Case Report

Dilemmas of an Anesthesiologist to assure a patient with Myasthenia Gravis safely walks the tightrope through the peri-operative course.

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Abstract

Background: Myasthenia gravis [MG] is an autoimmune disorder of neuromuscular transmission. A significant percentage of patients diagnosed with this disease benefit from thymectomy. It poses unique peri-operative challenges to the anaesthesiologists. **Case:** A 27 year old male diagnosed with MG-stage III, on Pyridostigmine, Azathioprine & Methylprednisolone, was posted for thoracoscopic thymectomy. This case report documents our experience about managing the patient's ongoing treatment peri-operatively, judicious use of neuromuscular blockers assisted by neuromuscular & bis monitoring; management of intra-operative complications such as ventricular tachycardia and continuously rising end tidal carbon dioxide. Reversal of the neuromuscular blockade was guided by monitoring the train of four count / ratio.**Conclusion:** The perioperative concerns include-Assessment of Airway & respiratory muscle strength, implications of superior mediastinal mass, managing the neuromuscular blockers intra-operatively & identifying the risk factors to decide the need of postoperative ventilation. Neuromuscular monitoring is an absolute must.

Keywords: Myasthenia gravis; thymectomy; thoracoscopic surgery; Acetylcholine receptors; mechanical ventilation; neuromuscular blocking agents

Introduction

Myasthenia gravis is an uncommon autoimmune neuromuscular disorder presenting with varying degrees of muscle weakness. Thymectomy is indicated to achieve remission in a significant proportion of these patients. Perioperative management brings forth several issues to deal with.Maintaining optimum neuro-muscular function is a fine balancing act, requiring cautious adjustment of drug doses and avoiding drugs / triggers that may worsen the myasthenic or cholinergic crisis. The neuromuscular blocking agents are best avoided or used judiciously. It is of utmost importance to identify the risk factors that predict the need of post-operative mechanical ventilation.

Case report

27 year old male, weighing 70 kg and height of 168 cm, was diagnosed with MG four months back. His symptoms improved with tab Pyridostigmine 240 mg/day, Azathioprine 50 mg BD and Methylprednisolone 4 mg BD with no history of ICU admission, plasmapheresis or immunoglobulin administration. His investigations revealed positive Acetylcholine receptor antibody test[AchR]. His pulmonary function test [PFT] showed FVC of 3.82 L, FEV1/FVC-81.9 & FEF 25/75-3.29. Routine blood investigations, thyroid profile, ECG, 2D-ECHO & X-Ray Neck were normal. His CECT thorax showed left anterior mediastinal lesion that measured 4.4 cm x 3.4 cm x 1.7 cm, but trachea and bronchi were normal.His steroid was continued and pyridostigmine was omitted on day of surgery. Preoperatively, patient was nebulised with 4% lignocaine to prevent response to passage of double lumen endotracheal tube (DLT).In OR, monitoring included ECG, NIBP, SPO2, neuromuscular monitoring, temperature, ETCO2, gas analysis, BIS monitoring & urine output. His baseline vitals were: HR - 54/min, BP: 120/70 mm Hg, ECG was normal, SpO2-100% on room air. Preoperatively, he was given Inj Atropine intra-muscularly. Two 18 gauge iv cannulae were secured and he was premedicated with Inj Pantoprazole, hydrocortisone 200 mg, Midazolam 1 mg and Fentanyl 50 micrograms iv slowly. Patient was induced with Inj Propofol 80 mg and Sevoflurane increased to 4%. At this point, TOF count was 2. Laryngoscopy was attempted & cords sprayed with 10% Lignocaine, cords were relaxed. Trachea was intubated with 37 F left sided DLT, without using NMBA. Position of DLT confirmed with fiberoptic bronchoscope. Anaesthesia was maintained with Oxygen: Nitrous Oxide 60:40 + Sevoflurane at MAC of 1.2-1.4. 50 micrograms Fentanyl was repeated. Intraoperatively, TOF ratio went up to 0.7 & patient started breathing spontaneously. Inj Atracurium 10 mg was given and TOF count reduced to zero.Intraoperatively, there were two episodes of non sustained ventricular tachycardia without hemodynamic compromise while working around heart. But it stopped as soon as surgeon stopped manipulation around heart. During extraction of thymoma, patient was in lighter plane of anaesthesia [BIS - 70 and showed TOF ratio of 0.8], which settled with increase in Sevoflurane concentration and Inj Propofol 20 mg. TOF ratio reduced to 0.4 and BIS to 50. Procedure was uneventful and lasted for 120 minutes.Inj Diclofenac 75 mg and Inj Paracetamol 1 gm was given intravenously with local port site infiltration for postoperative

