Summer 7-29-2022

# Myasthenia Gravis

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# Myasthenia Gravis

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## Introduction

- Myasthenia gravis (MG) is a neuromuscular disease thought to be autoimmune, and "mediated by acetylcholine receptor (AchR) antibodies that act at the neuromuscular junction (NMJ)" (McCance & Heather, 2014, p. 674).
- MG is manifested by "skeletal muscle weakness, fatigability on effort, and at least partial restoration of function after rest" (Nagelhout & Elisha, 2018, p. 768).
- Subtypes of autoimmune myasthenia gravis (McCance & Heather, 2014, p. 675).
  - *Generalized*: involves proximal musculature with either periodic remission, a slowly progressive course, a rapidly progressive course, or a fulminating course
  - *Neonatal:* 10-15% of infants whose mothers have MG will show transitory signs
  - *Ocular:* weakness of eye myscles and eyelids and may include swallowing difficulties and slurred speech as well

## Why MG?

- 25-125 people in every 1 million worldwide with increasing prevalence (Nagelhout & Elisha, 2018, p. 768).
- MG is also associated with "an increased incidence of other autoimmune diseases, including systemic lupus erythematous, rheumatoid arthritis, polymyositis, and thyrotoxicosis" (McCance & Heather, 2014, p. 674)
- It is important to study and understand MG as "patients with neuromuscular diseases can present as complicated anesthetic cases, often requiring specific and tailored perioperative considerations" (Collins et al., 2020, p. 485).

## Signs and Symptoms

- Fatigability or weakness of voluntary muscles
  - Seen primarily on "repeated or continual action of the muscles and the symptoms decrease on rest" (Binu et al., 2022, p. 64).
  - Symptoms worsen as day progresses (Thanvi, 2004, p. 694).
- Ocular weakness is most common and results in eyelid drooping, or ptosis, and blurry vision (Binu et al., 2022, p. 64)
- Dysphagia is common due to the weakening of muscles involved in chewing and swallowing (Berrih-Aknin et al., 2014, p. 143).
- Cogan's lid twitch: causes "upper eyelids to twitch or slowly droop when the patient attempts to move the eyes from downward position to primary position by a vertical saccade" (Binu et al., 2022, p. 64).
- With facial muscle involvement, patients might lose the ability to make certain facial expressions due to the corners of the mouth not pulling up and gives the appearance of a "snarl" rather than a smile (Binu et al., 2022, p. 64).
- Dyspnea on exertion if respiratory muscles and diaphragm involvement is included (Binu et al., 2022, p. 64).
- A weak voice due to weakening of muscle of the voice box (Binu et al., 2022, p. 64).
- Symptoms follow craniocaudal direction of weakness (ex. from head to limbs) (Binu et al., 2022, p. 64).

## Diagnosis

- Insidious onset (McCance & Heather, 2014, p. 676).
- Diagnosis occurs with "response to edrophonium chloride (Tensilon), results of repetitive single-fiber EMG, and detection of AchR and MuSK antibodies" found in 80% of generalized autoimmune myasthenia cases (McCance & Heather, 2014, p. 676).
  - IV administration of Tensilon improves muscle strength for 5-10 minutes
  - EMG shows muscle fiber weakening readily
  - CT & MRI may determine whether thymoma is present
- Various classifications of MG are listed below in Table 1

## Treatment

- *Cholinesterase inhibitors*: inhibit hydrolysis of acetylcholine, raising the concentration and enhances chances of reaching threshold potential at motor end plate (Nagelhout & Elisha, 2018, p. 770).
- *Corticosteroids*: effectiveness may reflect suppression of immunoglobulin production that binds to NMJ (Stoelting,
- *Plasmapheresis & intravenous immunoglobulin*: reduce concentration of circulating antibodies. This is a short-term solution (Nagelhout & Elisha, 2018, p. 770).
- *Thymectomy*: for adults with generalized disease and thymomas. Effectively "arrests or reverses the myasthenic process by removing a major source of antibody production" (Nagelhout & Elisha, 2018, p. 770).

**Clinical Classification of Myasthenia Gravis; Osserman Score System**

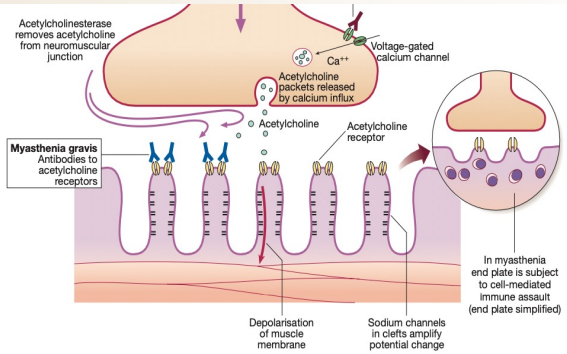
| Stage | Clinical Status |
|---|---|
| I | Only ocular involvement |
| IIa | Generalized muscle weakness |
| IIb | Generalized moderate muscle weakness and/or bulbar involvement |
| III | Acute, fulminant presentation and/or respiratory depression |
| IV | Severe, generalized myasthenia |

***Table 1. Clinical classification of myasthenia gravis (Nagelhout & Elisha, 2018, p. 770)***

## Underlying Pathophysiology

- The pathophysiology of MG is not completely understood
- Anti-AchR antibodies are identified as the primary cause of MG in 80-90% of patients (Binu et al., 2022, p. 63).
- These antibodies attack the NMJ by the following mechanisms (Binu et al., 2022, p. 63):
  - Forming crosslinks between ACh receptors
  - Endocytosis and degredation of receptors
  - Destruction of post-synaptic junctional folds
  - Blockade of the receptor by antibody (Figure 1)
- Some patients are shown to instead have antibodies against MuSK (Binu et al., 2022, p. 63).
- "MuSK is involved in rapsyn-mediated clustering of the Ach" and therefore interferes with muscle contraction (Binu et al., 2022, p. 63).
- A study by Makino et al. (2020) indicates that "B cells in peripheral blood may impact MG pathogenicity" as B cells are known to be the type of protein that is able to produce an antibody (p. 1).
- The thymus is suspected to play a role in MG pathogenesis as 75% of the patients diagnosed with myasthenia gravis have a thymic abnormality (Binu et al., 2022, p. 63).
  - This indicates why thymectomies are sometimes considered an appropriate treatment for MG

