rocuronium with no issues of cholinergic crisis. It reverses blockade in patients with MG within four minutes. The reversal with neostigmine for nondepolarizing NMBAs is unpredictable especially in the patients who are on anticholinesterase medication previously. Therefore, it should be titrated to effect to avoid a cholinergic crisis.

Anesthesiologists should be aware of the myriad of factors that can worsen MG. It is important to distinguish between the myasthenic crisis and the cholinergic crisis as their treatment is totally different. Myasthenic crisis treatment is neostigmine while cholinergic crisis occurs due to neostigmine.

The myasthenic crisis

It has certain peculiarities such as weakness of the respiratory muscle and/or bulbar muscles which severe enough to call for intubation or to delay the extubation. The main precipitants of this type of crisis are surgical stress, infection, residual anesthetics, withholding MG medications, few medications known to exacerbate MG like aminoglycosides, magnesium, beta-blockers, calcium channel blockers. The crisis is characterized by weakness of respiratory and bulbar muscles while the signs of impending crisis are dysphagia, change in phonation, weak cough, oral secretions. These patients will get improved with edrophonium. In case of myasthenic crisis, never hurry for extubation. Also, urgent rapid therapy with plasma exchange or immunoglobulins can certainly be done in them.

The cholinergic crisis

Patients who receive anticholinesterases are at risk for this type of crisis. The two crises are distinguished by
edrophonium test which improves symptoms if myasthenic crisis and worsens symptoms if cholinergic crisis. The symptoms of cholinergic crisis are described using the acronym “SLUDGE”: Salivation, lacrimation, urination, defecation, gastrointestinal distress, and emesis. It should always be noted that prolonged paralysis can occur in a cholinergic crisis. Further anticholinesterase should be withheld. The treatment comprises endotracheal intubation, Inj atropine and holding the cholinesterase inhibitors.[9]

CONCLUSION

MG patient for OPCAB is challenging as along with managing the OPCAB surgery and hemodynamics, explicit management of the myasthenic disease also needs to be carried out simultaneously. The postoperative period is still more challenging from respiratory, hemodynamics and muscle power, point of view.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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