Ocular Myasthenia Gravis: Diagnosis, Management, and Risk of Disease Progression

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Abstract:

Myasthenia gravis (MG) is an autoimmune disorder that causes muscle weakness and is categorized by four factors: the antibodies involved, the location of muscle weakness, the age of onset, and therapeutic status. Ocular myasthenia gravis (OMG) is a subtype that specifically affects the muscles of the eye and can cause droopy eyelids or double vision.

Diagnosing OMG remains challenging due to its overlap with other neurological and ophthalmologic conditions. Common diagnostic approaches include bedside assessments such as the ice-pack test, the single-fiber EMG test (SFEMG), and the acetylcholine receptor (AChR) test. Among these, the ice-pack test offers a rapid and sensitive screening method, while SFEMG provides high diagnostic accuracy as a confirmatory test.

Management strategies focus on both symptomatic relief and prevention of disease progression. Pyridostigmine is typically used as first-line therapy, while corticosteroids such as prednisone are introduced when symptoms persist or worsen. Evidence suggests that certain factors, including adult-onset disease, abnormal repetitive nerve stimulation (RNS), AChR antibody positivity, and thymoma, are associated with an increased risk of progression from ocular to generalized MG.

Understanding these diagnostic tools and risk factors is essential for guiding clinical decision-making, optimizing treatment strategies, and reducing disease risk. This review synthesizes current evidence to provide a comprehensive overview of the diagnosis, management, and risk of progression in ocular myasthenia gravis.

Introduction

Myasthenia gravis is a chronic autoimmune disorder that affects the neuromuscular junction, where nerves communicate with muscle. As a result, myasthenia gravis leads to muscle weakness and fatigue. This occurs when autoantibodies disrupt communication at the neuromuscular junction. Typically, nerves release a chemical messenger called acetylcholine, which binds to receptors on the muscle and causes it to contract. However, in an individual with myasthenia gravis, antibodies block or damage these receptor-related proteins, impairing muscle contraction. This can lead to symptoms such as diplopia, ptosis, trouble swallowing, and weakness in the arms or legs (Tannemaat, 2024; Hughes, 2004).

Myasthenia gravis is classified differently depending on the type of antibodies present, the muscles involved, the age of onset, or associated conditions. These subtypes respond differently to treatment and have varying long-term outcomes, making their distinction clinically important (Tannemaat, 2024).

The first classification of myasthenia gravis is based on the detection of autoantibodies in a patient's blood. The first subtype, AChR-positive MG, is the most common form of this disease; antibodies target acetylcholine receptors on the muscle surface, which prevents proper nerve-muscle communication (Meriggioli & Sanders, 2009). Another subtype, MuSK-positive MG, is less common but often more severe because antibodies target MuSK, a protein required for the formation and maintenance of the neuromuscular junction. Patients usually have more prominent weakness in the face, neck, and respiratory muscles (Guptill et al., 2011; Evoli et al., 2018). An even rarer form of myasthenia gravis is associated with LRP4-positive MG, in which antibodies target LRP4, another protein essential for the neuromuscular junction, and symptoms may overlap with those of other forms of the disease (Yan et al., 2018; Bacchi et al., 2018). The last form determined by autoantibodies is seronegative MG. With this type, patients test negative for known antibodies, including AChR, MuSK, and LRP4, but still exhibit clinical features of myasthenia gravis. Seronegative MG is believed to be caused by other, less well-studied antibodies (Tannemaat, 2024).

Myasthenia gravis is also classified by the muscles involved. Ocular myasthenia gravis is a subtype where weakness is limited to the eye muscles, causing double vision and droopy eyelids. About half of patients with ocular MG start with ocular symptoms but later progress to generalized myasthenia gravis (Guo et al., 2021; Li et al., 2018). The other main form is generalized MG, in which weakness extends beyond the eyes to the face, arms, legs, and throat, and sometimes to the respiratory muscles. Severity ranges from mild to life-threatening depending on the individual (Tannemaat, 2024).

Finally, MG can be classified by associated conditions or age of onset. Thymoma-associated MG occurs when a thymic tumor is related to the disease. Since the thymus plays a vital role in the immune system, abnormalities in its function can contribute to MG (De Rosa et al., 2021; Álvarez-Velasco et al., 2021). Age of onset is also essential. Juvenile MG affects children and adolescents and, although rare, requires early recognition, as treatment and outcomes may differ from those in adults. On the other hand, late-onset MG is diagnosed later in life, usually after age 50 or 60, and its prevalence has been increasing, likely due to better recognition and longer life expectancy (Tannemaat, 2024).

The primary objective of this paper is to focus on ocular myasthenia gravis, with symptoms limited to the eye muscles. While many articles and case reports are available, most focus on a single test or treatment option, making the information scattered and difficult to compare. The goal of this paper is to synthesize existing literature on both diagnostic testing and management. By organizing various studies and case reports into a clear structure, I aim to make it easier to see which testing methods and treatment strategies work best, where they have limitations, and how they compare. This paper provides a comprehensive overview by consolidating key diagnostic and management strategies. (Giannoccaro et al., 2020; Behbehani et al., 2022; Monte et al., 2021).

