# Perianesthetic Implications and Considerations for Myasthenia Gravis

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*Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disease in which antibodies against the post-nicotinic acetylcholine receptor at the neuromuscular junction develop. Although the exact cause of MG remains unknown, the thymus is a common factor in many cases. Patients with underlying junctional disease, such as MG, have greater anesthesia-related risks because of their known predisposition toward prolonged muscle weakness. Medications given in the perioperative period, such as anesthetic agents, antibiotics, cardiovascular drugs, and corticosteroids, affect neuromuscular transmission that contributes to muscle weakness. Judicious use of neuromuscular blocking agents for patients with MG must be considered. This patient population is at high risk for respiratory failure, and therefore must be carefully assessed throughout the perioperative period to ensure that a regular spontaneous respiratory pattern is sufficient to provide adequate oxygenation. Perianesthesia providers must consider anesthetic, ventilatory, and pharmacologic implications when proposing, providing, and recovering anesthesia for the patient with MG.*

**Keywords:** *myasthenia gravis, autoimmune neuromuscular disorder, neuromuscular junction, perianesthesia, continuing education.*



**OBJECTIVES—1. DESCRIBE THE** presenting characteristics of the patient with myasthenia gravis; 2. Discuss the signs and symptoms of a patient with myasthenia gravis that is in postoperative distress; 3. Discuss perianesthetic approaches to minimize risks for the surgical patient with myasthenia gravis.

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Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disease in which antibodies develop against the post-nicotinic acetylcholine receptor (nAChR) at the neuromuscular junction (NMJ). The action of these antibodies results in decreased capacity of the neuromuscular end plate to transmit nerve signals.[1] Antibodies (IgG) against the nAChRs are found in most patients with generalized MG.[2] The resulting signal interference at the NMJ is evidenced as the patient exhibits signs of muscle weakness and rapid fatigue of voluntary muscles with repetitive use.[3] Although the exact cause of MG is unknown, the thymus, a gland involved in immune function, is a common factor and thought to produce acetylcholine receptor (AChR) antibodies responsible for MG. In the United States, the prevalence of MG is estimated at 14 to 20 cases per 100,000, yet this is likely underestimated because of MG being underdiagnosed.[4] Women are more commonly affected than men, with the highest incidence occurring in women during their third

decade.[2] Although less common in men, MG typically is seen in males older than 60 years.[3] Roughly, 5% of patients with MG present with other autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, and pernicious anemia.[5] Approximately 10% to 15% of MG patients present with a tumor, called thymoma, which is usually benign.[5] Clinical classification of MG is based on skeletal muscle involvement and severity of symptoms and assessed using the Osserman and Genkins classification system.[6]

### *Presentation and Diagnostics*

Presenting characteristics of patients with MG may include the following: fatigued voluntary muscles affecting the extraocular eye muscles (diplopia) and eyelids (ptosis), bulbar symptoms including difficulty chewing and swallowing (dysphagia), mild to severe generalized weakness, slurred speech, and respiratory failure.[7,8] The patient's history may reveal diagnostic cues of MG, although diagnosis is ultimately confirmed through a variety of tests. Confirmation can be made from clinical, electrophysiological, immunologic, and pharmacologic testing.[6] The most common tests for confirmation of MG include electromyography (EMG), edrophonium (Tensilon), and regional curare.[6] Patients with MG are unable to produce sustained or repeated muscle contractions when stimulated by EMG. Although EMG testing is the most specific test for MG, it is limited to only specific muscle groups.[6] If EMG testing results are inconclusive, the edrophonium test is performed. Administration of this acetylcholinesterase inhibitor to a patient with MG may increase strength as degradation of ACh is reduced. Patients without MG will see no improvement in muscle strength with edrophonium testing.[6] Inconclusive edrophonium test results use regional curare to confirm the presence of MG. With this confirmatory test, a tourniquet is used to isolate a limb in which very small doses of curare are administered.[6] Patients with MG will exhibit a decreased response to repeated muscle stimulation by EMG.[6]