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analgesia.Towards end, TOF ratio continued to come up, as Sevoflurane was gradually reduced. When patient started breathing spontaneously and TOF ratio was 0.6, reversal was achieved with Neostigmine 1.5 mg intravenously and TOF ratio came up to 1. The patient opened his eyes spontaneously and moved all limbs, TV was 350 ml, inspiratory pressure-30 cm H2O, RR 16/min and regular; trachea was extubated and patient was shifted to PACU. His pyridostigmine, azathioprine and methylprednisolone were resumed. Patient was followed up for five days with no complications reported.

Discussion

MG is autoimmune disorder of skeletal muscle neuromuscular junctions that is caused by antibodies against nicotinic AchR. More than 70% of these patients have thymus hyperplasia and about 10% have thymomas[1,2]. It is commonest disorder of neuromuscular transmission, with prevalence of 150 to 250 per million[1].

It usually presents with ocular symptoms and progresses to bulbar involvement and skeletal muscle weakness. It worsens with activity and improves with rest. Association of muscle weakness with AchR antibodies confirms diagnosis. American MG Foundation has classified MG in stages [Table1].

Different treatment modalities described in literature include pyridostigmine for symptomatic management, plasmapheresis and immunoglobulin for rapid/bridging therapy and immuno-modulators. Thymectomy is indicated for thymomas and thymic hyperplasia [3,4].

Pre-operative concerns include assessing the patient's ability to protect and maintain airway [Bulbar involvement] and avoidance of myasthenic and cholinergic crisis by optimizing neuromuscular transmission. Risk factors that can exacerbate MG peri-operatively includes infection, fatigue, medications including antibiotics, type of surgery, preoperative bulbar symptoms and opioids[5,6]. The respiratory muscle strength can be evaluated with the help of PFT. As thymoma is an anterior mediastinal mass, tracheal compression, deviation and vascular compression needs to be assessed using CT thorax. Maximum inspiratory and expiratory flow volume loops with the patient in supine and upright position will serve as a guide for any respiratory compromise. Also it will be helpful to know whether the obstruction is fixed or dynamic.

Autoimmune diseases associated with MG are rheumatoid arthritis, autoimmune thyroiditis, SLE , polymyositis and blood cytopenia [7]. Hypothyroidism is likely to exacerbate symptoms of MG.It is imperative to rule out hypertension, deranged blood sugar and osteoporosis in patients who are chronically on steroids.

Besides,they often need peri-op steroid supplementation.

If patient is on Azathioprine, CBC and liver functions need to be monitored. Hypokalemia exacerbates muscular weakness and should be checked.These patients are on anticholinesterases, which is likely to cause bradycardia, salivation and alter effects of NMBA. There is often dilemma, whether anticholinesterases should be continued or not, peri-operatively. If symptoms are mild, preferably discontinue them, as these drugs increase susceptibility to vagal arrhythmias and increase need of NMBA. They also prolong duration of action of Succinylcholine. But when patient is dependent on these medications, it is advisable to continue anticholinesterases peri-operatively.

It is best to use sedatives, anxiolytics and opioids in a titrated manner as these patients are sensitive to their respiratory depressant effects. Intra-operatively, monitoring should include ECG, BP, SPO2,temperature &ETCO2. Invasive BP may be considered depending on the likelihood of intra-operative haemodynamic fluctuations and need for monitoring ABG. Neuromuscular monitoring is mandatory,irrespective of whether NMBA is being used or not. Hyperthermia may cause muscle weakness hence normothermia is preferred[8].

Intraoperatively, opioids should be used cautiously. It would be better to use regional anaesthesia technique, wherever possible, in order to avoid risk of prolonged duration mechanical ventilation. Awake thymectomy under thoracic epidural anaesthesia have been conducted for trans-sternal approach[9]. Thoracoscopic thymectomy is usually done using DLT under general anaesthesia; where spontaneous ventilation is not advisable. Hence small doses of NMBA are needed to facilitate mechanical ventilation[10].