Methods

To gather sources for this paper, a structured, stepwise approach was used to identify relevant literature. The first step was to define the focus of my research. I wanted to focus specifically on ocular myasthenia gravis, with an emphasis on two main areas: diagnosis and treatment. Keeping the topic focused on these two parts helped me filter out unrelated studies and made the searches more manageable.

Search terms were iteratively refined to improve specificity and relevance. At first, I tried extensive searches like “ocular myasthenia gravis diagnosis,” but these often returned too general results. To improve this, I refined the search strings by adding the names of specific tests or medications. For example, I searched terms like “ocular myasthenia gravis ice test SFEMG RNS” for diagnostics and “ocular myasthenia gravis pyridostigmine prednisone azathioprine” for treatment. This process required iterative refinement to balance sensitivity and specificity, since I had to avoid searches that were too broad or too narrow.

I then searched PubMed for these terms. To make the results more relevant, I applied filters: I limited the publication dates to the last 10–15 years and prioritized review papers and case reports. However, I also included older articles when they were essential, such as early studies on antibody testing or pharmacological tests that shaped the field.

From there, I went through each search result in two stages. First, I checked the title to see if it specifically mentioned ocular myasthenia gravis. If the title seemed relevant, I moved to the abstract. Reading the abstract helped me decide if the study provided valuable information, such as test sensitivity and specificity for diagnostic papers or treatment outcomes for management papers. Studies that focused solely on generalized MG and did not address ocular cases were excluded. Studies containing relevant data on ocular myasthenia gravis were retained.

After selecting papers, I organized them into two main categories: one for diagnostic and screening methods and another for treatment and management strategies. The diagnostic group included bedside tests (like the ice-pack test and forced eyelid closure), antibody assays (AChR, MuSK, LRP4), and electrophysiological tests (RNS and SFEMG). The treatment group included first-line drugs like pyridostigmine, corticosteroids such as prednisone, steroid-sparing agents like azathioprine and mycophenolate, and more recent biologic therapies.

For each paper, I extracted key details. Across all search strings, 230 papers were identified. After title screening, 160 were excluded, leaving 70 papers for abstract review. During abstract review, 45 additional papers were excluded, leaving 25 studies with precise, usable data on ocular myasthenia gravis for full review. In diagnostic studies, I documented sensitivity, specificity, sample size, and the test’s place in the diagnostic process. In treatment studies, I recorded how the drug works, typical dosing ranges, how long it takes to show an effect, typical side effects, and whether the drug was considered first-line or used later in therapy. When two studies reported different statistics for the same test, I included both and noted possible reasons for the differences, such as variations in patient populations or methods.

Finally, I combined the information into a structured narrative. Specifically, the review began with the challenges of diagnosing ocular myasthenia gravis, discussed the order of screening and confirmatory tests, and then transitioned to treatment and management strategies. This method permitted organization of scattered information into a precise sequence, making it easier to understand how each test or treatment fits into the overall picture.

Screening and Diagnostic Testing in Ocular Myasthenia Gravis

Ocular myasthenia gravis (OMG) is a challenging neurological condition to diagnose because its symptoms often mimic those of other common eye or nerve disorders (Álvarez-Velasco et al., 2021; Meriggioli & Sanders, 2009). Patients with myasthenia gravis present with drooping eyelids, double vision, or eye-movement problems (Tannemaat, 2024). However, these presentations are non-specific, as they can also occur in other disorders, such as thyroid eye disease, cranial nerve palsies, or chronic progressive external ophthalmoplegia (Meriggioli & Sanders, 2009). Because of this overlap, no single test can definitively diagnose myasthenia gravis. Thus, physicians usually use a systematic process that starts with simple, safe bedside screening, then moves to blood antibody tests, and finally ends with advanced studies like electromyography if the case remains uncertain (Tannemaat, 2024).

The first step in evaluating OMG usually begins with bedside maneuvers that are fast, noninvasive, and inexpensive (Tannemaat, 2024). Even though these tests do not provide 100% certainty, they help doctors decide whether more specialized testing is warranted. The best-known of these is the ice-pack test, which has been used clinically since the 1970s. In this test, a doctor places an ice pack on the patient’s drooping eyelid for 2 to 5 minutes, then checks whether the eyelid lifts (Giannoccaro et al., 2020). The cooling effect slows acetylcholinesterase, the enzyme that usually breaks down acetylcholine at the neuromuscular junction (Hughes et al., 2004). Rather than slowing movement, reduced temperature decreases enzyme activity, allowing acetylcholine to remain in the gap longer and enabling weak muscle fibers to contract more effectively. If the eyelid rises at least 2 millimeters, the test is positive.