## Preoperative Considerations

### *Treatment Options*

Treatment modalities for MG include anticholinesterase medications, thymectomy, immunosuppressive therapy, and plasmapheresis. Anticholinesterases inhibit the acetylcholinesterase enzyme that increases the portion of ACh available for muscle contraction at the NMJ. Pyridostigmine (Mestinon), edrophonium (Tensilon), and neostigmine (Prostigmin) are anticholinesterases used for first-line MG treatment.[3] The anticholinesterase Physostigmine is not used as this drug/acetylcholinesterase inhibitor crosses the blood-brain barrier and produces unwanted central nervous system effects.[6] Recall that patients with MG have fewer properly functioning nAChRs, making them extremely sensitive to nondepolarizing neuromuscular blocking agents (NNBAs). As such, careful titration of NNBAs should be based on peripheral nerve stimulator (PNS) monitoring, specifically, quantitative PNS monitoring.[6] In contrast to their response to NNBAs, MG patients have a resistance to the depolarizing muscle relaxant succinylcholine.[3] The exact mechanism of action of the succinylcholine resistance is unknown, but thought to be related to the decreased number of postsynaptic nAChRs[3] as patients with MG can have up to 70% to 80% fewer usable receptors at the end plates of the affected muscles.[6]

In the event that anticholinesterase drug therapy proves ineffective, immunosuppressive therapy with corticosteroids is considered. Although helpful with immunosuppression, corticosteroid treatment is associated with the greatest likelihood of side effects, such as hypertension, hyperglycemia, osteoporosis, and adrenal insufficiency.[3,9] The thymus gland is involved in immune function and thought to ultimately produce AChR antibodies responsible for MG.[10] Thymectomy, the surgical removal of the thymus gland, is performed with the goal of inducing remission of the disease process or to at least allow for reduced immunosuppressant dosages required by patients with MG.[3]

One treatment used for short term with transient symptom improvement for patients with MG is plasmapheresis. Plasmapheresis has provided extreme yet short-lived symptom improvement in 45% of patients.[6] Removal of circulating antibodies does not change the destruction of nAChRs, and the benefits must be weighed against the risks associated with repeated plasmapheresis, including infection, hypotension, and pulmonary embolism.[3]

### *Preoperative Evaluation*

Patients with MG require careful preoperative evaluation. Optimally, surgery should be scheduled when the patient is in remission or the disease is well controlled as surgical stress can exacerbate symptoms of MG.[6] Preoperative evaluation should include an assessment of the patient's disease course, drug therapy, muscle groups affected, and the ability to maintain and protect his or her airway and clear secretions.[2] Preoperatively, patients with known respiratory or bulbar involvement should have pulmonary function tests, be counseled along with family members by an anesthesia or appropriately trained health care provider regarding the increased risk of postoperative intubation and ventilation, and be informed that if postoperative intubation is necessary, the patient will be admitted to a monitored unit for postoperative observation and extubation.[6] Anesthesia providers should inform managers of monitored units before and the day of surgery (DOS) that the patient may require postoperative disposition to that unit. Another preoperative consideration for the MG patient who is at increased risk for pulmonary aspiration is the administration of metoclopramide to decrease gastric volume and either a histamine-2 receptor antagonist such as Ranitidine or nonparticulate antacid (eg, Bicitra) to decrease the intragastric concentration of hydrogen ions (increase pH), all of which have been theorized to minimize complications if aspiration occurs (eg, minimize degree of caustic injury to bronchioles resulting from aspiration pneumonitis)[2,11,12] and are supported by the American Society of Anesthesiologists' current guidelines.[13] Additional methods to decrease risk of pulmonary aspiration include rapid sequence rather than standard induction, consideration of local anesthesia with intravenous (IV) sedation or regional anesthetics, both of which permit spontaneous respirations throughout the perioperative period, and consideration of an awake fiberoptic intubation during which the MG patient may receive topical anesthetic and maintains spontaneous respirations until correct placement of an endotracheal tube or other secure airway device is verified.

Previous recommendations were to hold anticholinesterase medications[7] the DOS, yet more recent recommendations are to continue these medications on the DOS to avoid respiratory distress postoperatively.[9] The anesthetist or provider from the anesthesia preoperative clinic, in accordance with established protocols, should consult with the patient's neurologist regarding whether immunosuppressive therapy should be continued on the DOS.[1] Providers must consider the interaction of acetylcholinesterase therapy with NNBAs and depolarizing muscle relaxants as the response may be amplified or diminished, respectively.[6] Recall that the MG patient has impaired neuromuscular transmission. This impairment decreases laryngeal and pharyngeal muscle function and protective airway reflexes, all of which predispose the patient not only to aspiration, but also to upper airway obstruction. Hence, cautious administration of opioids, anxiolytics, or other medications with the potential to cause respiratory depression is warranted with MG patients.[1,2]

