

A REVIEW ON MYASTENIA GRAVIS

Dr. D. Rama Brahma Reddy¹, P. Sukanya², A. Bindu Madhavi³

¹Principal & Professor, Dept. of Phytochemistry, Nalanda Institute of Pharmaceutical Sciences, Kantepudi, Sattenapalli.

²Assistant professor, Dept. of Pharmaceutics, Nalanda Institute of Pharmaceutical Sciences, Kantepudi Sattenapalli ³Student, Nalanda Institute of Pharmaceutical Sciences, Kantepudi, Sattenapalli

ABSTRACT

Myasthenia gravis (MG) is an auto immune neurological disorder characterized by defective transmission at the neuromuscular junction. The incidence of the disease is 4.1 to 30 cases per million person-years, and the prevalence rate ranges from 150 to 200 cases per million. MG is considered a classic example of antibody-mediated auto immune disease. Most patients with MG have autoantibodies against the acetylcholine receptors (AChRs). Less commonly identified autoantibodies include those targeted to muscle-specific kinase (MuSK), low-density lipoprotein receptor-related protein 4 (Lrp4), and agrin. These autoantibodies disrupt cholinergic transmission between nerve terminals and muscle fibers by causing downregulation, destruction, functional blocking of AChRs, or disrupting the clustering of AChRs in the postsynaptic membrane. The core clinical manifestations vary according to the type of autoantibody, and whether a thymoma is present. The autoantibodies targeted neuromuscular junction (NMJ) molecules, such as nicotinic acetylcholine receptor (AChR), muscle-specific kinase (MuSK), and low-density protein related lipoprotein receptor 4 (Lrp4) that altera in tissue architecture and decrease the density or functionality of AChR and decrease neuromuscular transmission by various mechanisms. Therefore, a serious weakness of the fatigued skeletal muscle.

Key Words: Myasthenia gravis, acetylcholine receptor, autoantibodies, cytokines, B cells, T cells.

1. INTRODUCTION

MYASTENIA GRAVIS: In 1672, for the first time, Thomas Willis described the disease as spurious palsy. The name 'Myasthenia Gravis pseudo paralytica was proposed by the German neurologist Friedrich Jolly in 1895. In response to repeated stimulation of the innervating nerve, jolly also showed a decrease in myasthenia gravis (MG) muscle contraction. The chemical inherent in neurotransmissions has been identified during the 1920s and acetylcholine (ACh) was recognized as a neuromuscular transmitter medication. In 1934, when there were clinical parallels between MG and curare poisoning, Mary Walker successfully treated MG patients with one of the acetylcholinesterase inhibitors (AChEI), physostigmine, and also the curare antidote. An autoimmune mechanism was proposed during the following decades to resolve thymus defects and the reported high incidence of other ADs in patients with MG. The Scottish neurologist John A, demonstrated a theory of autoantibodies directed toward an endplate protein at the NMJ Simpson in 1960. In the 1970s, however, Jim Patrick and Jon Lindstrom finally consolidated the autoimmune hypothesis when acetylcholine receptor (AChR) immunized rabbits and showed an elevation of AChR directed antibodies. The autoantibodies targeted neuromuscular junction (NMJ) molecules, such as nicotinic acetylcholine receptor (AChR), muscle-specific kinase (MuSK), and low-density protein related lipoprotein receptor 4 (Lrp4) that altera in tissue architecture and decrease the density or functionality of AChR and decrease neuromuscular transmission by various mechanisms. Therefore, a serious weakness of the fatigued skeletal muscle. MG tends to be affected by sex and age; below 40 years, the female: male ratio is around 3: 1; however, the ratio is approximately equal when the age is between 40 and 50 years or during puberty. MG is more likely to occur in males in 50 years. In Europe and North America, childhood MG is uncommon (10 % -15 % only). In Asian countries, however, up to 50 % of patients, primarily with purely ocular symptoms, have an onset below 15 years of age.[1]