Several studies have demonstrated the diagnostic accuracy of the ice-pack test. Fakiri et al. (2013) reported 92% sensitivity and 79% specificity in patients with ptosis, while Lertchavanakul et al. (2001) found 95% sensitivity and 100% specificity. A newer version by Kee et al. (2019), in which patients held their eyes in upgaze before ice was applied, had 73.3% sensitivity and 96.7% specificity in patients with mild ptosis. Although the ice-pack test is simple, quick, and low-cost, it still requires a clinician's time and proper materials, and minor risks such as temporary skin reactions may occur. Nonetheless, the ice-pack test remains the first-line bedside tool for OMG. In another bedside test, the forced eyelid closure test, a physician asks the patient to close their eyes tightly for about 30 seconds, then reopen them; if ptosis temporarily improves, the result is considered positive. Smaller reports, typically involving fewer than forty participants, report 70–90% sensitivity for this maneuver (Wong et al., 2020). Another practical clinical observation is Cogan’s lid twitch sign. In this test, a patient looks down for ten to fifteen seconds, then back to primary gaze; if the eyelid overshoots briefly before sagging again, the test is considered positive. This sign shows 75–80% sensitivity (Meriggioli & Sanders, 2009), though it is not very specific, as similar twitching can occur in other eye disorders. The peek sign is another valuable clue. When a patient tries to keep their eyes tightly closed, fatigue of the orbicularis oculi muscle causes the eyelids to drift apart, giving the impression of "peeking slowly." These bedside signs and maneuvers are not perfect, but together they give doctors a crucial early impression. If the results are strongly positive, doctors move forward to confirm the suspicion with blood tests. If they are negative but suspicion remains, further testing is still warranted, especially when symptoms fluctuate or mimic other disorders.

Before modern antibody testing and electromyography were widely available, doctors often relied on pharmacological tests to confirm a diagnosis of myasthenia gravis (MG). The most commonly used test was the edrophonium test (Meriggioli & Sanders, 2009). Edrophonium is a short-acting acetylcholinesterase inhibitor that temporarily boosts acetylcholine at the neuromuscular junction. The effects of this usually begin within 30 to 45 seconds and last for approximately 5 minutes. It was given intravenously, and patients with MG often showed rapid, visible improvement in ptosis or double vision. Sensitivity in OMG was reported to be 71–95% (Meriggioli & Sanders, 2009), but the test carried risks, including bradycardia and arrhythmias, which occurred in up to 12-20% of patients, so it required continuous monitoring and emergency readiness. Because of these safety issues, it has mostly fallen out of use. The neostigmine test was a slower but safer alternative. Neostigmine is another acetylcholinesterase inhibitor, commonly injected intramuscularly or intravenously, with improvement observed after 30–60 minutes. Its accuracy is similar to that of edrophonium, but because it takes longer to act, it is less dramatic. Today, both edrophonium and neostigmine testing are rarely used, except in resource-limited settings where antibody or electrophysiological testing is unavailable (Tannemaat, 2024). They are still historically significant because they helped establish that ocular myasthenia gravis symptoms can be rapidly reversible with acetylcholinesterase inhibition (Meriggioli & Sanders, 2009).

Once bedside testing raises suspicion, doctors usually order serological testing to look for specific antibodies. The most common is the acetylcholine receptor antibody assay. A positive test is specific for MG, but the sensitivity in ocular-only disease is much lower than in generalized MG. Behbehani et al. (2022) reported positivity in about 50% of OMG patients, while Monte et al. (2021) found similar rates of 38–50% depending on age and disease duration. In their study, older patients and those with longer-standing symptoms were more likely to test positive. In contrast, younger patients and those with very recent onset had lower detection rates, reflecting the slower buildup of circulating antibodies over time.

In contrast, Chung et al. (2021) reported 80% sensitivity and 99% specificity with high-quality binding assays. The standard method worldwide is radioimmunoassay, but newer, more sensitive cell-based assays are emerging, as they can detect antibodies that RIA misses (Meriggioli & Sanders, 2009). Other antibodies can also play a role, though they are less common in ocular-only disease. MuSK antibodies are found in fewer than 5% of patients with isolated ocular symptoms but are more often seen in generalized MG with bulbar weakness

(Guptill et al., 2011; Evoli et al., 2018). LRP4 antibodies are also rare, but their presence can help identify patients who would otherwise be classified as seronegative (Yan et al., 2018; Bacchi et al., 2018). While antibody testing provides valuable confirmation, negative results are frequent in OMG, which is why it cannot stand alone to rule out the disease.

If bedside and serological tests do not provide a clear answer, doctors may use electrophysiological studies to assess nerve and muscle function. The first option is repetitive nerve stimulation. In this test, doctors repeatedly stimulate a motor nerve and record how much the muscle response decreases with each signal. A drop greater than 10% is considered abnormal (Padua et al., 2004). However, RNS has low sensitivity in ocular MG. Padua et al. (2004) found that only 27.8% of 90 OMG patients had abnormal results. Costa et al. (2004) confirmed similar findings. Because RNS has low sensitivity, it is primarily used as a secondary confirmatory tool and is more helpful in generalized MG. The single-fiber electromyography (SFEMG) is considered the gold standard for diagnosing OMG (Padua et al., 2004). SFEMG measures "jitter," or the variability in how muscle fibers respond to repeated nerve signals (Padua et al., 2004). This test is highly sensitive and can detect abnormalities even when antibodies and RNS are negative: Padua et al. (2004) reported that SFEMG abnormalities were found in 83.3% of frontalis muscles and 61.1% of extensor digitorum communis muscles. Giannoccaro et al. (2020) found SFEMG had 94% sensitivity and 79% specificity, compared with the ice test's 86% sensitivity and 79% specificity. When both tests were combined, diagnostic sensitivity increased to 98% (Giannoccaro et al., 2020). Even though SFEMG requires special equipment, technical skill, and is mildly invasive (Giannoccaro et al., 2020), its accuracy makes it a strong confirmatory tool, especially for seronegative or hard-to-diagnose patients.

