

Title	An Overview of Myasthenia Gravis
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Purpose

The goal of this course is to provide an understanding about myasthenia gravis and the treatments used for its control.

Objectives

1. Describe the signs and symptoms of myasthenia gravis.
 2. Explain types of medications used to treat myasthenia gravis.
 3. Describe two diagnostic tests used in myasthenia gravis.
 4. Differentiate between a myasthenic crisis and a cholinergic crisis.
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MYASTHENIA GRAVIS

Myasthenia gravis (MG) is an autoimmune neuromuscular disease that affects people from all nationalities and can occur at any age. Over the past 20 years the number of people affected has increased and in the United States MG affects 0.5-14.2 people per 100,000 population (5). It is not contagious, and is not hereditary. Myasthenia gravis, if not properly treated, can lead to death. It is the most common primary disorder of neuromuscular transmission. The onset is usually gradual and progresses over an average period of six years. Periods of remissions and exacerbations can occur.

It affects more females than males. While it can affect anyone, it most commonly affects women under 40 and men over 60. MG has considerable impact on the individual affected because it hinders voluntary control and alters facial appearance. Individuals affected with MG are able to lead normal lives with treatment; the health care worker can help promote a healthier lifestyle for these individuals by teaching them about the disease process, as well as, the medications and treatments to control symptoms of MG.

WHAT CAUSES MYASTHENIA GRAVIS?

The characteristic sign of MG is muscle weakness. It is caused by an interruption of impulses between nerve and muscle. In the human body, every muscle movement originates as a result of an impulse between nerve and muscle at the neuromuscular junction. In order for an impulse to create change, acetylcholine (ACh), a neurotransmitter, must join to the acetylcholine receptors that exists at the neuromuscular junctions. This binding action allows ion exchanges in the muscle that then leads to contraction. In myasthenia gravis, the receptors at the neuromuscular junction are impaired because the immune system produces antibodies that bind to these acetylcholine receptor sites. As time progresses, more and more receptor sites are occupied or destroyed, thereby, decreasing the potential for muscle activity and leading to loss of muscle control. For this purpose treatment with anti-cholinesterase inhibitors and immunosuppressant medications are used. Together these medications function to decrease

damage to the acetylcholine receptor sites. Thyroid disease is seen in about 10 percent of patients with myasthenia gravis – either hyper or hypothyroidism (5).

For those who are treated properly, life expectancy is not altered in those with myasthenia gravis (1, 2). With improper treatment, risk of respiratory complications including aspiration pneumonia increases. In some cases of MG, individuals may experience remission of the disease. It is not known what triggers this remission.

WHAT ARE THE SYMPTOMS OF MYASTHENIA GRAVIS?

Sufferers of MG complain of such symptoms as: muscle weakness, fatigue, ptosis, diplopia, ocular motor disturbance, dysarthria, weak cough, swallowing and chewing difficulty, loss of facial muscle control, difficulty sitting upright, shortness of breath, and unsteady gait (1, 2, 3, 4, 5). It typically takes about one year from onset of symptoms until diagnosis because muscle weakness – which is present in many other conditions – is a common presenting symptom in many disease states (1). Symptoms often vary in duration; they worsen with repeated use of the muscles and usually are relieved after rest. Any factor that produces stress, emotional or physical, can aggravate symptoms and may lead to a myasthenic crisis if not addressed. A myasthenic crisis occurs when muscular weakness becomes severe and causes inadequate respiratory function. If respiratory support is not provided, respiratory arrest ensues.

HOW IS MYASTHENIA GRAVIS DIAGNOSED?

Myasthenia gravis can often be mistaken for other illnesses. Diagnosis is not dependent on subjective findings only; the physician performs a neurological exam, evaluates blood test results for antibodies to the

acetylcholine receptors (AChR). He can perform an edrophonium chloride test (Tensilon test). The test is positive if muscle control improves in the affected area for a brief period of time after injection with a chemical. Computed topography exam and magnetic resonance imaging are used to assess for thymus gland abnormalities (thymus abnormalities are common in individuals with MG), normal studies do not rule out thymoma.