Myasthenia gravis (MG) is the most common autoimmune disorder that affects the neuromuscular junction. MG is largely a treatable disease but can result in significant morbidity and even mortality. This can usually be prevented with a timely diagnosis and appropriate treatment of the disease. MG is a heterogeneous disease from a phenotypic and pathogenesis standpoint. The spectrum of symptoms ranges from a purely ocular form to severe weakness of the limb, bulbar and respiratory muscles. The age of onset is variable from childhood to late adulthood with disease peaks in younger adult women and older men. MG is considered a classic example of antibody-mediated autoimmune disease. It can also be viewed as an example of a class II hypersensitivity reaction, as IgG autoantibodies react with intra or extracellular antigens, leading to end-organ damage. Most patients with MG have auto antibodies against the acetylcholine receptors (AChRs), and a minority are seropositive for antibodies directed to muscle-specific kinase (MuSK), low-density lipoprotein receptor-related protein 4 (Lrp4) or agrin. These antibodies also provide the basis for defining disease subgroups and help delineate phenotypic variants. In a subgroup of MG patients, striational antibodies

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have also been identified, which include antibodies against titin, ryanodine receptor, and the alpha subunit of the voltagegated K+ channel (Kv1.4). These antibodies mostly serve as biomarkers of disease severity and are often detected in patients with late-onset MG or with thymoma, and some of them have concomitant myositis and/or myocarditis. Although MG is mediated by autoantibodies, different subtypes of T cells and their cytokines also play important roles in the pathogenesis.

One of the most prevalent conditions that interfere with neuromuscular transmission is myasthenia gravis (MG). Its distinctive symptoms, which are mostly brought on by an immune response against the post synaptic membrane of the neuromuscular junction (NMJ), include acute weakness and exhaustion, ocular muscles, bulbar functions, as well as limb and respiratory muscles. Most people with MG initially experience ocular symptoms. At least one symptom aggravation will occur in most MG patients at some point during their disease. In Asia, the prevalence of the disease is rising. The disease is becoming more widely recognized in persons over 50. Autoimmune NMJ disorders can be diagnosed using various approaches, including imaging, pharmacological, electrophysiological, and serological antibody tests. The clinical course of MG is significantly influenced by age and gender, so patient management of these variables requires special attention. The first year or two of the disease causes the greatest degree of weakness and high death rate; however, many patients recover after that. Identification of the clinical features is essential for an early diagnosis. Delays of one to two years before diagnosis are not unusual due to the disease's low incidence in clinical practice and frequently undiagnosed symptoms. Given its strong correlation with the severity of the disease, weariness is likely a contributing factor to the MG symptomatology.[2]

CAUSES OF MYASTENIA GRAVIS:

- Myasthenia gravis begins to develop later in life when normal receptors on the muscle attack antibodies in the body. This blocks a chemical stimulation for muscle contraction.
- When a woman with myasthenia gravis passes the antibodies on to the fetus, a temporary form of myasthenia gravis may develop in the fetus, but generally, it resolves within 2 to 3 months.
- The main causes of this disease are antibodies and thymus. Normally, the immune system produces proteins called antibodies that help preventing or frightening the infection.
- Specific autoimmune disorder characterized by weakness of voluntary muscle caused by autoantibodies to the postsynaptic membrane at neuromuscular junction against the nicotinic acetylcholine receptor (AChR).
- > The second cause of the MG is thymus. In anti-AChR antibody-positive MG, the thymus is an important pathogenicrole, with thymichyperplasia present in 65% of the cases and thymoma present in 10% of the cases.

In addition, MG presents a paraneoplastic phenomenon in 30% of patients with thymoma.

CLASSIFICATION OF MYASTENIA GRAVIS

- Subtypes of MG are broadly classified as follows:
- 1. Early-onset MG: age at onset<50 years. Thymic atrophy, mainly males, usually females,
- 2. Late-onset MG: age at onset >50 years. Thymic atrophy, mainly males,
- 3. Thymoma-associated MG: (10%–15%)
- 4. MG with anti-MUSK antibodies,

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- 5. ocular MG (oMG): symptoms only affecting extra ocular muscles,
- 6. MG with no detectable AChR and muscle-specific tyrosine kinase (MuSK) antibodies.

MG patients with Thymoma almost always have detect able AChR antibodies in serum. Thymoma-associated MG may also have additional para neoplasia-associated antibodies (e.g., antivoltage-gated K+ and Ca++ channels, anti-Hu, anti dihydro pyrimidinase-related protein 5, and antiglutamic acid decarboxylase antibodies.

