New Therapeutic Strategies in Myasthenia Gravis

Myasthenia gravis (MG) is an autoimmune neuromuscular disease that causes progressive skeletal muscular weakness, particularly in the eyes, mouth, throat, and limbs. “Manifestations range from isolated double vision and droopy eyelids to profound paralysis requiring artificial ventilation,” says Henry J. Kaminski, MD, the Meta A. Neuman Professor of Neurology at George Washington University. Early onset of MG, between ages 20–45, is predominantly seen in women. Later onset, after ages 45–50, is typically seen more often in men.

Approximately 10–15% of people with MG have a thymus gland tumor, called thymoma. About 30–50% of the time, the tumor expresses what Dr. Kaminski calls “self-proteins” that are then attacked by the immune system as it reacts to the tumor. Resecting it may alleviate symptoms but doesn’t cure the autoimmune disease.

There are now several FDA-approved therapies for MG, including established treatments such as pyridostigmine, prednisone, azathioprine, mycophenolate, tacrolimus, methotrexate, cyclophosphamide, rituximab, intravenous immunoglobulin (IVIG) and plasma exchange. In the past decade, the FDA has approved eculizumab, zilucoplan, ravulizamab, rozanolixizumab, and efgarligomad. Common treatments include cholinesterase inhibitors like pyridostigmine (Pyridostigmine), which are given as a first-line treatment and work by helping nerves and muscles communicate. “Symptoms can improve in about 30 minutes, but action wanes over four hours, so redosing is necessary,” says Dr. Kaminski.

Other treatments considered lifesaving that can be used as chronic treatments are a blood-filtering process called plasmapheresis, IVIG, antibody treatment, and plasma exchange. “IVIG and plasma exchange essentially remove circulating antibodies and are used for severe exacerbations,” says Dr. Kaminski. “They can work quickly, from days to two to three weeks.”

Research continues to explore additional therapeutic strategies. Several research studies are recruiting to test potential MG treatments, including:

- A phase 3 study of a new form of oral cladribine in adults testing the long-term safety and efficacy of the drug.
- A phase 2 study looking at the safety and efficacy of Descartes-O8 CAR-T cells for MG in adults.
- A phase 1 study evaluating various doses of MuSK-CAART in people diagnosed with muscle-specific tyrosine kinase (MuSK) myasthenia gravis, a rare but potentially severe disease where patients develop pathogenic autoantibodies that specifically target the MuSK protein in the neuromuscular junction.

One of Dr. Kaminski’s colleagues, Linda L. Kusner, PhD, published the results of a study on survivin, which promotes the survival of autoreactive immune cells. The research found that there is elevated

expression of survivin in thymic and peripheral lymphocytes in MG patients, Dr. Kaminski says. Dr. Kusner's work eliminated these cells using a survivin vaccination approach and an antibody approach with animals having elimination of weakness. "She and colleagues at Mimivax are humanizing an antibody to survivin in anticipation of human studies in MG. This treatment would be expected to only eliminate autoreactive cells and save normal cells from removal," Dr. Kaminski says.

Resources:

- MDA webinar: Myasthenia Gravis: Clinical Features & Differential Diagnosis
- MDA webinar: Optimizing Care in Myasthenia Gravis
- The Myasthenia Gravis Foundation of America
- The Myasthenia Gravis Rare Disease Network
- Myasthenia Gravis Foundation's Global MG Patient Registry
- Australia's MGBase Patient Registry