While not diagnostic of ocular myasthenia gravis itself, other tests are often included to provide a complete picture. Chest CT or MRI is performed to check for thymoma, a tumor of the thymus gland that occurs in approximately 10–15% of patients with myasthenia gravis and can worsen autoimmune activity (Benatar & Kaminski, 2022).

Thyroid function testing is also routine, as autoimmune thyroid disease co-occurs with MG in 10–15% of cases (Álvarez-Velasco et al., 2021).

Test	Purpose	Pros	Cons/limitations	Order of use
Clinical Exam	Assess ptosis, diplopia, fatigue pattern	Quick, noninvasive, initial assessment	Subjective; mild cases can be missed	First
Ice Pack Test	Confirm fatigable ptosis by cooling eyelid (↑ ACh function)	Simple bedside test, high specificity	Short duration relief, less reliable for diplopia	First-line bedside
Edrophonium (Tensilon) Test	Temporarily improves weakness via AChE inhibition	Strong indicator if positive	Short-acting, side effects (bradycardia, syncope), less used now	Optional confirmatory
Acetylcholine Receptor (AChR) Antibody Test	Detects autoimmune antibodies	High specificity for MG	May be negative in pure ocular cases	Early laboratory test
MuSK / LRP4 Antibody Tests	Detects antibodies in seronegative patients	Helps subtype classification	Lower prevalence in OMG	If AChR-negative
Repetitive Nerve Stimulation (RNS)	Measures decrement in muscle response	Objective, supports NMJ dysfunction	Less sensitive in ocular MG	Intermediate diagnostic
Single-Fiber EMG (SFEMG)	Measures neuromuscular transmission jitter	Highest sensitivity	Requires expertise, limited availability	Gold standard if diagnosis unclear
CT/MRI of Chest (Thymus)	Detect thymoma or hyperplasia	Guides thymectomy decisions	Radiation exposure	Post-diagnosis evaluation

Table 1. This table summarizes the primary diagnostic tests used in evaluating ocular myasthenia gravis, outlining each test's clinical purpose, advantages, limitations, and recommended order of use.

Taken together, the diagnostic workflow for ocular myasthenia gravis begins with bedside tests such as the ice-pack test and the forced eyelid closure test, and with signs such as Cogan's lid twitch, because these are quick, safe, and low-cost. Antibody testing proceeds if suspicion remains high, starting with AChR assays and, when available, adding MuSK or LRP4 to catch less common cases. A positive antibody result provides strong confirmation, whereas a negative result requires electrophysiological testing. In this stage, repetitive nerve stimulation can sometimes support the diagnosis. However, it has relatively low sensitivity, while single-fiber EMG offers the best accuracy and is considered the gold standard when certainty is essential. Imaging for thymoma and thyroid blood work round out the evaluation, helping detect conditions that often accompany MG and ensuring nothing important is overlooked.

Treatment and Management of Ocular Myasthenia Gravis

The management of ocular myasthenia gravis requires a carefully structured approach that considers both short-term symptom relief and long-term disease control. Because symptoms such as ptosis and diplopia can vary widely in frequency and severity, physicians typically begin treatment with the least invasive methods and gradually escalate based on patient response, tolerance, and the likelihood of disease progression. The overall goal of therapy is to strengthen the affected ocular muscles, reduce fatigue, prevent the spread of weakness to other muscle groups, and minimize medication-related toxicity while preserving the patient's quality of life (Evoli et al., 2020).

The most common initial therapy is pyridostigmine bromide, a reversible acetylcholinesterase inhibitor that increases acetylcholine concentration at the neuromuscular junction (Meriggioli & Sanders, 2009). This allows for more effective communication between nerve terminals and muscle fibers, improving muscle contraction and temporarily reducing symptoms such as eyelid drooping and double vision (Benatar & Kaminski, 2022). Pyridostigmine is particularly effective in patients with mild or purely ocular forms of the disease, with about 70–80% of patients experiencing meaningful symptom relief (Benatar & Kaminski, 2022). It is often the first medication prescribed after diagnosis.

The standard oral dosage typically ranges from 30 to 60 mg every 4–6 hours, with adjustments based on the individual's tolerance and response (Benatar & Kaminski, 2022). Its effects begin within about 30 minutes and last for several hours (Benatar & Kaminski, 2022). While generally well tolerated, pyridostigmine may produce cholinergic side effects, including abdominal cramping (20–30%), diarrhea (15–25%), excessive salivation (10–20%), and sweating (10–20%) (Meriggioli & Sanders, 2009). When needed, clinicians may add glycopyrrolate to control excessive secretions. Because pyridostigmine addresses only symptoms rather than the underlying autoimmune process, it is commonly used alongside or as a bridge to it for long-term disease control. (Evoli et al., 2020).