About 15% of generalized MG patients do not have anti AChR antibodies in current lab assays. In 40% of this sub group, antibodies to MuSK and another postsynaptic neuromuscular junction (NMJ) protein, are found. They have atypical clinical features like selective facial, bulbar, neck, or respiratory muscle weakness with occasional marked muscle atrophy and with relative sparing of the ocular muscles. Respiratory crises are more common with involvement of muscle groups like paraspinal and upper esophageal muscles. Enhanced sensitivity, nonresponsiveness, or even clinical worsening to anticholinesterase medications has also been reported. Disease onset is earlier with female predominance and thymus histology is usually normal. Seronegative MG lacks both anti-AChR and anti-MuSK antibodies and forms a clinically heterogenous group with purely ocular, mild generalized, or severe generalized disease. Some patients may have low-affinity anti-AChR antibodies, nondetectable by current assays. They are essentially indistinguishable from patients with anti-AChR antibodies in terms of clinical features, pharmacological treatment response, and possibly even thymic abnormalities.

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Thymomas are frequently associated with autoimmunity. Neoplastic epithelial cells in thymomas express numerous selflike antigens including AChR-like, titin-like, and ryanodine-receptor-like epitopes. These antibodies react with epitopes on the muscle proteins titin and ryanodine receptor, are found mainly in association with thymoma and late-onset myasthenia gravis, and may correlate with myasthenia gravis severity. These striational antibodies are principally detected only in the sera of patients with MGand rarely found in AChR antibody-negative MG. The frequencies of striational antibodies in thymoma-associated MG patients are high. Antititin antibodies are detected in 49%–95% of thymic-associated MG, antiryanodine receptor antibodies in 70%–80%, and anti-KV1.4 (VGKC) in 40–70% of the cases. Since the presence of striational auto antibodies is associated with a more severe disease in all MG subgroups, these antibodies can therefore be used as prognostic determinants in MG patients.

To establish the diagnosis of MG, necessary investigations include- AChR antibodies, MuSK antibodies, and CT/MR of anterior mediastinum for thymoma. Neurophysiological examination with repetitive nerve stimulation and jitter measurements are important in establishing the initial diagnosis, especially in patients without detectable antibodies.[3]

EPIDEOMOLOGY:

MG is a rare neurological disease and pediatric MG is even more uncommon. Both incidence and prevalence have significant geographical variations, but it is believed that MG incidence has increased worldwide over the past seven decades. The prevalence of MG was estimated at 1 in 200,000 from 1915 to 1934, increased to 1 per 20,000 after the introduction of anticholinesterase drugs in 1934, and rose to 1 per 17,000 population after the discovery of AChR antibodies in 1969. Prevalence rates range from 150 to 200 cases per million, and they have steadily increased over the past 50 years, at least partly due to improvements in recognition, diagnosis, treatment, and an overall increase in life expectancy. More recent studies addressing incidence rates have been conducted in Europe and show a wide range from 4.1 to 30 cases per million person-years.

The annual rate is lower in studies coming from North America and Japan, with the incidence ranging from 3 to 9.1 cases per million. Lower incidence and prevalence rates have been reported in a large study from China at 0.155–0.366 per million, and 2.19–11.07 per 1,00,000, respectively. Two population-based studies from Korea showed a prevalence of 9.67–10.42 per 1,00,000 people in 2010, which increased to 12.99 per 1,00,000 in 2014. On the other hand, a smaller study using records of a hospital-based Health Maintenance Organization estimated an incidence of MG at 38.8 per 1,00,000 person-years for the Argentinian population. Different study methodologies, including diagnostic criteria and other sources of bias, such as the small size of the study population and the underestimation of patients with milder disease, likely play a factor in the significant variability of incidence rates over time and across different geographical regions.

Incidence rates have a bimodal distribution in women, with peaks around age 30 and 50. In men, the incidence increases steadily with age and with the highest rates between age 60 and 89. Women are more commonly affected before age 40, with a female: male ratio of 3:1 for early-onset MG. In the fifth decade of life, women and men are equally affected, while men have a higher proportion after age 50, with a male: female ratio of 3:2. Around 10% of cases are pediatric, which is defined as onset before age 18. MG can affect people of all race and ethnic backgrounds and is slightly more prevalent in patients of African ancestry. Furthermore, MG phenotype may vary depending on the ethnic background. In a retrospective study from South Africa, black patients were more likely to have treatment-resistant ophthalmoplegia and ptosis than whites, whereas the whites were more likely to develop treatment refractory generalized MG. The age at diagnosis was 17 years higher in Caucasians than non-Caucasians in another cohort of patients with ocular MG. In a US study, Oh et al. found that MG started earlier and had a more severe phenotype in African Americans than in Caucasians. The seronegative African Americans had a higher percent of MuSK seropositivity in that study (50% vs. 17% in the whites). On the other hand, patients of Asian ancestry have higher rates of MuSK antibodies compared to Caucasians and individuals of African ancestry. MuSK-associated MG is also more prevalent among those living in latitudes closer to the equator.