### *Steroid Stress Dosing*

Many patients with MG take chronic corticosteroids for immunosuppressive therapy, making steroid stress dosing before surgical incision an important consideration. Chronic steroid use suppresses the hypothalamic-pituitary-adrenal axis; therefore, reducing the release of cortisol from the adrenal glands.[14] Cortisol plays an important role in the effectiveness of catecholamines. Abrupt discontinuation of steroid use may significantly worsen the patient's clinical status, as cortisol production from surgical stress can be insufficient for hemodynamic stability.[15] Providers should administer a single IV dose of corticosteroid to patients who have received long-term steroids before surgery.[14] The dosage of corticosteroid depends on the anticipated degree of surgical insult.[14] Although side effects must be considered, a recent study recommended that preoperative high-dose steroid therapy for the control of MG symptoms stabilizes postoperative patient status.[9]

## Intraoperative Considerations

### *General Versus Regional Anesthesia*

Patients with MG have many pharmacologic implications that must be considered when formulating and delivering an anesthetic plan. Several general anesthetic techniques have been used, yet no single technique has been shown to be superior. Some clinicians prefer to avoid muscle relaxants

and use potent inhalational agents, both for facilitating tracheal intubation and providing muscle relaxation for surgery.[16,17] Use of inhalational agents allows for neuromuscular transmission to recover as these volatile anesthetics are rapidly eliminated at the end of surgery.[17] It has been theorized that desflurane and sevoflurane may offer some advantages because of their low blood solubility in comparison to isoflurane.[16]

Medications that potentiate muscle weakness with general anesthesia include certain potent volatile anesthetics (isoflurane), hypnotics (sodium pentothal), opioids, and muscle relaxants.[8] Interactions with these medications that weaken neuromuscular transmission have led some providers to advocate for the use of regional anesthesia with MG patients.[4,15] Local anesthetics (LA) used in regional anesthesia are thought to potentiate neuromuscular blockers by decreasing the sensitivity of the postjunctional membrane to ACh.[1,18] This potentiation may cause weakness in MG patients if LA blood levels are sufficient, particularly with ester LA, which are metabolized by plasma cholinesterase and could present problems in patients taking anticholinesterases.[19,20] Regional and LA should be administered using reduced doses of amide LA to avoid increased blood amide levels (Table 1). Spinal anesthesia has the advantage of reduced drug dosage, whereas epidural techniques facilitate easier control of blockade level and may obviate the need for opioids in postoperative pain management.[18] Epidural analgesia has been used during labor for MG patients with success, but high dermatome levels produced by epidural analgesia can compromise the patient's respiratory function and increase the risk for postoperative mechanical ventilation.[1,18] It is suggested that the anesthetist avoid blockade of intercostal muscle innervation to minimize the risk of respiratory muscle weakness[18]; however, the safe and successful use of thoracic epidural blockade with bupivacaine for intraoperative anesthesia and postoperative analgesia for transsternal thymectomy has been reported.[6]

**Table 1. Local Anesthetics**

| Amides | Esters |
|---|---|
| Bupivacaine | Benzocaine |
| Etidocaine | Chloroprocaine |
| Lidocaine | Procaine |
| Levobupivacaine | Cocaine |
| Mepivacaine | Tetracaine |
| Prilocaine | |
| Ropivacaine | |

### *Induction Options*

General anesthesia is induced by IV or inhalational methods. With either, protective airway reflexes are lost. During induction, the overall goal is to minimize the length of time patients have an unprotected airway. General anesthesia coupled with decreased pharyngeal and laryngeal muscle strength associated with MG further diminishes the ability of this patient population to protect their airway, placing them at increased risk for aspiration.