Other diagnostic tools, such as, nerve conduction velocity testing (NCV), electromyography (EMG) and muscle biopsies can be used. The NCV test is used to assess nerve conduction speed, as well as, nerve action potential and the EMG test is used to measure muscle action potentials. In addition, a muscle biopsy can reveal anatomical features, which are characteristics of neuromuscular disease.

DRUGS USED TO TREAT MYASTHENIA GRAVIS

Cholinesterase inhibitors are the preferred choice in treating MG. Just as symptoms differ in each person, type of medication; dose and frequency are different for each individual. Medication dose and frequency are adjusted to obtain optimal therapeutic effects with minimal side effects. Cholinesterase inhibitors improve muscle contraction by increasing the amount of acetylcholine (Ach) at the neuromuscular junction. The more Ach, the more likely nerve impulses will be transmitted. It is important to note that these medications do not increase or protect the acetylcholine receptor sites (AChR).

Table 1: Cholinesterase Inhibitors

Generics	Common Side effects

Neostigmine, Pyridostigmine, Ambenonium	Nausea, diarrhea, vomiting, diaphoresis, abdominal cramps, increased salivation, increased bronchial secretions
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Cholinesterase inhibitors can be taken with food or milk to prevent gastrointestinal upset. Increased muscle strength is usually evident within one hour after medication administration. It is important to emphasize compliance with medication administration as ordered by the physician. Taking less medication than prescribed can exacerbate muscular weakness and taking more medications than prescribed can lead to overdose and result in a cholinergic crisis.

In a cholinergic crisis there is severe muscle weakness, which can lead to respiratory arrest. Signs of overdose are: confusion, severe diarrhea, severe nausea, increase in salivation, blurred vision, urinary retention, hot dry skin, tachycardia, hypertension, abdominal cramps, seizures, and an increase in respiratory rate. Treatment is supportive and may consist of gastric lavage, activated charcoal administration, intravenous fluids, urinary catheterization, withdrawal of cholinesterase inhibitors and administration of atropine (antidote).

In caring for an individual with MG, it is important to notify the physician if the individual is also showing symptoms of urinary tract infection, or intestinal/urinary obstruction. These conditions are worsened with the use of cholinesterase inhibitors. Also, some medications can worsen symptoms of MG, they include: anesthetics, antibiotics, antiarrhythmics, muscle relaxants, psychotropic drugs, morphine, quinine, beta-blockers, calcium channel blockers, iodinated contrast agents, aminoglycosides and novocain (6). Medications, such as, D-penicillamine, alpha-interferon, and botulinum toxin can cause a crisis situation and/or induce MG (6). It is believed that the drug induces MG because of changes it produces in the immune system. This is referred to as drug-related myasthenia gravis. When MG results after a bacterial or viral infection, it is referred to as viral/bacterial myasthenia gravis.

In order to protect acetylcholine receptor sites, medications that suppress the immune system are administered, in addition to cholinesterase inhibitors. By suppressing the immune system, the formation of antibodies that affect the acetylcholine receptors decrease. Dosages are titrated to suppress the immune system production of antibodies and at the same time allow the immune system to protect the body against infections. Corticosteroids and other immunosuppressive medications, such as, azathioprine (Imuran), cyclophosphamide (Cytoxan) and cyclosporine (sandimmune) are used. The use of corticosteroids should be accompanied by the use of a bisphosphonates (such as alendronate [Fosamax] or risedronate [Actonel]) and the use of an antacid (4). Side effects to long-term corticosteroid use are of concern. Some examples are: osteoporosis, weight gain, cataracts, memory changes, and hypertension.

For patients who are being considered for long-term use of corticosteroids a co-administered immunosuppressant medication should be administered. This will allow a decreased dose of the corticosteroid. Reducing the use of corticosteroids results in lesser exposure to the medications' side effects. Azathioprine (Imuran) is the drug of choice as a steroid suppressant medication. Some do not respond to this medication or are intolerant and may be switched to another immunosuppressive medication (4).

Bronchodilators, beta-agonists and anticholinergics, are sometimes used in the treatment of respiratory complications of MG. These medications treat respiratory distress and bronchospasm from the medications used to treat myasthenia gravis. Sometimes one, sometimes both medication are needed for bronchodilation.