The mortality rate of MG has dramatically declined from the early 20th century after the availability of acetylcholine esterase inhibitors, immunosuppressants, intravenous immunoglobulin and advanced respiratory care. However, the mortality rate from the disease remains at 5–9%, being slightly higher in males than females. Using the US Nationwide Inpatient Sample (NIS) database for the years 2000 to 2005, the overall in-hospital mortality rate was estimated as 2.2%, but higher in those with MG crisis (4.7%), with the main predictors of death being older age and the presence of respiratory failure.[4]

ETIOLOGY:

Myasthenia gravis, similar to other autoimmune disorders, occurs in genetically susceptible individuals. Precipitating factors include conditions like infections, immunization, surgeries, and drugs. The commonly implicated proteins in the

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NMJ against which autoantibodies are produced include the nicotinic acetylcholine receptors (n-AChR's), musclespecific kinase (MuSK), and lipoprotein-related protein 4 (LPR4). Agrin–LRP4–MuSK protein complex is essential for the formation and maintenance of NMJ, including the distribution and clustering of the AChR. Approximately 10% of patients with MG have a thymoma, and it is implicated in the production of autoantibodies.



PATHOPHYSIOLOGY:

The pathophysiologic mechanisms in MG are dependent on the type of antibodies present. In n-AChR MG, the antibodies are of the IgG1 and IgG3 subtype. They bind to the n-ACh receptor present in the postsynaptic membrane of the skeletal muscles and activate the complement system leading to the formation of the membrane attack complex (MAC). MAC brings about the final degradation of the receptors. They may also act by functionally blocking the binding of ACh to its receptor or by enhancing the endocytosis of the antibody-bound n-ACh receptor. In MusK MG and LPR4 MG, the antibodies are of the IgG4 subtype and do not have the complement activating property. They bind to the Agrin–LRP4–MuSK protein complex in the NMJ, whose primary function is the maintenance of the NMJ, including the n-ACh receptor distribution and clustering. The inhibition of the complex leads to a reduced number of n-ACh receptors. The ACh released at the nerve terminal, in turn, is unable to generate the postsynaptic potential required to generate an action potential in muscle due to a reduced number of n-ACh receptors leading to the symptoms of muscle weakness. The weakness is more pronounced with the repeated use of a muscle group since it causes depletion of the ACh store in the NMJ.

Clinical Classification: The Myasthenia Gravis Foundation of America (MGFA) clinical classification divides MG into 5 main classes based on the clinical features and the disease severity. Each class carries different prognoses or responses to therapy.

- Class I: Involves any ocular muscle weakness, including weakness of eye closure. All other muscle groups are normal.
- Class II: Involves mild weakness of muscles other than ocular muscles. Ocular muscle weakness of any severity may be present.
- Class IIa: Involves predominant weakness of the limb, axial muscles, or both. It may also involve the oropharyngeal muscles to a lesser extent.
- Class IIb: Involves mostly oropharyngeal, respiratory muscles, or both. It can have the involvement of limb, axial muscles, or both to a lesser extent.
- Class III: Involves muscles other than ocular muscles moderately. Ocular muscle weakness of any severity can be present.
- Class IIIa: involves the limb, axial muscles, or both predominantly. Oropharyngeal muscles can be involved to a lesser degree.
- Class IIIb: Involves oropharyngeal, respiratory muscles, or both predominantly. The limb, axial muscles, or both can have lesser or equal involvement.
- Class IV: Involves severe weakness of affected muscles. Ocular muscle weakness of any severity can be present.
- Class IVa: Involves limb, axial muscles, or both predominantly. Oropharyngeal muscles can be involved to a lesser degree.
- Class IVb: Involves oropharyngeal, respiratory muscles, or both predominantly. The limb, axial muscles, or both can have lesser or equal involvement. It also includes patients requiring feeding tubes without intubation.
- Class V: Involves intubation with or without mechanical ventilation, except when employed during routine postoperative management.[5]

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COMPLICATIONS:

