

TOP 10 FACTS

Top ten facts you need to know about anesthetic management of Myasthenia gravis patients

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Keywords: Myasthenia, general anesthesia, anesthetic medications, myasthenic crisis, cholinergic crisis.

<https://doi.org/10.67225/001c.129850>

Journal of the Mississippi State Medical Association

Vol. 65, Issue 11/12, 2024

Myasthenia gravis (MG) is a neuromuscular disorder related to autoimmune mechanisms that produce antibodies directed against acetylcholine receptors at the neuromuscular junction. It leads to impairment of neuromuscular transmission, which leads to weakness of muscles (visual disturbances, difficulty breathing, swallowing, motor weakness of extremities). The course of MG is often variable; the patient's symptoms may deteriorate when they are exposed to stress, infections, surgery, pregnancy, and medications (antibiotics, anesthesia medications). In this article, we would like to discuss the top ten facts about anesthetic management of myasthenia gravis patients.

Introduction

Myasthenia gravis (MG) was described in the 17th century when Thomas Willis, an Oxford physician, recognized it in a patient with generalized muscle weakness that improved with rest. However, London physician Samuel Wilks gave the modern description in 1877. Anesthetic management of patients with MG is challenging, related to the disease itself, medications to treat the condition, and anesthetic medications that interfere with neuromuscular function.¹

1. Myasthenia gravis is an autoimmune disorder in which autoantibodies target acetylcholine receptors, disrupting their activation. Specifically, the antibodies target the α -subunit of the nicotinic acetylcholine receptor (AChR) at the neuromuscular junction.
2. Over 85% of patients have antibodies against the acetylcholine receptors, and the remaining patients have antibodies against other proteins at the postsynaptic terminal, such as muscle-specific tyrosine kinase (MuSK) or lipoprotein-related protein 4 (LRP4). About 5% of patients have no detectable antibodies.² ([Table 1](#))
3. Myasthenia gravis initially presents with diplopia, ptosis, dysarthria, fatigue, and proximal limb muscle weakness. Though any muscle can be affected, patients classically have

bulbar symptoms and suffer from proximal limb muscle weakness that worsens with activity.³ ([Table 2](#)) 20-30% of patients will have a myasthenic crisis in the course of their disease that results in profound muscle weakness, respiratory failure, and cardiac abnormalities such as left ventricular diastolic dysfunction, atrial fibrillation, focal myocarditis, or atrioventricular (AV) conduction delays.

4. Diagnosis is primarily based on clinical history, serodiagnostic testing, physical exam, and electrodiagnostic testing. Treatment of myasthenic crisis includes cholinesterase inhibitors (e.g., pyridostigmine), corticosteroids, intravenous immunoglobulin, and plasmapheresis.
5. Preoperative assessment of Myasthenia patients includes determining which muscle groups are involved, the recent disease course, medications, and associated medical problems. Patients with myasthenia class III to V with moderate to severe pulmonary and bulbar involvement are at increased risk of aspiration.³ These patients were treated with proton pump inhibitors and prokinetic agents (Metoclopramide). The patient should continue the medications (pyridostigmine, steroids) to reduce the chances of worsening symptoms. Preoperative lung function tests and other blood tests are recommended for these patients.
6. Local and regional anesthesia is recommended for MG patients when possible. Amide local anesthetics (LAs) were chosen over ester-linked LAs because anticholinesterase medications (pyridostigmine) impair hydrolysis of ester-linked LAs. Mid-thoracic or higher levels of neuraxial anesthesia with a high concentration of LAs are avoided to reduce respiratory muscle dysfunction. Interscalene brachial plexus may impair diaphragm function (Phrenic nerve involvement), which may worsen the respiratory function.⁴
7. During general anesthesia in patients with untreated myasthenia gravis, the motor endplates are resistant to the effects of succinylcholine due to the downregulation of AChRs. Generally, these patients require a higher intubating dose of succinylcholine. Patients with uncontrolled myasthenia gravis are sensitive to nondepolarizing neuromuscular blocking agents, as small doses can result in profound respiratory muscle weakness. When possible, nondepolarizing neuromuscular blocking agents should be avoided or limited to reduced doses of rocuronium if sugammadex is available.²

