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Myasthenia Gravis and implications for the Certified Registered Nurse Anesthetist

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Introduction

In healthcare and, specifically anesthesia, there are many conditions that require various considerations by the prudent provider. An example of a condition requiring special attention is myasthenia gravis. Myasthenia gravis is an autoimmune disease in which skeletal muscle weakness and rapid fatigue result from destruction of nicotinic acetylcholine receptors [7]. Although the prevalence is not overwhelmingly high with most recent estimates of prevalence around 14 to 20 per 100,000 people in the United States [5] and 20 per 100,000 worldwide [9], inappropriate perioperative management of those with this ailment can result in serious consequences. Understanding the pathophysiology, various treatments (both surgical and medical), and anesthetic implications can result in better outcomes for individuals with myasthenia gravis that require surgery.

Case Study

Mr. Smith, a 52-year-old male, presents to his primary care physician whom he hasn't seem in nearly ten years because not only does he need a physical before his carpal tunnel surgery planned for next month, but also because he has not been feeling well. Mr. Smith has been experiencing generalized muscle weakness that, at times, leaves him feeling short of breath. In addition to fatigue that does seem to resolve with rest, Mr. Smith has also been experiencing double vision, a "fluttering" sensation of his heart, difficulty swallowing, and drooping of his eyelid. After several blood tests were negative, including normal glucose and thyroid panel, and a thorough neurological examination was performed, Mr. Smith's physician suspected myasthenia gravis so he ordered a tensilon test, which confirmed the diagnosis of myasthenia gravis.

Mr. Smith presents with classic symptoms of myasthenia gravis and is within the typical age range for disease presentation in men, which is between 50 and 60 years of age [8]. Weakness commonly affects the muscles of one or both eyes leading to ptosis and diplopia [4] and the age of onset in men is typically Visual disturbances affect more than half of patients with myasthenia gravis. Fatigue that resolves with rest and arrhythmias that result of inflammation of the myocardium are also symptoms common to the patient with myasthenia gravis [8]. Diagnosis of myasthenia gravis is not always straightforward and can be difficult at times. Various blood tests exist which include measurement of serum antibodies against acetylcholine receptors and muscle-specific receptor tyrosine kinase (MuSK) with the latter being present in nearly 40% of individuals with myasthenia gravis. Perhaps the most well known diagnostic for myasthenia gravis is the tensilon test in which tensilon, also known as edrophonium, is administered which inhibits the breakdown of acetylcholine. The increased amount of acetylcholine in an individual with myasthenia gravis will cause a momentary improvement of weakness. Other tests that can assist in the diagnosis of myasthenia gravis include electromyography, radiologic imaging of the chest and neck to assess for thymus alterations, and pulmonary function tests [10].

Pathophysiology

To understand the pathophysiology of myasthenia gravis, one must first have an understanding of skeletal muscle depolarization and the receptors involved. When an electrical impulse reaches the presynaptic nerve terminal, an influx of calcium triggers the release of presynaptic acetylcholine. Approximately 150 to 200 vesicles that contain nearly 10,000 molecules of acetylcholine each are released into the synaptic cleft and bind to nicotinic acetylcholine receptors. Nicotinic acetylcholine receptors are located on postsynaptic folds on motor end plates, which are located in close proximity to skeletal muscle. The binding of acetylcholine to the alpha sub-unit of the nicotinic acetylcholine receptor causes a conformational change in the receptor, opening a channel that allows for a rapid influx of sodium ions. The rapid influx of sodium ions depolarizes the motor end plate and skeletal muscle, which allows for muscular contraction [8]. The following picture depicts the neuromuscular junction and acetylcholine's role in action potential propagation.

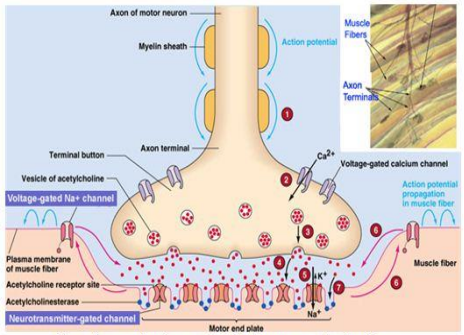


Figure 1: axon of motor neuron at the neuromuscular junction

[1]

As mentioned earlier, myasthenia gravis is an autoimmune disorder in which antibodies target the nicotinic acetylcholine receptors and other proteins resulting in their destruction. Specifically, nearly 85% of people with myasthenia gravis have antibodies that target nicotinic acetylcholine receptors. Of the 15% that do not have anti-acetylcholine antibodies, 70% have antibodies targeting other proteins involved in neuromuscular transmission that includes muscle specific tyrosine kinase. Regardless of the type of autoantibody muscle membrane destruction is caused by antibody activation of complement, disintegration of the postsynaptic membrane, and elimination of the postsynaptic folds (the primary location of nicotinic acetylcholine receptors). Investigation of thymus abnormalities (thymomas, atrophy, or hyperplasia) is warranted in patients with myasthenia gravis because the thymus major site for antibody production [2].

