Diagnosis of Myasthenia Gravis

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KEYWORDS

- Myasthenia gravis • Edrophonium test • Repetitive nerve stimulation
- Single-fiber electromyography • Acetylcholine receptor–binding autoantibodies
- Muscle-specific tyrosine kinase (MuSK)
- Low-density lipoprotein receptor–related protein 4 (LRP4) • Agrin

KEY POINTS

- Edrophonium testing is rarely used to confirm due to logistical barriers as atropine has to be kept in the clinic and this needs a crash cart and code team to be available.
- Autoantibodies to acetylcholine receptor binding are highly sensitivity and specific in generalized myasthenia gravis (MG).
- Slow repetitive nerve stimulation is a helpful tool to document an impaired safety factor of neuromuscular transmission in MG.
- Single-fiber electromyography is tedious and has the highest sensitivity in both generalized and ocular MG, particularly in weak muscles.

Myasthenia gravis (MG) diagnosis depends on clinical symptoms, examination findings, and the following diagnostic testing. In most instances the clinician makes the diagnosis of MG based on the neurologic history and examination findings, and the diagnostic tests are usually performed to confirm the clinical diagnosis.

Disclosure Statement: Drs M. Pasnoor and C. Farmakidis have nothing to disclose. Dr M.M. Dimachkie is on the speaker's bureau or is a consultant for Alnylam, Baxalta, Catalyst, CSL-Behring, Mallinckrodt, Novartis NuFactor, and Terumo. He has also received grants from Alexion, Biomarin, Catalyst, CSL Behring, FDA/OPD, GSK, Grifols, MDA, NIH, Novartis, Orphazyme, Sanofi, and TMA. Dr R.J. Barohn is a consultant for NuFactor and is on the advisory board for Novartis. He has received an honorarium from Option Care and PlatformQ Health Education. He has received research grants from NIH, FDA/OOPD, NINDS, Novartis, Sanofi/Genzyme, Biomarin, IONIS, Teva, Cytokinetics, Eli Lilly, PCORI, ALSA, and PTC. This work was supported by a CTSA grant from NCATS awarded to the University of Kansas for Frontiers: University of Kansas Clinical and Translational Science Institute (# UL1TR002366) The contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH or NCATS.
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Neurol Clin 36 (2018) 261–274
https://doi.org/10.1016/j.ncl.2018.01.010 **neurologic.theclinics.com**

ICE PACK TEST

This test is commonly performed by ophthalmologists and generally thought to have good sensitivity and specificity, however, more subject to false-positive and false-negative results than the edrophonium chloride test. This test is often used in cases whereby patients are either old or medically unstable for the edrophonium test or if edrophonium testing is not available.

Method: A cold ice pack, disposable glove, or specimen filled with ice is applied to the ptotic eyes for 1 to 2 minutes. Improvement of ptosis shortly after application of ice indicates a positive result.

A cooler temperature inhibits acetylcholinesterase enzyme activity,[1] leading to a decreased breakdown of released acetylcholine in the neuromuscular junction (NMJ), thus, improving NMJ transmission.

COGAN LID TWITCH TEST

This test consists of a brief overshoot twitch of lid retraction following sudden return of the eyes to the primary position after a period of downgaze.[2] The lid will briefly twitch upward then settle back to its previous position. This sign is used to evaluate MG; however, it is not diagnostic for this and may be seen in other conditions. One study by Singman and colleagues[3] showed a sensitivity of 75% and a specificity of 99% of the Cogan lid twitch in evaluating MG.

EDROPHONIUM CHLORIDE (ENLON) TEST

Edrophonium chloride is a short-acting, reversible acetylcholinesterase inhibitor. It inhibits the breakdown of acetylcholine, which is a neurotransmitter that is released at the synaptic junction, thus, increasing the availability of acetylcholine at the NMJ leading to increased binding of acetylcholine to postsynaptic receptors, causing an alteration in the ion channels; this leads to generation of the action potential. Edrophonium testing was introduced in the 1950s. Before that, diagnostic testing for MG was done with physostigmine and neostigmine (prostigmine), both introduced by Mary Walker.[4,5]

Edrophonium testing is a useful diagnostic test for myasthenia gravis; however, this cannot be used for adjusting the medical treatment. An objective way to measure weakness should be present before considering this testing, and this is usually ptosis. A response of ocular movement can also be seen; but it is difficult to determine if the test is positive unless diplopia reduces extremely, which is infrequent. Therefore, ptosis is the best sign to measure at the bedside.

The edrophonium test is a simple test that can be performed easily in the outpatient setting and does not need to be done in the hospital setting. The intravenous (IV) administration of up to 10 mg of edrophonium chloride is a diagnostic test in the evaluation of potential patients with MG. The details of the testing are presented in **Box 1**. It is not used as frequently now with the advent of antibody testing. The edrophonium test can have several pitfalls. The most common mistake is that the physician performing the test does not have an objective parameter to measure before and after edrophonium administration. As noted earlier, the most useful parameter is the degree of ptosis in each eye. The palpebral fissure should be measured before the drug is administered. The best indication of a positive test is a significant increase in the palpebral fissure aperture or the opening of a completely ptotic eye (**Figs. 1** and **2**). If no ptosis is present, the edrophonium test may be difficult to interpret even in clear-cut cases of MG. If patients have a