When pyridostigmine alone does not provide adequate relief, or when symptoms begin to interfere with daily functioning and vision, corticosteroids are typically introduced (Benatar & Kaminski, 2022). Prednisone and prednisolone are the most frequently used corticosteroids for ocular myasthenia gravis. These medications suppress inflammation and inhibit cytokine and autoantibody production at the neuromuscular junction, thereby reducing immune-mediated damage to muscle receptors (Evoli et al., 2020). Their efficacy is well documented, with 60-80% of patients achieving partial or complete remission following corticosteroid therapy (Benatar & Kaminski, 2022). The dosing regimen varies depending on symptom severity. For mild cases, treatment often begins with a low daily dose of 10-20 mg, whereas more severe cases may require up to 1 mg/kg per day. Once symptoms are controlled, the dose is gradually tapered to minimize side effects while maintaining stability. Corticosteroids typically produce noticeable clinical improvement within days to weeks, which is faster than that of most other immunosuppressive drugs (Luo et al., 2022).

Despite their high efficacy, corticosteroids carry significant risks when used long-term. In clinical studies, long-term is typically defined as twelve months or more of continuous therapy, and adverse effects become increasingly common after this period (Mantegazza & Antozzi, 2020). Potential adverse effects include weight gain, hypertension, mood swings, glucose intolerance or diabetes, osteoporosis, and increased susceptibility to infections. These effects are not rare, with about 20-40% of patients on chronic corticosteroids developing metabolic complications and up to 50% experiencing weight gain or mood-related side effects (Mantegazza & Antozzi, 2020; Lascano et al., 2021). To reduce these risks, physicians often use corticosteroids as a temporary or “bridge” therapy while initiating slower-acting immunosuppressants that provide sustained immune regulation. Patients on prolonged corticosteroid therapy require regular monitoring for metabolic and bone changes, and most are advised to supplement with calcium and vitamin D to help maintain bone density. Preventive measures such as exercise, dietary modifications, and periodic bone density scans are also recommended to reduce the risk of complications (Mantegazza & Antozzi, 2020).

For long-term disease management, steroid-sparing immunosuppressants play a central role in maintaining remission while minimizing corticosteroid exposure. Common agents include azathioprine, mycophenolate mofetil, and calcineurin inhibitors, which provide sustained immune regulation.

Azathioprine is one of the most widely used agents in this category (Evoli et al., 2020). It inhibits purine synthesis, thereby suppressing the proliferation of T and B lymphocytes that generate pathogenic autoantibodies (Evoli et al., 2020). Although its clinical effects develop gradually, often requiring 3 to 6 months, and sometimes up to a year, it is widely used because it provides long-term disease control and reduces relapse frequency (Luo et al., 2022). Studies show that 70–80% of patients experience partial or complete improvement, making it one of the most effective steroid-sparing therapies for ocular myasthenia gravis (Benatar & Kaminski, 2022). However, because azathioprine can cause bone marrow suppression and liver toxicity, patients require regular monitoring of liver function tests and complete blood counts. When well-tolerated, it is often continued for years to maintain remission, allowing corticosteroid doses to be reduced or discontinued entirely.

Mycophenolate mofetil is another commonly prescribed steroid-sparing agent. It inhibits inosine monophosphate dehydrogenase, thereby selectively blocking lymphocyte proliferation and causing fewer hepatic side effects compared with azathioprine (Luo et al., 2022). Studies suggest that 40 to 60 percent of patients with ocular myasthenia gravis achieve sustained remission or significant clinical improvement with mycophenolate, particularly when combined with low-dose corticosteroids (Lennon et al., 2021). Unlike azathioprine, it has a faster onset of action, though it can still take several months to reach full effect. As with all immunosuppressants, patients on mycophenolate require periodic monitoring for cytopenias and infections, but severe toxicity is uncommon.

When azathioprine or mycophenolate are ineffective or poorly tolerated, calcineurin inhibitors such as cyclosporine and tacrolimus are considered. Both drugs inhibit interleukin-2 production, thereby preventing T-cell activation, which plays a key role in sustaining the autoimmune response in myasthenia gravis. Tacrolimus, in particular, has shown encouraging results even at low doses, sometimes leading to faster clinical improvement than azathioprine (Luo et al., 2022). However, both agents must be used cautiously because of their potential to cause nephrotoxicity, hypertension, and other systemic effects. Blood pressure and kidney function should be monitored routinely throughout therapy. For patients who fail to respond to conventional immunosuppressants or who cannot tolerate their side effects, methotrexate may be prescribed off-label. As a folate antagonist with immunosuppressive and anti-inflammatory properties, methotrexate can help maintain disease stability in refractory cases, though evidence in ocular myasthenia gravis remains limited (Benatar & Kaminski, 2022).

When traditional immunosuppressive therapies fail to achieve satisfactory results, biologic and targeted agents may be introduced. These newer treatments act at specific points within the immune system to disrupt the pathogenic mechanisms underlying myasthenia gravis. Rituximab, a monoclonal antibody targeting CD20-positive B cells, is particularly effective in refractory and MuSK-positive myasthenia gravis. By depleting B cells, rituximab lowers the production of pathogenic antibodies and reduces inflammation at the neuromuscular junction. Although large-scale studies in purely ocular myasthenia remain limited, smaller clinical series have demonstrated that rituximab can induce remission, prevent disease progression, and improve ocular symptoms in difficult-to-treat cases (Nowak et al., 2021).