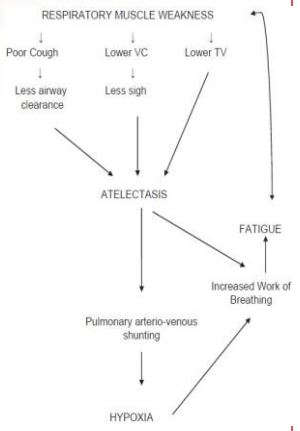
Significance of Pathophysiology

- Most frequent symptom is muscle weakness.
- Weakness occurs when 70%-90% of nicotinic acetylcholine receptors are lost [6].
- Myasthenia gravis can classified, or staged, according to severity and muscles affected by the Osserman Staging system seen below.

Class I	Patients with ocular involvement alone
Class II	Mild muscular weakness, not incapacitating
Class III	Moderate muscular weakness, not incapacitating, including oropharyngeal and respiratory muscle weakness
Class IV	Incapacitating weakness of any muscle system, including oropharyngeal and respiratory muscle weakness
Class V	Life-threatening respiratory insufficiency requiring ventilatory assistance (crisis)

[3]

Of significant importance is respiratory muscle weakness in patients with myasthenia gravis. Ineffective respiratory muscle function can cause a multitude of problems both perioperatively and in day-to-day life. The following schematic is a great representation of the pathologic effects that can result from respiratory muscle weakness.



[3]

Nursing Implications

Decreased numbers of nicotinic acetylcholine receptors and the associated skeletal muscular weakness have important implications for the nurse anesthetist caring for the patient with myasthenia gravis perioperatively. A medication type frequently utilized by the nurse anesthetist to facilitate tracheal intubation and provide a motionless surgical field for the surgeon is neuromuscular blockers (NMBs). The two types of paralytics utilized today are depolarizing NMBs and non-depolarizing NMBs [11]. The only depolarizing NMB in use today is succinylcholine. Chemically, succinylcholine is composed of two molecules of acetylcholine (known as diacetylcholine) and causes muscular paralysis by joining to a nicotinic acetylcholine receptor causing a sustained muscular depolarization, preventing further action potentials from propagating. It differs from acetylcholine in that it is metabolized by pseudocholinesterase rather than acetylcholinesterase [8]. Due to the similarities between succinylcholine and acetylcholine, it is not surprising that patients with myasthenia gravis are often resistant to this medication, necessitating increased dosages to achieve acceptable paralysis (usually 2.5 times more).

Patients with myasthenia gravis, however, are considerably more sensitive to non-depolarizing NMBs, which achieve paralysis by binding to nicotinic acetylcholine receptors and preventing depolarization [8]. For example, in patients with myasthenia gravis, the potency of atracurium and vecuronium, two non-depolarizing NMBs, potency is increased two times. Because of the increased potency, caution must be used with non-depolarizers. If a non-depolarizing agent is needed, the initial dose should be reduced by 50-67% and closely monitored with a peripheral nerve stimulator. Intravenous induction agents like propofol or etomidate and/or volatile anesthetics like desflurane can be used to facilitate endotracheal intubation, however, the degree of respiratory depression can be magnified so caution needs to be exercised with these agents as well. Similar to induction agents, opioids can cause exacerbate respiratory muscle weakness and too need to be used with caution. Because of the profound respiratory weakness than can result postoperatively, ventilator support is frequently needed in patients with myasthenia gravis [11]. Some experts recommend discontinuation of cholinesterase inhibitors, medications used to treat myasthenia gravis, preoperatively in those with mild disease as these agents can complicate anesthetic management. Reversal of non-depolarizing neuromuscular blockers in these patients can result in a cholinergic crisis. It should be noted that discontinuation of cholinesterase inhibitors remains controversial. Finally, adequate return of muscular strength must be ensured prior to extubation so respiratory distress/ failure dose not occur [8].

Conclusion

Myasthenia gravis is a disease process that can cause profound weakness both perioperatively and in every day life. Understanding the pathophysiology of the disease, as is seen in the case of Mr. Smith, can provide the nurse anesthetist with a sound basis so as to optimally manage the anesthetic.

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