Patients at increased risk for aspiration often have a rapid sequence induction with cricoid pressure, unlike a standard induction, which involves mask ventilation without cricoid pressure. Inhalational induction with Sevoflurane has successfully been used with MG patients as an alternative to the standard IV induction.[1] Volatile anesthetics, to varying degrees, also possess muscle relaxation properties that facilitate endotracheal intubation without the use of NBAs.[3] In addition, MG patients are more sensitive to the relaxant effects of volatile anesthetics, which decrease neuromuscular blocker requirements, thus making inhalational induction a viable option.[1] When IV induction is desired, anesthetic agents, such as propofol, ketamine, etomidate, and barbiturates, have been shown to be safe.[6]

### *Neuromuscular Blockade*

The use of NBAs to facilitate intubation of MG patients must be cautiously considered. Patients with MG show resistance to depolarizing agents because of a decreased availability of functional postsynaptic AChR.[21] This decrease in receptors also results in a decreased safety margin of remaining AChRs available for neuromuscular transmission.[17] Succinylcholine, the only depolarizing NBA used in the United States at doses of 1 to 1.5 mg/kg, has been successfully used in rapid sequence intubations; however, both anticholinesterase drugs and plasmapheresis contribute to decrease pseudocholinesterase, leading to prolonged duration or phase II block.[6] NNBAs have increased potency with MG patients, making reduced doses of

1/10th the usual dose necessary.[6,22] Relatively small amounts of NNBA can produce profound and prolonged NMJ blockade in MG patients. Patients with MG are less sensitive to succinylcholine, the only depolarizing NBA used in the United States, than NNBAs, yet either class of drug, depolarizing or nondepolarizing NBAs, can exacerbate the disease or unmask the disease in patients who are undiagnosed. It is essential that neuromuscular transmission is monitored closely.

Exacerbations of weakness are characteristic of MG. Immediately before an anesthetic induction that includes succinylcholine, providers may elect to administer a defasciculating dose of an NNBA in an attempt to prevent myalgias associated with succinylcholine. A defasciculating dose is 1/10th of an intubating dose of NNBA, yet this small dose is sufficient to compound existing weakness and lead to respiratory distress in the MG patient.[6] Sensitivity to NNBAs has been described in the full spectrum of MG patients, including those with minimal disease such as ocular symptoms only, to those in apparent remission or those with subclinical undiagnosed myasthenia.[2,3] A safe alternative to the administration of NBAs to patients with MG includes volatile anesthetics that possess muscle relaxant properties.[23] Volatile anesthetics are thought to inhibit ACh release and intracellular calcium increase needed for muscle contraction, thereby, causing airway smooth muscle relaxation.[21,23]

One drug that may revolutionize NNBA use in patients with neuromuscular disease is Sugammadex.[24] Before the development of Sugammadex, acetylcholinesterase inhibitors that block the normal breakdown of ACh were solely used to reverse neuromuscular blockade. Sugammadex, Food and Drug Administration approved in 2015, uses an encapsulation approach that inactivates the action of steroidal NNBAs (eg, vecuronium, rocuronium, and pancuronium) to effectively and safely reverse neuromuscular blockade and has been shown to reduce the incidence of residual blockade among patients with MG.[19,25-27]

### *Medications That Exacerbate MG*

In addition to NBAs, many commonly used drugs affect neuromuscular transmission to a small degree. In healthy patients, this is usually of no clinical significance, although it can have great effects on the MG patient. Perioperatively administered antibiotics, cardiovascular drugs, and corticosteroids are among the most well-known offenders of decreased neuromuscular transmission given during the perioperative period.[5]

Antibiotics can induce or exacerbate symptoms of MG.[5] Oral and IV aminoglycoside antibiotics are known to impair neuromuscular transmission and produce clinically significant weakness in a dose-dependent fashion, via a wide range of presynaptic and postsynaptic mechanisms.[5] Weakness produced by aminoglycosides can be partially reversed using cholinesterase inhibitors, a calcium infusion, and aminopyridines.[5] In vitro studies demonstrate that various other antibiotics, including tetracyclines, sulfonamides, penicillins, and fluoroquinolones are associated with anecdotal reports of increased myasthenic weakness or potential problems.[5] Regardless of class, most antibiotics have the potential to affect nerve transmission, resulting in weakness. The effects of antibiotics on neuromuscular transmission are complex and can pose a challenging decision for providers. If the patient with MG requires perioperative antibiotic treatment, the provider should be cognizant of and monitor for clinically significant adverse effects.