Another class of biologic therapies includes complement inhibitors such as eculizumab and ravulizumab. These monoclonal antibodies bind to the complement protein C5 and block the formation of the membrane attack complex, which damages acetylcholine receptors. Although they are primarily approved for AChR-positive generalized myasthenia gravis, emerging evidence suggests that they may also benefit patients with severe or stubborn ocular presentations (Howard et al., 2022). These agents are generally well-tolerated but are associated with high cost and require infusion-based administration under medical supervision. A newer therapy, efgartigimod, represents a novel approach by targeting the neonatal Fc receptor (FcRn). By inhibiting this receptor, efgartigimod accelerates the degradation of pathogenic IgG antibodies, thereby reducing their concentration in the bloodstream. Clinical trials have demonstrated that efgartigimod leads to rapid symptom improvement, good tolerability, and minimal adverse effects, making it a promising therapeutic option for patients with ocular myasthenia gravis who fail to respond to conventional treatment (Howard et al., 2022). Although biologics are powerful tools, their use is generally reserved for patients who have not responded to standard therapy because of their expense, infusion requirements, and limited long-term safety data.

In situations of acute worsening, impending crisis, or preoperative preparation, rapid-acting rescue treatments such as intravenous immunoglobulin and plasmapheresis may be utilized. IVIG involves the intravenous administration of pooled donor antibodies that neutralize harmful autoantibodies and modulate immune function. This treatment typically leads to noticeable improvement within one to two weeks and is particularly useful for achieving short-term stabilization (Benatar & Kaminski, 2022). Plasmapheresis, on the other hand, physically removes circulating autoantibodies and immune complexes from the bloodstream. This approach provides fast and often dramatic relief, though the benefits are temporary. Both treatments are especially valuable during severe exacerbations or in preparation for thymectomy when rapid symptom control is necessary. Because they require hospital-level monitoring, specialized equipment, and can cause complications such as hypotension or infection, these interventions are reserved for short-term use before transitioning patients back to maintenance therapy.

Alongside pharmacologic treatment, supportive and lifestyle measures are critical for optimizing patient outcomes. Fatigue, emotional stress, infection, and elevated temperatures are known to worsen muscle weakness, so patients are advised to maintain adequate rest, manage stress, and avoid overheating. Balancing physical activity with recovery periods can help prevent symptom flare-ups. Simple assistive measures such as wearing sunglasses to reduce light sensitivity, using prism lenses or eye patches to minimize double vision, and arranging the environment to reduce visual strain can substantially improve daily functioning. Psychological support is also essential, as chronic conditions like ocular myasthenia gravis can affect self-image and mental health. Regular neurological follow-up is necessary, particularly during the first 2 years after diagnosis, as approximately half of patients with ocular myasthenia gravis eventually progress to generalized disease (Evoli et al., 2020). Early detection of systemic involvement enables timely adjustments to the treatment plan, helping prevent complications and maintain patient stability.

For selected patients, particularly those with thymoma or refractory disease, surgical removal of the thymus gland, or thymectomy, is an established therapeutic option. The thymus plays a central role in immune regulation and T-cell maturation, and abnormalities in its function or structure can contribute to persistent autoantibody production. Thymectomy is routinely recommended for thymoma patients. It is increasingly considered for AChR-positive patients without thymoma, as it has been shown to reduce antibody levels and lower the likelihood of progression to generalized myasthenia gravis (Suzuki et al., 2019). Although less frequently performed for purely ocular presentations, several studies have reported that it can lead to gradual clinical improvement and, in some cases, complete remission over time. Postoperative improvement typically occurs over months to years, supporting the thymus's role in perpetuating autoimmune activity. The procedure is now often performed through minimally invasive approaches, which reduce recovery time and surgical risk compared to traditional open techniques.

In summary, the management of ocular myasthenia gravis is a dynamic, individualized process that evolves with disease severity, patient response, and treatment tolerance. The first-line medication, pyridostigmine, provides rapid symptomatic relief by enhancing neuromuscular transmission. Corticosteroids such as prednisone and prednisolone are then introduced to suppress the immune response and achieve more sustained disease control. For long-term maintenance, steroid-sparing immunosuppressants such as azathioprine, mycophenolate mofetil, cyclosporine, and tacrolimus are used to prevent relapse while minimizing corticosteroid toxicity in patients who do not respond adequately or experience significant side effects. Biologic therapies such as rituximab, eculizumab, ravulizumab, or efgartigimod offer new and effective alternatives. During acute exacerbations, IVIG and plasmapheresis provide rapid stabilization and are often used as bridges to slower-acting maintenance therapies. For patients with thymoma or refractory disease, thymectomy may yield long-term improvement and remission. Complementing these pharmacologic and surgical interventions, lifestyle modifications and supportive measures remain essential for symptom management and quality of life. When implemented together in a coordinated, stepwise manner, these strategies enable physicians to achieve meaningful symptom control, prevent disease generalization, and promote long-term stability in patients with ocular myasthenia gravis.