8. Induction agents (propofol, etomidate, and ketamine) are used in MG patients with no issues. Short-acting opioid agents (Remifentanyl, fentanyl) are preferable during general anesthesia. Intraoperative inhalational agents (sevoflurane and desflurane) were used in MG patients with no significant concerns. Intraoperative use of some medications may worsen muscle weakness in MG patients. Use of such medications perioperatively cautioned. These medications interfere with presynaptic and postsynaptic ion channels at the neuromuscular junction.⁴ ([Table 3](#))
9. A myasthenic crisis is caused by improper medication use (Pyridostigmine), stress, hyperthermia, or infection and is characterized by respiratory failure with muscle weakness. Severe crises may require intubation and mechanical ventilation. Cholinergic crisis, on the other hand, is caused by preoperative excess anticholinesterase medications (pyridostigmine) or intraoperative neostigmine use. Symptoms of cholinergic crisis include muscle weakness, excess salivation, lacrimation, urination, and gastrointestinal distress (defecation, emesis). Cholinergic crisis is treated with intravenous atropine (0.4-2 mg) or glycopyrrolate (0.2-1 mg).⁵
10. Muscle strength in the postoperative period may deteriorate in patients with MG despite adequate strength to meet extubation criteria. The factors that correlate with the requirement for postoperative mechanical ventilation are disease duration for six years or longer, presence of chronic obstructive pulmonary disease unrelated to MG, daily total pyridostigmine dose greater than 750 mg per day, and preoperative forced vital capacity less than 2.9 L.⁴

Perioperative Management of MG patients requires a multidisciplinary approach. The goal is to understand the patient's pathophysiology, associated medical problems, medications, and disease progress. The goals during anesthetic management include avoiding stressors, preventing the worsening of muscle weakness, and preserving respiratory function.

Submitted: August 15, 2024 CDT. Accepted: December 19, 2024 CDT. Published: December 19, 2024 CDT.

Table 1. Myasthenia Gravis (MG) Variants

Type	Age group
Early-onset MG	<50 years with thymic hyperplasia
Late-onset MG	>60 years with thymic atrophy
Thymoma associated MG	Around 50 years
MG with anti-MuSK antibodies	Most common late 30s (17-81 years)
Ocular MG	Juvenile onset (<18 years), early (18-49 years), Late (>50 years)
MG with no detectable AchR and MuSK antibodies	Two peaks, one at age 30 and another at age 70-80 years
Lambert-Eaton syndrome variant	Underlying malignancy (small cell cancer lung). Affects voltage-gated calcium channels (older age>50 years)

Table 2. Myasthenia Gravis Foundation of America Classification

Class	Symptoms
Class I	Ocular muscle weakness only
Class II	Ocular and mild systemic weakness
Class III	Ocular and moderate systemic weakness
Class IV	Ocular and severe systemic weakness
Class V	Myasthenic crisis with respiratory failure requiring intubation
Subtypes ^a	a= Predominately affecting limb and axial muscles (oropharyngeal muscles may be affected to a lesser extent). b= Predominantly affecting oropharyngeal and respiratory muscles (limb and axial muscles may be affected to a lesser extent).

^a Applies to classes II to IV

Table 3. Medications that aggravate myasthenia symptoms

Drug class	Drugs
Anesthetic medications	Nondepolarizing muscle relaxants
Anti-arrhythmic agents	Procainamide, Propafenone, Peruoside, Etafenone
Antibiotics	Aminoglycosides, Fluoroquinolones, Penicillins, polymyxins, Tetracyclines, Imipenem, Vancomycin,
Antiepileptics	Carbamazepine, Gabapentin, Phenytoin, Trimethadione
Beta-blockers	Atenolol, Nadolol, Propranolol, Sotalol
Calcium channel blockers	Amlodipine, felodipine, Nifedipine, Verapamil
Chemotherapy agents	Cisplatin, Doxorubicin, Etoposide
Corticosteroids	Hydrocortisone, Methyl prednisone, Prednisone
H2- Receptor blockers	Cimetidine, Ranitidine
Interferons	Alpha and Beta interferons
Psychotropics agents	Carbamazepine, Haldol, Lithium, Tricyclic anti-depressants (TCAs)

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SUPPLEMENTARY MATERIALS

Table 1: Myasthenia Gravis (MG) Variants

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Table 2: Myasthenia Gravis Foundation of America Classification

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Table 3: Medications that aggravate myasthenia symptoms

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