- The complication of myasthenia gravis includes myasthenic crisis, usually secondary to infections, stress, or acute illnesses.
- Treatment complications include long term steroid effects like osteoporosis, hyper glycemia, cataracts, weight gain, hypertension, and avascular necrosis of the hip.
- There is also the risk of lymphoproliferative malignancies, as well as opportunistic infections such as systemic fungal infections, tuberculosis, and Pneumocystis carinii pneumonia with chronic immunosuppressive therapy.
- Cholinergic crisis presents due to excessive ACh at nicotinic and muscarinic receptors secondary to the use of cholinesterase inhibitors.
- Symptoms include cramps, lacrimation, increased salivation, muscular weakness, muscular fasciculation, paralysis, diarrhea, and blurry vision.

CLINICAL FEATURES:

The cardinal feature of MG is fluctuating weakness that is fatigable, worsening with repetitive activities and improving with rest. Weakness is worsened by exposure to heat, infection, and stress. The fluctuating feature distinguishes MG from other disorders that present with a similar weakness. Typically, the weakness involves specific skeletal muscle groups. The distribution of the weakness is generally ocular, bulbar, proximal extremities and neck, and in a few patients, it involves the respiratory muscles. In patients with MG, the weakness is mild in 26%, moderate in 36%, and severe in 39%, associated with dysphagia, depressed cough, and reduced vital capacity. [6] Ocular muscle weakness is by far the most common initial symptom of MG, occurring in approximately 85% of patients. Generalized progression will develop in 50% of these patients in two years. It presents with fluctuating ptosis and diplopia or sometimes blurry vision. Diplopia can be elicited by having the patient look laterally for 20-30 seconds resulting in eye muscle fatigue uncovering myasthenic weakness. The ptosis can be unilateral or bilateral, fatigues with upgaze, and sustained upgaze for 30 or more seconds will usually induce it. The ptosis can be severe enough to totally occlude vision if it is bilateral. The most commonly involved extraocular muscle is the medial rectus. On clinical examination, usually more than one extraocular muscle is weak with pupillary sparing. The weakness does not follow any pattern of specific nerve or muscle involvement, distinguishing it from other disorders such as vertical gaze paresis, oculomotor palsy, or internuclear ophthalmoplegia (INO). Bulbar muscle involvement during the course of the disorder can be seen in 60% of the patients, presenting as fatigable chewing, particularly on chewing solid food with jaw closure more involved than jaw opening. Bulbar symptoms with painless dysphagia and dysarthria may be the initial presentation in 15% of patients. The lack of ocular involvement in these patients may be mis diagnosed as motor neuron disease. Weakness involving respiratory muscles is rarely the presenting feature in the first 2 years of onset. Respiratory muscle weakness can lead to myasthenic crisis which can be life threatening, requiring mechanical ventilation and naso-gastric (NG) tube feeding. It can be precipitated by infections and certain medication such as aminoglycosides, telithromycin, neuromuscular blocking agents, magnesium sulfate, beta blockers, and fluoroquinolone antibiotics.



Fig (1): (a)Photograph of a patient with MG showing partial right ptosis. The left lid shows compensatory pseudolid retraction because of equal innervation of the levator palpabrae superioris (Herring's law). (b) Post-Tensilon test: note the improvement in ptosis.

DIAGNOSIS:

Tensilon (Edrophonium Chloride) Test: Edrophonium chloride is a short-acting acetylcholinesterase inhibitor that prolongs the duration of action of acetylcholine at the NMJ. Edrophonium is administered intravenously and the patient is observed for objective improvement in muscle strength particularly the eyelid ptosis and/or extraocular muscle movement. Only unequivocal improvement in strength of a sentinel muscle should be accepted as a positive result. Patients must be connected to cardiac and blood pressure monitors prior to injection because of possible risk of arrhythmia and hypotension. Atropine should be available at bed side for use if an adverse event like severe bradycardia (heart rate below 37) develops. Side effects from Edrophonium include increased salivation and sweating, nausea, stomach cramping, and muscle fasciculation. Hypotension and bradycardia are infrequent and generally resolve with rest in the supine position. Tensilon test has a sensitivity of 71.5%–95% for the diagnosis of MG.