Cardiovascular medications such as beta-adrenergic blocking and calcium channel blocking agents as well as statin medications have been associated with increased muscle weakness in MG patients.[28,29] Beta blocking agents have been shown to produce a dose-dependent reduction in neuromuscular transmission in rat skeletal muscle.[5] The specific mechanism for the beta blocker junctional effect is unclear; however, propranolol and atenolol are thought to have the most and least pronounced impairment of neuromuscular transmission, respectively.[5]

Although their effect on neurotransmission is not well established, studies have indicated that calcium channel blockers may adversely affect neuromuscular transmission because of a presynaptic reduction in ACh release.[5] Calcium channel blockers are known for their ability to potentiate the effect of NBAs by impeding nerve-evoked muscle action potentials and inhibit evoked synaptic transmission.[30] Statin medications are used to treat hyperlipidemia despite their association with muscle pain, aggravated muscle fatigue, elevated creatinine kinase,

and rhabdomyolysis.[28,29,31-33] These lipid-lowering agents have been shown to worsen MG, possibly by endogenous coenzyme Q10 reduction resulting in mitochondrial dysfunction, chloride channel deficiencies resulting in muscle membrane dysfunction, or interrupted glycoprotein synthesis.[33,34]

Regardless of whether a patient has a neuromuscular disease, many factors impact neuromuscular transmission in surgical patients including, but not limited to temperature, the concentration of hydrogen ions, age extremes, a recent burn, cerebral vascular accidents, electrolyte disturbances, inhaled anesthetics, and many medications.[21,35]

Corticosteroids are often used in the treatment of MG because of their ability to suppress migration and activation of lymphocytes; however, elderly patients with bulbar symptoms or severe weakness are at higher risk for MG exacerbations related to steroid use.[36]

### *Ventilation and Maintenance of Anesthesia*

Patients with MG are at high risk for respiratory failure and myasthenic crisis (MC).[2] The Leventhal criteria, commonly used preoperatively to determine the degree of risk for postoperative respiratory failure among patients with MG, includes MG disease duration of 6 years and/or greater, concomitant chronic respiratory disease, daily pyridostigmine dose greater than 750 mg, and vital capacity of 2.9 L or less.[2] Additional predictors of the need for postoperative ventilation include the presence of preoperative bulbar symptoms, a prior history of MC, preoperative anti-AChR antibody levels of greater than 100 nmol/L, intraoperative estimated blood loss of greater than 1,000 mL,[29] maximum expiratory pressure of less than 40 cm $H_2O$,[37] decremental orbicularis oculi response,[38,39] and preoperative muscle strength, swallowing ability, and respiratory function.[40] In a patient whose strength is normalized, their risk for postoperative respiratory complications will be similar to that of a non-MG patient undergoing a similar procedure.[2] Pressure support ventilation is preferred as it allows the patient to maintain spontaneous ventilation and retain respiratory drive, while decreasing the work of breathing. The degree of ventilatory support required is patient and procedure dependent.

### *Extubation of the MG Patient*

Patients who have MG are at high risk for respiratory failure, and thus, sufficient spontaneous breathing must be assessed before extubation. Extubation criteria for patients with MG are similar to standard extubation criteria and include return of the patient's baseline level of consciousness and respiratory status with tidal volumes of 5 mL/kg or greater, spontaneous ventilation with an end tidal carbon dioxide ($ETCO_2$) of 50 mm Hg or less, and peripheral capillary oxygen saturation ($SpO_2$) of 90% or greater. Beyond generic extubation criteria, some agree that consensus regarding extubation criteria for MG patients is lacking and must be based on clinical judgment.[37,41,42] At or near the conclusion of an anesthetic that includes an NBA, it is important to administer an antagonist and assess the degree to which the NBA was pharmacologically antagonized or reversed. The assessment may be qualitative with a PNS or quantitative with an EMG. Quantitative nerve monitoring is more specific, objective, and better able to detect residual blockade or incomplete reversal of the NBA, which can cause negative sequelae for the MG patient, such as impaired gas exchange, pulmonary dysfunction, and the need for reintubation and postoperative mechanical ventilation.[43-45]

Qualitative assessment of neuromuscular blockade involves monitoring baseline train of four with a PNS after the patient is induced and deemed unconscious before the administration of any type of muscle relaxant. Providers also conduct qualitative assessment of neuromuscular blockade during the intraoperative maintenance phase of anesthesia. Providers can evaluate the degree of neuromuscular blockade with the PNS in the unconscious patient, yet the assessment is subjective, relies on clinical signs, and is therefore less predictive of neuromuscular recovery from NBAs.[45] Whether assessment of neuromuscular blockade is quantitative or qualitative, complete NBA reversal is required to ensure adequate strength such that the patient maintains a patent airway, has an intact cough reflex, and sufficient strength to clear secretions before the removal of an established secure airway, most often, an endotracheal tube.

