What’s Hot off the Press in Neuromuscular Junction Disorders?

Introduction
Welcome back to our column highlighting some of the latest developments in research in neuromuscular junction disorders. We hope you enjoyed the last edition which appeared in the Spring 2014 Foundation Focus and look forward to keeping you updated on breakthroughs in the field.

Myasthenia Gravis Crisis
Myasthenic crisis is defined as impending or actual failure of the muscles of breathing or swallowing, usually severe enough to require placement of a breathing tube and artificial ventilation. It is estimated to occur in about 15-20% of patients with myasthenia gravis (MG).⁴ Crisis more commonly occurs in the first two years after MG is diagnosed and may be precipitated by a number of conditions, including infection, certain medications, trauma, or stress.⁵ A recent study performed in India examined the predictors and outcome of myasthenic crisis in their patient cohort.² Sixty-four patients with MG were identified in their database; 14 (21.9%) experienced crisis an average of 8.5 months after the time of diagnosis. The most common precipitating factor was infection. Of the 14 patients, 8 required prolonged artificial ventilation during crises for an average of 36 days. When further analyzing the data, the authors discovered that male gender, the presence of other medical illnesses, the severity of MG, weakness of the muscles of swallowing and speaking, high levels of acetylcholine receptor (AChR) antibodies, and the presence of thymoma were all associated with a greater likelihood of experiencing crisis. In addition, these patients were found to have a poorer quality of life at the time of discharge from the hospital, more frequent hospitalizations, and higher costs of medical treatment. These findings highlight the importance of aggressive management of MG in the time immediately following diagnosis. Another recent study reviewed the course of 38 patients with MG who were treated for severe crises.⁶ At an average follow-up of 4 years, nearly 20% were asymptomatic and another 50% had only disease involving the eyes or mild generalized disease. Younger and older patients did equally well. These findings suggest that with aggressive treatment, even those patients who initially have a rocky course usually do quite well the majority of the time.

The cholesterol-lowering medications known as statins are widely prescribed to reduce the risk of heart attack and stroke.⁵ Many of you may be on them. The development of a range of muscle diseases or muscle pain is a well-recognized complication of treatment with these medications.⁶ A recent paper described 2 patients who were prescribed statins and developed ACh receptor positive ocular myasthenia, which combined with prior reports, brings the number of reported cases to 7.⁷⁻¹⁰

The authors proposed that exposure to statins either unmasked underlying MG or induces a new autoimmune process. This report highlights the need to consider the diagnosis of MG in patients with fatigable muscle weakness after starting statins and to carefully monitor known patients with MG after they start these medications. Realize you should not stop statin medications on your own if you think they are causing problems — discuss this with your doctor.

West Nile Virus (WNV) is a virus transmitted to humans by mosquitos and is now endemic in the continental United States. It can cause a range of symptoms from fever, headache, and fatigue, to infection of the brain (encephalitis) or weakness of the muscles mimicking polio. A recent paper described 6 cases of ACh receptor positive MG developing 3-7 months after WNV infection.¹¹ All of these patients also had the more commonly seen muscle weakness resembling polio. As with statin medications, a viral-triggered autoimmunity may be responsible for the development of MG in these patients.
Several new articles have examined the role of antibodies in MG. Involvement of the heart or cardiovascular system is fortunately not common in MG. Antibodies to a potassium channel (Kv1.4) which is located on both heart and skeletal muscle have been found in patients with MG and inflammation of the heart muscle (myocarditis). In a series of 650 patients with MG, antibodies to Kv1.4 were found in just over 10% of patients, all of whom also had ACh receptor antibodies. The majority of patients with these antibodies had non-specific findings on electrocardiograms (EKGs), but 8 had clinically-suspected inflammation of heart muscle with life-threatening heart rhythm disturbances and heart failure. All of these 8 patients also had thymomas. The findings of this study make antibodies to Kv1.4 a potential marker for heart muscle inflammation in MG.

A common question that patients with MG ask their doctors is whether ACh receptor antibody levels correlate with clinical change. The age-old answer to this question has been no. A recent study out of Duke University examined this question. Using their database, the investigators reviewed results from 151 patients and found that antibody levels fell in 92% of patients who improved based on standard MG outcome measures, but they also fell in 63% of patients who did not improve. The percent fall in antibody levels did not differ between those patients who improved and those who did not. In conclusion, the investigators could not recommend commercially-used ACh receptor antibody assays as a marker for following MG clinical status in either the clinic or trial setting. So this is a reason why it is not crucial for your doctor to recheck your antibody level over and over again.

Thanks for reading and see you again next time!

References