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- Ice Pack Test: The ice pack test is a nonpharmacological test which could be considered in patients with ptosis when the Edrophonium test is contraindicated. It is per formed by placing an ice pack over the eye for 2–5 minutes and assessing for improvement in ptosis.
- Electrophysiological Tests: The two principal electro physiologic tests for the diagnosis of MG are repetitive nerve stimulation study and single fiber electromyography. Repetitive nerve stimulation tests neuromuscular transmission. It is performed by stimulating the nerve supramaximally at 2 3Hz. A 10% decrement between the first and the fifthevoked muscle action potential is diagnostic for MG. In the absence of the decrement, exercise can be used to induce exhaustion of muscles and document decrement. The test is abnormal in approximately 75% of patients with gMG and 50% of patients with oMG.[7]

MANAGEMENT OF MYASTENIA GRAVIS:

Management of MG should be individualized according to patient characteristics and the severity of the disease. There are two approaches for management of MG based on the pathophysiology of the disease. The first is by increasing the amount of Acetylcholine that is available to bind with the postsynaptic receptor using an acetylcholinesterase inhibitor agent, and the second is by using immunosuppressive medications that decrease the binding of acetylcholine receptors by antibodies.

- ✤ There are four basic therapies used to treat MG:
- > symptomatic treatment with acetylcholinesterase inhibitors.
- > rapid short-term immunomodulating treatment with plasmapheresis and intravenous immunoglobulin.
- > chronic long-term immunomodulating treatment with glucocorticoids and other immunosuppressive drugs.
- ➢ surgical treatment.
- Short-Term Immunomodulating Therapies: Plasma exchange and intravenous immunoglobulin have rapid onset of action with improvement within days, but this is a transient effect. They are used in certain situations such as myasthenic crisis and preoperatively before thymectomy or other surgical procedures. They can be used intermittently to maintain remission in patients with MG who are not well controlled despite the use of chronic immunomodulating drugs.
- Plasmapheresis: It improves strength in most patients with MG by directly removing AChR from the circulation. Typically, one exchange is done every other day for a total of four to six times. Adverse effects of plasmapheresis include hypotension, paresthesias, infections, thrombotic complications related to venous access, and bleeding tendencies due to decreased coagulation factors. Intravenous Immunoglobulin Therapy (IVIg). It involves isolating immunoglobulins isolated from pooled human plasma by ethanol cryo precipitation and is administered for 5 days at a dose of 0.4g/kg/day, fewer infusions at higher doses are also used. The mechanism of action of IVIg is complex. Factors include inhibition of cytokines competition with autoantibodies, and inhibition of complement deposition. Interference with the binding of Fc receptor on macrophages, Ig receptor on B cells, and interference with antigen recognition by sensitized T cells are other mechanisms. More specific techniques to remove pathogenic anti-AChR antibodies utilizing immunoadsorption have been developed recently, which offer a more targeted approach to MG treatment. Clinical trials showed significant reduction of blocking antibodies with concomitant clinical improvement in patients treated with immunoadsorption techniques.[8]

SURGICAL MANAGEMENT:

- Thymectomy: Surgical treatment is strongly recommended for patients with thymoma. The clinical efficacy of Thymectomy in other situations has been questioned because the evidence supporting its use is not solid. Surgical treatment is strongly recommended for patients with thymoma. The benefit of thymectomy evolves over several years. Thymectomy is advised as soon as the patient's degree of weakness is sufficiently controlled to permit surgery. Patients undergoing surgery are usually pretreated with low-dose glucocorticoids and IVIg. Thymectomy may not be a viable therapeutic approach for anti-MuSK antibody-positive patients because their thymi lack the germinal centers and infiltrates of lymphocytes that characterize thymi in patients who have anti-AChR antibodies. This supports a different pathologic mechanism in anti-MuSK Ab-positive and anti-AChR Ab positive MG. Most experts consider thymectomy to be a therapeutic option in anti-AChR Ab-positive gMG with disease onset before the age of 50 years.
- Rehabilitation: A rehabilitation program in combination with other forms of medical treatment can help relieve symptoms and improve function in MG. The primary goal is to build the individual's strength to facilitate return to work and activities of daily living. The intensity and progression of the exercise depend on the stage of the disease and overall health. An interdisciplinary approach including neuromuscular medicine, physical medicine and rehabilitation, and respiratory therapy is recommended. Physical therapy is beneficial for long-term restoration of muscle strength. Graded strengthening exercises help the individual remain as functional as possible. Occupational

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therapy helps the individual adapt to new ways of performing daily living tasks using energy conservation and compensatory techniques. There is speech therapy for training of esophageal speech following a tracheostomy. Vocational counseling may be needed if the current job requirements cannot be met. Psychological interventions to cope with the illness may be necessary.[9]

TREATMENT:

Various treatments, alone or together, can help with symptoms of myasthenia gravis. Your treatment will depend on your age, how severe your disease is and how fast it's progressing.