### *Postoperative Considerations*

Postoperative priorities for nurses and providers who care for the MG patient are to resume home medications once the patient is hemodynamically stable, ensure adequate oxygenation and ventilation, monitor respiratory function (auscultate breath sounds and note respiratory rate, $ETCO_2$, breathing pattern, use of accessory muscles, chest excursion, color, and pulse oximetry), and avoid medications that exacerbate MG, yet provide adequate postoperative analgesia. Two main concerns for the MG patient are risk for MC and the need for prolonged postoperative ventilatory support.

### *Home Medications*

Patients with MG are commonly treated with anticholinesterase medications such as pyridostigmine, oral steroids like prednisone, and immunosuppressive agents such as azathioprine, cyclosporine, cyclophosphamide, and methotrexate.[46] Patients who took pyridostigmine preoperatively should resume taking the medication as soon as possible postoperatively. Oral formulation is optimal although intramuscular and IV doses may be administered at 1/10th and 1/30th of the usual dose, respectively.[4] Immunosuppressants may be held the morning of surgery because of their long duration of action and started postoperatively with other oral medications.[4]

### *Respiratory Monitoring*

Hypoventilation and respiratory depression are potential complications for the patient with MG because of prolonged neuromuscular blockade and a generalized state of muscle weakness. Respiratory supplies, equipment, and trained staff should be available in the immediate postoperative recovery areas for patients with MG. Pulmonary hygiene such as deep breathing, incentive spirometry, percussion, and postural drainage should be considered and implemented in the immediate postoperative period to clear airways of mucus and secretions and prevent pulmonary complications. Postanesthesia care unit nurses must be cognizant of vital signs, alert to hypoventilation that may lead to hypoxia and hypercarbia, and vigilant to signs of airway obstruction as these patients are also susceptible to aspiration because of muscle weakness. Suction should be immediately available at all times.

### *Postoperative Pain Control*

Optimal postoperative pain management helps prevent stress-induced pain that could exacerbate MG symptoms.[1] Ideal pain treatment modalities do not decrease the respiratory drive, increase generalized weakness, or increase the risk of gastrointestinal adverse effects. The administration of some postoperative pain medications hinders the patient's ability to maintain or clear the airway of secretions that can lead to postoperative pulmonary complications. Providers must exercise caution when administering respiratory depressant medications to patients with MG; extreme caution is advised for those who exhibit bulbar symptoms such as nasal regurgitation and difficulty swallowing and talking. These difficulties can not only depress respiratory function, but also increase the patient's risk for aspiration.

Adjuncts for postoperative pain control that do not depress respiratory function include acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs). Opioid alternatives to pain relief shown to be effective and safe for the MG patient include but are not limited to cyclo-oxygenase-2 selective NSAIDS (celecoxib), triptans (sumatriptan and rizatriptan), tricyclic antidepressants (amitriptyline), anticonvulsants (valproic acid, gabapentin, and pregabalin), LAs (Lidocaine), and selective serotonin-norepinephrine reuptake inhibitors (Duloxetine).[47] If opioids are necessary, small doses of short-acting opioids should be used in lieu of long-acting medications in an attempt to prevent respiratory depression.[1] Regional anesthetic methods should be used whenever appropriate to help avoid opioids and their harmful effects on the gastrointestinal system in an effort to quickly restart oral home medication regimens.[1]

Despite pain control method choices, concurrent MG medication regimens must be considered as some combinations have varying levels of interactions and adverse effects. Simultaneous use of cyclo-oxygenase-2-selective and nonselective NSAIDS with corticosteroids such as dexamethasone and aspirin may increase the risk for gastrointestinal adverse effects, whereas combinations with cyclosporines may result in nephrotoxicity.[47]

Interactions for which other drug combinations must be considered include but are not limited to carbamazepine and cyclosporines (increased metabolism of cyclosporines and corticosteroids), lidocaine and tacrolimus (possible risk for QT prolongation and/or torsades de pointes), benzodiazepines and cyclosporines (relax skeletal muscle), opioids combined with cyclosporines that can result in adverse effects in the central nervous system.[47] Drugs that should be used with caution include Mexiletine, Baclofen, and Pregabalin.[47] Drugs that should be avoided include magnesium and gabapentin (unmask MG in a previously asymptomatic patient or exacerbate muscle weakness) as well as Orphenadrine (exacerbate muscle weakness in MG).[47]

