Myasthenia Gravis Needs Assessment

Overview

Myasthenia gravis (MG) is a neuromuscular junction disorder characterized by fluctuating, fatigable muscle weakness. Approximately 60,000 to 83,000 adults in the United States have been diagnosed with MG. In the pediatric population, the disorder has a lower prevalence, comprising about 10% of MG cases.[1-3] According to Billy Dunn, M.D., director of the Office of Neuroscience in the FDA's Center for Drug Evaluation and Research, "There are significant unmet medical needs for people living with myasthenia gravis."[4]

MG takes a toll on the physical, mental, social, and economic lives of affected individuals. The mean annual direct medical cost of MG per patient is $760 to $28,780, with cost per hospitalization estimated at $2,550 to $164,730.[7] In addition, absenteeism, reduced work productivity, and unemployment contribute to the overall economic impact of MG.[8]

From a clinical standpoint, MG is heterogeneous and can demonstrate fluctuating symptoms. Patients with MG may present with double vision, facial weakness, dysarthria, dysphagia, difficulty raising their hands, and neck weakness.[4] As a result, MG has a significant impact on the activities of daily living, with patients reporting symptoms such as difficulty holding a hair dryer, dressing themselves, completing homework, chewing food, or having a conversation.[4,5] Pediatric patients with juvenile MG are additionally at risk of developing strabismus and amblyopia.[6] The most severe complication of MG is respiratory weakness, which may require mechanical ventilation.

In terms of treatment, steroids and acetylcholinesterase inhibitors are first-line therapies. Non-steroidal immunosuppressives are used as second-line treatments.[9] While these therapies can be effective, it is not always the case. Studies have shown that more than 50% of patients receiving treatment continue to experience at least one moderate-to-severe symptom.[5] With continuing symptoms, patients are often made to negotiate "trade-offs" in vital areas of their lives, such as work and family planning, because of persistent symptoms.[5] In one survey, more than 50% of women with MG reported having refrained from having children.[10]

The ability to use steroids and immunosuppressives for MG treatment is at times limited by the side effect profiles of these medications. This can especially be the case for pediatric and pregnant patients, as well as patients with comorbidities. Experiencing medication side effects predisposes patients with MG to undertreatment and refractory disease, thus highlighting the importance of personalized therapy. In addition, the use of steroids is associated with growth restriction in children, mood disturbances, hypertension, diabetes, osteoporosis, and infections.

The side effects of immunosuppressive medications, such as azathioprine and mycophenolate mofetil, may include vomiting, diarrhea, liver dysfunction, and myelosuppression.[11]

The prevalence of refractory MG varies from 3% to 40%, depending on the definition used, while several criteria for the definitions have been proposed.[12] According to the international consensus guidance for the management of MG, refractory MG refers to cases with an MG Foundation of America post-intervention status that is unchanged or worse after corticosteroids and at least 2 other immunosuppressive agents in adequate doses for an adequate duration, with persistent symptoms or side effects that limit functioning, as defined by both patient and physician.[9]

The international consensus guidance for MG recommended treatment for refractory MG includes chronic intravenous immunoglobulin, chronic plasma exchange, cyclophosphamide, rituximab, and eculizumab.[9,13] However, since the 2020 guidance update, the US FDA has approved several new targeted therapies for MG. This development, coupled with emerging therapies underscores both the growing complexity and optimism in managing and treating MG. Available data for the use of the targeted MG therapies in juvenile MG and pregnancy is limited, but nipocalimab (NCT05265273), ravulizumab (NCT05644561), efgartigimod (NCT04833894), and zilucoplan (NCT06055959) are being studied in the pediatric population, which may lead to significant enhancement and maneuverability in pediatric MG management protocols.[20-22] In pregnancy, nipocalimab has demonstrated efficacy in improving outcomes in allo-immunized pregnant individuals at high risk of severe hemolytic disease of the fetus and newborn (NCT05912517) and is potentially safe for use in pregnant individuals who have MG.[23] Ravulizumab is currently being evaluated in a clinical trial involving pregnant patients with MG (NCT06312644), with active recruitment underway.

Despite these advancements, the absence of updated guidelines may pose challenges for physicians in integrating new therapies into personalized treatment plans for patients with MG. We therefore propose continuing education for clinicians that addresses the following gaps to optimize care and improve outcomes among individuals affected by MG:

Summary of Needs, Gaps, Data, and Intended Outcomes

	Educational Needs	**Learning Objectives**	**Desired Outcome**
Gap 1 Clinicians often face challenges in diagnosing myasthenia gravis (MG) due to its heterogeneous clinical presentation and fluctuating symptoms, leading to diagnostic	Clinicians need updated, continuing education to formulate precise diagnostic plans for the optimal diagnosis of patients in special populations with MG. These plans should be specifically	Formulate diagnostic plans based on identified clinical patterns in pediatric and pregnant MG populations.	Facilitate prompt diagnosis and early treatment by improving recognition of clinical patterns and symptoms of MG in pediatric and pregnant patients.

delays and late initiation of treatment.	designed to reveal clinical patterns indicative of MG in pediatric and pregnant patients.		
Gap 2 Clinicians require insights into identifying unmet treatment needs for patients with MG in special populations.	For the effective management and treatment of pediatric and pregnant patients with MG, clinicians require continuing education on the underappreciated physiological and environmental patient-specific factors that contribute to unmet treatment needs in these populations.	Outline individual patient factors that may reveal unmet treatment needs in pediatric and pregnant patients with MG.	Use knowledge of patient-specific factors that influence treatment outcomes to identify and rectify unmet treatment needs in pediatric and pregnant patients with MG to determine the applicability and potential efficacy of new, emerging therapies.
Gap 3 Clinicians need continuing, updated information on new, emerging therapies to provide personalized treatment plans to pediatric and pregnant patients with MG.	Clinicians need updated information on new, emerging therapies for pregnant and pediatric patients with MG to formulate personalized treatment plans.	Design personalized treatment strategies for pregnant and pediatric patients with MG.	Clinicians will demonstrate increased proficiency in personalizing treatment regimens for pregnant and pediatric patients with MG to provide optimal care.