A myasthenic crisis is also an exacerbation of weakness that can lead to respiratory arrest. It is often caused by a stressor, such as, infection, fever, or an adverse medication reaction. Support is directed towards maintaining the airway and providing adequate ventilation until muscle strength returns and administering neostigmine. Death rates from a myasthenic crisis

are about five percent when diagnosis is prompt and treatment is appropriate (5).

How can one distinguish between a myasthenic crisis and a cholinergic crisis? This is done by means of the edrophonium (Tensilon) test. The individual is administered the test dose; if muscle strength improves then the crisis is a myasthenic crisis. In a cholinergic crisis, symptoms worsen.

OTHER MEASURES TO RELIEVE SYMPTOMS OF MYASTHENIA GRAVIS

Most myasthenia gravis sufferers have an abnormal thymus gland. Some people develop thymomas. A thymoma is a tumor of the thymus gland that can become malignant. After excision of the thymus, MG symptoms may decrease and typically do. In fact, symptoms are reduced in more than 70 percent of patients after removal of the thymoma and some are cured (1). Because of its invasiveness, there are risks involved with this procedure.

Administration of immune globulin can also reduce symptoms temporarily by decreasing the amount of antibodies produced by the immune system.

Plasmapheresis, which works by removing the antibodies that attack the acetylcholine receptor sites also provide short-term relief of symptoms, such as, muscle weakness. This procedure is used more often to assist in recovery during a crisis (7).

MEASURES TO PREVENT INJURY

In order to prevent injury, certain measures can provide safety in and outside the home setting. Neck muscles, arms, and legs become weaker with repetitive use; to avoid becoming excessively fatigued, the health care worker can encourage adequate nutrition and regular nap periods throughout the day. To prevent falls encourage removal of throw rugs, use of a cane or walker, if needed, and installation of nightlights to help illuminate rooms and hallways at night. Practicing safety measures is a key factor in the prevention of fractures resulting from falls.

Due to weakness in the tongue and jaw muscles, swallowing can often be difficult. At times liquids are regurgitated nasally. To improve muscle strength during meals administer medication 30 minutes before meals. Encourage sitting upright during meals, changing food consistency to soft, and taking small sips of liquid with food to help promote swallowing. If weak neck muscles affect the individual, a cervical collar could be used for support. It is very important to avoid aspiration; if not prevented it can lead to aspiration pneumonia.

Visual problems usually result from diplopia or ptosis. Bright light tends to increase eye tearing, encourage sunglasses for prevention. Covering an eye with an eye patch may help if suffering from double vision. Exposure to extremes in temperatures can also increase fatigue and should be avoided.

The health care worker should also encourage the use of a medical alert bracelet. Maintaining a list of medications the individual is taking is also advisable. This information facilitates treatment in cases of emergency medical attention, and prevents medication errors.

CONCLUSION

Myasthenia gravis is a progressive disease that can be fatal. Death is often due to aspiration pneumonia or another respiratory complication. Good treatment is necessary in order to prevent death and disability. Because the disease is not extremely common, referral to a physician who has experience treating it is encouraged.

New research is looking at improved ways to treat this disease. Hopefully, with further studies, new treatments will become available to further improve the quality of life for all those affected by myasthenia gravis.

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Course Exam

1. Myasthenia gravis is a musculoskeletal disorder.
 True False
2. In myasthenia gravis the neurotransmitter fails to bind to the receptor sites in the neuromuscular junction.
 True False
3. In myasthenia gravis the immune system produces antibodies, which prevent muscle contraction.
 True False
4. Older women (over 70) are the more commonly affected by myasthenia gravis than younger women.
 True False
5. Muscle weakness is a common symptom of myasthenia gravis.
 True False
6. A cholinergic crisis can be caused by an overdose of an anticholinesterase medications, such as, pyridostigmine.
 True False

7. An EMG is a test used to measure muscle action potential.
- True False
8. Treatment with azathioprine (Imuran) is usually administered to suppress immune response in order to decrease release of antibodies that affects the AChR sites.
- True False
9. A myasthenic crisis can be caused by an emotional stressor.
- True False
10. In most adults with myasthenia gravis the thymus gland is abnormal.
- True False