Medications:

- Cholinesterase inhibitors: Medicines such as pyridostigmine (Mestinon, Regonal) improve communication between nerves and muscles. These medicines aren't a cure, but they can improve muscle contraction and muscle strength in some people. Possible side effects include gastrointestinal upset, diarrhea, nausea, and too much salivation and sweating.
- **Corticosteroids:** Corticosteroids such as prednisone (Rayos) block the immune system, making it less able to produce antibodies. Use of corticosteroids over a long period of time, however, can lead to serious side effects. These include bone thinning, weight gain, diabetes and higher risk of some infections.
- Immunosuppressants: Your provider also might prescribe other medicines that change your immune system. These medicines could include azathioprine (Azasan, Imuran), mycophenolate mofetil (Cellcept), cyclosporine (Sandimmune, Gengraf, others), methotrexate (Trexall) or tacrolimus (Astagraf XL, Prograf, others). These medicines, which can take months to work, might be used with corticosteroids. Side effects of immunosuppressants, such as higher risk of infection and liver or kidney damage, can be serious.[10]

2. CONCLUSION

MG is a relatively uncommon illness that destroys the communication between the nervous system and the muscles. A lack of specific essential molecules for the body brings on this illness. When someone is affected by it, they become exhausted. This disease can strike at any age, even in childhood, but older males over 60 and young adult women under 40 are more at risk. An individual may need to undergo specific physical examinations and several other tests to confirm the precise origin of the disease, depending on the symptoms, infectious diseases, and different past medical histories. MG is a difficult ailment that can range in severity and have an impact on all facets of life. MG has no treatment options and it is managed with the help of medicine, plasmapheresis, thymus gland removal, IVIG, and rest to reduce muscle weakness. Treatment aims to manage symptoms and modulate immune system activity. Individuals can manage symptoms and have fulfilling lives with the help of appropriate medical care, emotional support, and lifestyle changes. Early diagnosis is crucial to the management of this illness. While avoiding eating and breathing issues, the treatment aims to improve general muscle function. In most cases, people with MG can regain muscle strength and live ordinary or near-ordinary everyday lives. There are emerging new therapies that target particular immune pathways. Future treatments may benefit from research into gene-based medicine.

3. REFERENCE

- [1] Mishra A K, Varma A. Myasthenia Gravis: A Systematic Review. Cureus. 2023.15(12). 21-34.
- [2] Ashith kumar Beloor Suresh; Ria Monica D. Asuncion. Myasthenia Gravis. National Library of Medicine. 2023.14(9). 24-34.
- [3] AnnapurniJayamTrouth, AlokDabi, Noha Solieman, MohankumarKurukumbi, and Janaki Kalyanam. Myasthenia Gravis: A Review. ResearchGate. 2012. 13(12). 223-300.
- [4] Laura Dresser, Richard Wlodarski, Kourosh Rezania and BettySoliven. Myasthenia Gravis: Epidemiology, Pathophysiology and Clinical Manifestations. Journal of Clinical Medicine. 2021. 10(8). 22 35.
- [5] Phillips, L.H. The Epidemiology of Myasthenia Gravis. Ann. N. Y. Acad. Sci. 2020, 998(19). 407–412.
- [6] Martínez Torre S, Gómez Molinero I, Martínez Girón R: An update on myasthenia gravis [Article in Spanish]. Semergen. 2018, 44(33). 351-4.
- [7] Vincent A, McConville J, Farrugia ME, Newsom-Davis J: Seronegative myasthenia gravis. Semin Neurol. 2004, 24(16). 125-33.
- [8] Murthy JMK. Myasthenia Gravis: Do the Subtypes Matter? Ann Indian Acad Neurol. 2020. 23(1). 54-60.
- [9] Juel VC: Myasthenia gravis: management of myasthenic crisis and perioperative care. Semin Neurol. 2021, 24(12). 75-81.
- [10] Stetefeld HR, Schroeter M: Myasthenic crisis [Article in German]. Fortschr Neurol Psychiatr. 2018, 86(35). 301 7.