Treatment	Purpose	Benefits	Limitations	Order of use
Pyridostigmine (Acetylcholinesterase inhibitor)	Increases acetylcholine at the neuromuscular junction to improve muscle contraction	Rapid symptom relief; effective for ptosis and diplopia; works within ~30 minutes	Does not treat underlying autoimmune cause; side effects include diarrhea, sweating, abdominal cramping	First - line medication
Corticosteroids (Prednisone / Prednisolone)	Suppress immune response and reduce autoantibody production	Strong clinical improvement; 60–80% of patients improve	Long-term side effects: weight gain, osteoporosis, hypertension, infection risk	Used if symptoms persist after pyridostigmine
Azathioprine	Suppresses T and B lymphocyte proliferation to reduce autoantibody production	Effective long-term control; steroid-sparing	Slow onset (3–12 months); requires liver and blood monitoring	Long-term maintenance therapy
Mycophenolate Mofetil	Inhibits lymphocyte proliferation through purine synthesis blockade	Fewer liver side effects than azathioprine; effective for sustained remission	Takes months for full effect; infection risk	Alternative steroid-sparing therapy
Calcineurin Inhibitors (Cyclosporine, Tacrolimus)	Block T-cell activation and cytokine production	Can help patients resistant to other immunosuppressants	Kidney toxicity, hypertension; requires monitoring	Used in refractory cases
Biologic Therapies (Rituximab)	Targets CD20-positive B cells to reduce antibody production	Effective for refractory or MuSK-positive cases	Expensive; limited long-term data	Advanced therapy

Treatment	Purpose	Benefits	Limitations	Order of use
Complement Inhibitors (Eculizumab, Ravulizumab)	Block complement protein C5 to prevent damage to acetylcholine receptors	Effective in severe antibody-positive disease	High cost; infusion therapy required	Severe or resistant cases
FcRn Inhibitor (Efgartigimod)	Accelerates degradation of pathogenic IgG antibodies	Rapid symptom improvement; targeted therapy	New treatment with limited long-term data	For patients not responding to standard therapy
Intravenous Immunoglobulin (IVIG)	Modulates immune system and neutralizes autoantibodies	Rapid symptom improvement within weeks	Temporary effect; hospital administration	Acute exacerbations or pre-surgery
Plasmapheresis	Removes circulating autoantibodies from blood	Very fast symptom relief	Temporary benefit; invasive procedure	Severe worsening or crisis
Thymectomy	Surgical removal of thymus to reduce autoimmune activity	Can reduce symptoms and disease progression	Surgical risks; benefits may take months to years	Selected patients (thymoma or refractory disease)

Table 2. The tables summarize the stepwise management of ocular myasthenia gravis, outlining major pharmacologic, biologic, and surgical treatments along with their mechanisms, benefits, limitations, and typical order of use in clinical practice.

Discussion

Despite advances in understanding and treating myasthenia gravis, ocular myasthenia gravis remains one of the most complex forms to diagnose and manage effectively. Current diagnostic and therapeutic methods have improved patient outcomes, but several key gaps still hinder early detection, personalized treatment, and equitable access to care. These challenges highlight the biological complexity of the disease and underscore the need for more focused research on ocular forms of MG (Tannemaat, 2024; Evoli et al., 2020).

A significant challenge involves the limitations of current diagnostic methods. While bedside tests like the ice-pack test and antibody assays are helpful, none is completely definitive. Nearly half of patients with ocular MG test negative for antibodies to the acetylcholine receptor, muscle-specific kinase, or low-density lipoprotein receptor-related protein 4 (Yan et al., 2018; Bacchi et al., 2018). This often means doctors must rely on clinical judgment and specialized testing such as single-fiber electromyography, which can detect subtle communication problems between nerves and muscles. However, SFEMG is costly, technically demanding, and available only in specific specialized centers (Padua et al., 2004). Because of these barriers, many patients experience delayed or missed diagnoses, increasing their risk of progression to generalized MG and causing prolonged discomfort or vision issues. To improve this, future research should focus on faster, more accessible diagnostic tools, such as highly sensitive cell-based antibody tests or portable electrophysiology devices, that can be used in community settings and smaller hospitals (Tannemaat, 2024).

Another ongoing issue is the complexity and variability of treatment response. Many patients initially improve with pyridostigmine or corticosteroids, but others experience ongoing or fluctuating symptoms that are difficult to control (Benatar & Kaminski, 2022). Immunosuppressive drugs like azathioprine or mycophenolate mofetil can be effective but often take several months to work, leaving patients in a difficult waiting period where symptoms remain uncontrolled (Luo et al., 2022). Long-term corticosteroid use also brings complications such as weight gain, hypertension, osteoporosis, and infection, forcing doctors to balance effectiveness with potential harm. Most current treatment guidelines are based on studies of generalized MG rather than ocular MG, creating uncertainty about how long to treat, what combinations work best, and when to taper medications. To fill this gap, large-scale clinical trials focused solely on ocular MG are needed to define optimal dosing, safe tapering schedules, and long-term maintenance strategies (Evoli et al., 2020).