However, NMBAs are rarely required for laryngoscopy and intubation,if patient is adequately anaesthetized and deeper plane of anaesthesia assured.Two factors influence management of NMBA - inherent disease itself and treatment with anticholinesterases. Those not receiving anticholinesterases usually need larger than normal doses of succinylcholine, due to decreased number of functional AchR; whereas those on anticholinesterases have decreased plasma cholinesterase activity and hence, decreased succinylcholine metabolism, thereby resulting in prolonged neuromuscular block, from 4 to 87 minutes, leading to phase II block. On other hand, reduced AchR increase their sensitivity to non-depolarising NMBAs. Hence, giving it in small increments corresponding to 10 to 20% of the ED95 until desired effect is achieved is recommended. Also it would be wise to use intermediate and shorter acting NMBA. All sources of potential error including neuromuscular monitoring should be verified by verifying proper functioning of the device as well as appropriate site selection.Maintenance of anaesthesia may be planned as - Oxygen + Nitrous + Inhalational agent ± iv anaesthetic infusion ± Intermediate/short acting NMBA. Amongst inhalational agents, Sevoflurane as well as Desflurane can be used. However, Sevoflurane is preferred due to lower incidence of airway events and because, it depresses EMG response, when used in more than one MAC. Complete reversal of neuromuscular blockade can be achieved using Sugammadex, with no risk of cholinergic crisis. However lack of strong evidence for its routine use in MG patient and its cost and availability makes it unlikely first choice[11,12]. Extubation should not be planned until patient is awake and responsive, strong & negative inspiratory force is at least -30 cm H2O.Maintenance of anaesthesia may be planned as - Oxygen + Nitrous + Inhalational agent ± iv anaesthetic infusion ± Intermediate/short acting NMBA. Amongst inhalational agents,Sevoflurane as well as Desflurane can be used. However, Sevoflurane is preferred due to lower incidence of airway events and because, it depresses EMG response, when used in more than one MAC. Complete reversal of neuromuscular blockade can be achieved using Sugammadex, with no risk of cholinergic crisis. However lack of strong evidence for its routine use in MG patient and its cost and availability makes it unlikely first choice[11,12]. Extubation should not be planned until patient is awake and responsive, strong & negative inspiratory force is at least -30 cm H2O.Post-operatively, full medical regimen for MG is restarted immediately and continued till remission which takes months to years. In case of post-operative weakness, differential diagnosis includes Myasthenic crisis, residual effects of anaesthetic drugs, non-anaesthetic drugs interfering with neuromuscular transmission and cholinergic crisis. Cholinergic crisis will present with SLUDGE i.e. increased salivation, lacrimation, urinary frequency, diarrhea, vomiting, needing anti-cholinergic and respiratory support while myasthenic crisis presents with respiratory insufficiency needing ventilatory support. Severity of disease, anti-AchR antibodies, history of myasthenic crisis, vital capacity < 2.9 L and presence of thymoma are independent risk factors for predicting need of postoperative ventilation[13].Postoperative

analgesia can be managed with regional anaesthesia techniques and multimodal analgesia.To sum up, pertinent perioperative concerns include-Assessment of Airway and respiratory muscle strength, understanding implications of superior mediastinal mass, knowledge about drug interactions with disease process and implications of drugs used for management of MG. It is best to avoid depolarising NMBA. If at all needed, non-depolarising shorter acting NMBA must be used cautiously in increments of 10-20% of ED95. Neuromuscular monitoring is an absolute must. And finally preoperative treatment must be resumed as early as possible, post operatively.

Table 1: Myasthenia Gravis foundation of America classification

Stage	Clinical Status
I	Only ocular movement
II	Generalized mild muscle weakness IIa: Limb and axial muscles IIb: Bulbar involvement or respiratory weakness
III	Generalized moderate muscle weakness IIIa: Limb and axial muscles IIIb: Bulbar involvement or respiratory weakness
IV	Generalized severe muscle weakness IVa: Limb and axial muscles IVb: Bulbar involvement or respiratory weakness
V	Tracheal intubation or mechanical ventilation

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