***Figure 1. Myasthenia gravis consists of antibodies blocking acetylcholine receptors at the neuromuscular junction (Nagelhout & Elisha, 2018, p. 769).***




## Significance of Pathophysiology

- The primary outcome of immune-mediated destruction of the acetylcholine receptors at the neuromuscular junction is "a decreased number of functional postsynaptic ACh receptors," leading to a decrease in the movement and an increased fatigue of the muscles (Nagelhout & Elisha, 2018, p. 769).
- In order for muscle contraction to occur, acetylcholine must bind to receptors at the motor end plate (Nagelhout & Elisha, 2018, p. 769).
- The series of steps that must occur are listed in Figure 2.
- Without properly functioning receptors, these steps cannot continue past step 3.

**Steps of Neurohumoral Transmission and Excitation-Contraction Coupling**

1. An action potential reaches the motor nerve ending.
2. $Ca^{2+}$ enters the motor nerve ending; ACh is released into the synaptic cleft.
3. ACh binds to a postsynaptic cholinergic receptor at the motor end plate.
4. The motor end-plate membrane depolarizes (the EPP).
5. An action potential is generated at the perijunctional muscle membrane.
6. The action potential spreads along the muscle membrane and inward to the transverse tubules.
7. Depolarization of the T tubules causes $Ca^{2+}$ release from the sarcoplasmic reticulum.
8. $Ca^{2+}$ triggers actomyosin complex cross-bridge formation; the sarcomere shortens; the muscle contracts.

*ACh*, Acetylcholine; *T*, transverse.

***Figure 2. Steps of neurohumoral transmission and excitation-contraction coupling (Nagelhout & Elisha, 2018, p. 767).***

## Implications for Nursing Care

Due to the side effects and treatments associated with MG, nurses should keep some of the following things in mind when caring for these patients:

- Understand the progression of MG throughout the day and how symptoms might be better in the morning
- "Effective cough requires deep inspiration followed by glottic closure and appropriate expiratory muscle strength to generate sufficient intrathoracic pressure and obtain high expiratory flows" and therefore might be difficult for those with MG to perform (Racca et al., 2019, p. 498).
- Additionally, "clearing airway secretions and airway mucus can be a continual problem for patients with generalized muscle weakness and for those who cannot swallow saliva or food without aspiration" (Racca et al., 2019, p. 498).
- Due to the inability of some MG patients to express themselves effectively, nurses should avoid relying on nonverbal communication and be sure to clarify directly with the patient
- Corticosteroids might cause the following side effects (Nagelhout & Elisha, 2018, p. 770):
  - Osteoporosis
  - Gastrointestinal bleeding
  - Suppression of endogenous cortisol release
  - Cataracts
  - Increased susceptibility to acute infections
  - Hypertension
  - Glucose intolerance
- Cholinesterase inhibitors when used in excess may cause myasthenic crisis, "which is a severe exacerbation of myasthenic symptoms resulting in respiratory distress" (Nagelhout, & Elisha, 2018, p. 770).

## Anesthesia Considerations

According to Nagelhout & Elisha (2018), the following considerations are important for the patient with MG who will be receiving anesthesia (p. 771):

- Assess patient several days before and immediately before surgery for disease control
- Avoid anxiolytics or opioids preoperatively if possible
- Consider effects of anticholinesterase medications if taken the day of surgery
- Consider risk for aspiration regarding pharyngeal weakness and inability to clear secretions
- If possible, use only local or regional anesthesia
- For general anesthesia, small doses of short-acting nondepolarizing muscle relaxants should be used
- Ensure full return of respiratory strength prior to extubation

Sugammadex is considered useful in reversing steroidal muscle relaxants. However, there is still an unpredictability of response when given to those with neuromuscular disease, and the optimal dose is not agreed upon. The patient should have neuromuscular monitoring to ensure complete reversal when sugammadex is used (Gurunathan et al., 2019, p. 1).

## Continuing Research

- New research is happening frequently regarding myasthenia gravis and emerging treatment possibilities.
- One study that investigates a new treatment is by Makino et al. (2020) and validates "pathogenic anitbodies as a molecular target of MG treatment" by "using single cell technology and novel high-throughput cell-based binding assays" (p. 1).
- Monoclonal antibodies, such as rituximab, are resulting in good therapeutic effect and appears to be promising for severe generalized myasthenia gravis (Nagelhout & Elisha, 2018, p. 770).

## Conclusions

- Myasthenia gravis is a neuromuscular disease with increasing prevalence due to better diagnosis (Collins et al., 2020, p. 485).
- Pathophysiology is not completely understood but likely revolves around antibodies that attack different proteins of the NMJ (Naglehout & Elisha, 2018, p. 768).
- Symptoms include muscle weakness, eyelid drooping, lack of facial expressions, and sometimes, respiratory complications such as aspiration and dyspnea
- Due to the above symptoms, nurses and anesthesia providers should be cognizant of the possible complications and considerations of treatment while caring for a patient with myasthenia gravis
- Treatments are available, but more research continues to be done regarding the most effective options to improve the quality of life for these patients

## References and Additional Sources

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