The high cost and limited access to biologic and targeted therapies also pose serious challenges for many patients. Drugs such as rituximab, eculizumab, ravulizumab, and efgartigimod have shown substantial efficacy in refractory MG (Howard et al., 2022), but their high cost and need for intravenous administration make them difficult to access outside major medical centers. For patients with ocular MG, insurance approval is often denied because these biologics are approved primarily for generalized MG. This leaves many patients without effective options when traditional drugs fail to control symptoms. Addressing this issue will require policy reform to improve coverage and continued research into affordable biosimilars or oral alternatives that could make advanced therapies more widely available (Nowak et al., 2021).

Another area in need of attention is the underrepresentation of specific patient subgroups in clinical research. Many trials exclude children, older adults, and patients with seronegative MG, limiting understanding of disease behavior across populations (Guo et al., 2021). For example, juvenile MG may progress differently or respond less predictably to immunosuppressive treatments. At the same time, older adults with late-onset MG often face additional health issues that make treatment more complicated (Álvarez-Velasco et al., 2021). Because these groups are underrepresented, doctors often rely on generalized MG data that may not accurately reflect ocular disease. Expanding clinical research to include these populations and using precision-medicine approaches, such as studying genetic, immune, and imaging biomarkers, could help personalize treatment and improve long-term outcomes.

To overcome these challenges, management of ocular myasthenia gravis should focus on improved coordination, fairness, and individualized care. Doctors and researchers need systems that connect diagnostic tools, such as antibody tests and clinical evaluations, into a single, straightforward workflow. Treatment should also be more accessible so that patients can receive proper care no matter their background or location. Finally, care should become more personalized by using biological markers to predict which treatments will be most effective for each patient. Achieving these goals will depend on collaboration across research centers, open data sharing, and more funding for clinical and translational studies. By bridging the diagnostic, treatment, and equity gaps, the field can move from simply managing symptoms to delivering proactive, precision-based care that truly improves both patient outcomes and quality of life for those with ocular myasthenia gravis.

Conclusion

Ocular myasthenia gravis remains a uniquely challenging disorder due not only to its severity but also to its variability and unpredictability. What often begins as a localized ocular condition can evolve into a more widespread neuromuscular disease, making early recognition and precise management essential. Advances in understanding its autoimmune basis have significantly improved diagnostic accuracy and expanded therapeutic options, transforming patient outcomes in meaningful ways.

However, progress has not eliminated uncertainty. Limitations in diagnostic sensitivity, inconsistent treatment responses, and barriers to accessing advanced therapies continue to complicate care. Furthermore, the underrepresentation of diverse patient populations in clinical research leaves critical gaps in understanding how the disease presents and responds across different groups.

Ultimately, the future of ocular myasthenia gravis lies in precision and accessibility. By advancing early detection methods, expanding equitable access to treatment, and developing individualized, mechanism-based therapies, medicine can move beyond managing symptoms toward truly optimizing patient outcomes. In doing so, a condition once defined by uncertainty may become one characterized by control, stability, and improved quality of life for those affected.

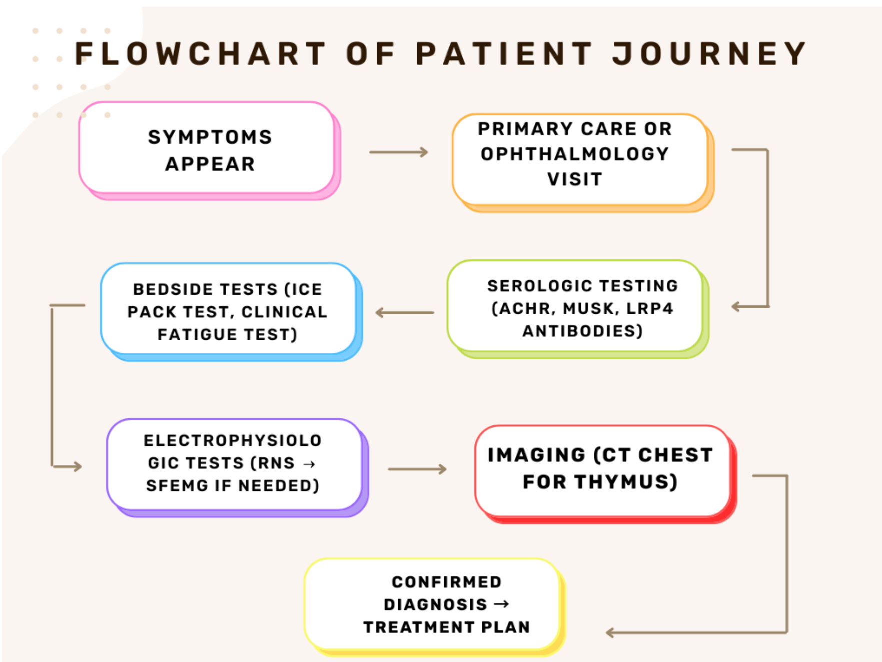

Figure 1. The flowchart illustrates the sequential diagnostic pathway for patients presenting with ocular symptoms suggestive of myasthenia gravis.

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