### *Myasthenic Crisis*

MC is an exacerbation of MG, often occurring during the postoperative period and characterized by worsened muscle weakness that leads to respiratory failure and requires endotracheal intubation and mechanical ventilation. Wendell and Levine list common precipitants of MC, some of which are closely affiliated with the perioperative period, including physical stressors, sleep deprivation, surgery, pain, temperature extremes, aspiration pneumonitis, infection, and emotional stress such as the fear of surgery.[41,48] Many factors can lead to MC, including infection, surgery, pain, stress, and the administration of certain medications (Table 2).

One differential diagnosis to be ruled out when MC is suspected is cholinergic crisis. There are two ways to differentiate between the two, and they are to check pupillary size and perform an edrophonium challenge test.[6] MC is characterized by dilated pupils and will respond to low doses of edrophonium (2 to 10 mg) with improved strength. Conversely, cholinergic crisis will result in constricted pupils and will show no change or an exacerbation of symptoms with edrophonium administration.[6] MC treatment includes IV immunoglobulin and plasmapheresis along with ventilator support.[49]

**Table 2. Stressors Precipitating Myasthenic Crisis**

| | |
|---|---|
| Physical stressors | Aspiration pneumonitis |
| Infection | Perimenstrual state |
| Pregnancy | Sleep deprivation |
| Surgery | Environmental stressors |
| Pain | Temperature extremes |
| Tapering of immune-modulating medications | |

## Conclusion

Patients with MG are at higher risk for anesthesia and perioperative-related complications, yet various anesthetic approaches have been used successfully. The primary recommendation is that perioperative providers minimize the risk of respiratory muscle weakness and subsequent respiratory failure.[7] NBAs, antibiotics, opioids, and anxiolytics are among the medications that must be used with caution in this patient population as they are known to cause prolonged muscle weakness. Careful preoperative evaluation is essential to optimize patients with MG. Knowing surgical stress can exacerbate symptoms, careful planning should lead providers to schedule surgery when the patient is in remission, or the disease process is well controlled in an attempt to avoid symptom exacerbation brought on by surgical stress.[6] The patient's ability to maintain and protect their airway must be assessed before and throughout the perioperative period, preoperative pulmonary function tests should be considered, and the neurologist should be consulted regarding immunosuppressive therapy.[1] There are many considerations for the MG patient throughout the perioperative period; however, careful planning and optimization make it feasible to safely anesthetize this population and minimize perioperative complications.

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### Perianesthetic Implications and Considerations for Myasthenia Gravis

**1.5 Contact Hours**

**Purpose of the *Journal of PeriAnesthesia Nursing***

To facilitate communication about and deliver education specific to the body of knowledge unique to the practice of perianesthesia nursing.

**Outcome of this CNE Activity**

To enable the nurse to increase knowledge on the care of the patient with myasthenia gravis.

**Target Audience**

All perianesthesia nurses.

**Article Objectives**

1. Describe the presenting characteristics of the patient with myasthenia gravis
2. Discuss the signs and symptoms of a patient with myasthenia gravis that is in postoperative distress
3. Discuss perianesthetic approaches to minimize risks for the surgical patient with myasthenia gravis

**Accreditation**

American Society of Perianesthesia Nurses is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

Additional provider numbers: Alabama #ABNP0074, California #CEP5197

**Contact hours**

Registered nurse participants can receive 1.5 contact hours for this activity.

**Disclosure**

All planners and authors of continuing nursing education activities are required to disclose any significant financial relationships with the manufacturer(s) of any commercial products, goods or services. Any conflicts of interest must be resolved prior to the development of the educational activity. Such disclosures are included below.

**Planners and Author Disclosures**

The members of the planning committee for this continuing nursing education activity do not have any financial arrangements, interests or affiliations related to the subject matter of this continuing education activity to disclose.

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## Directions

A multiple-choice examination, designed to test your understanding of **Perianesthetic Implications and Considerations for Myasthenia Gravis** according to the objectives listed, is available on the ASPAN Website: https://www.aspan.org/Education/CE-Articles-Online/

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