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Review Article

Myasthenia Gravis and its Physiotherapeutic Management

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Abstract

Myasthenia gravis is caused by a breakdown in the normal communication between nerve and muscles. In this disease neurotransmission is impaired by antibodies against the acetylcholine receptors in the post-synaptic membrane of the muscle. It is considered to be an organ specific autoimmune disease and also due to the thymic abnormalities. In this disease there is weakness of leg and arm muscles, double vision, drooping eyelids and difficulties with speech, chewing, swallowing and breathing.

As there is no specific treatment of myasthenia gravis, so physiotherapeutic management can reduce sign and symptoms. However, suppression of production of cyclohexamide receptor antibodies by administrating corticosteroid and immunosuppressive drugs like prednisolone and azoathioprine etc. help in improving myaesthenia gravis. As in some cases, thymoma are frequently associated with autoimmunity so thymectomy may cause reduction of myasthenia gravis as it decreases plasma cell producing antibodies. Because of the various treatment there is marked reduction in the myasthenia gravis.

Keywords: Myaesthenia Gravis; Acetylcholine; Neurotransmission; Thymus; Thymoma; Thymectomy; Immunosuppression; Autoimmunity; Autoantibodies; Neuromuscular

Abbreviation

Ach: Acetylcholine; MUSK: Muscles-specific Receptor Tyrosine Kinase; MG: Myasthenia Gravis; Th Cell: T Helper Cell

Introduction

Although Thomas Willis (1672) [27] was not the first to describe patients with weakness of limb muscles which become greater during the course of the day and progressive tongue weakness stimulated by "long, hasty or laborious speaking" but he was the first to recognise myaesthenia gravis as distinct clinical entity [28]. Later on, a complete description of myasthenia gravis including severity, prognosis and different presentation of the cases was presented by Samuel Goldflam in 1893.

Myasthenia gravis (MG) is an autoimmune disorder because of a postsynaptic defect of neuromuscular transmission due to biomolecular mimicry. Myasthenia gravis occured in the majority of patients having autoantibodies designated against the postsynaptic nicotinic acetylcholine receptor (AChR) [3].

Myasthenia Gravis is a relatively rare, long term condition and an autoimmune neuromuscular disease caused by circulating antibodies that interrupt acetylcholine receptors at the postsynaptic neuromuscular junction, inhibiting the excitatory effects of the neurotransmitter acetylcholine on nicotinic receptors at neuromuscular junctions causing to altering muscle weakness and fatigue which is more marked in the afternoon. It is generalized muscle

weakness and the most common muscles impressed are muscles that control the eyes and eyelids, facial expressions, chewing, swallowing, and speaking, respiratory muscles can be affected and may require quick intervention. Myasthenia gravis mocks people at any age but it is common to affect women under 40 [8].

Most cases are due to immunoglobulin G1 (IgG1) and IgG3 antibodies that assault AChR in the postsynaptic membrane, leading complement-mediated damage and muscle weakness [19].

Aetiology

Thai and LO (2004) reported the following causes of myasthenia gravis:

- Abnormal immune reaction i.e. antibody mediated autoimmune response.
- Passive transfer of maternal anti AchR antibodies may result in transient neonatal myasthenia gravis.
- Many drugs like D-penicillamine may induce myasthenia gravis.
- Congenital myasthenia syndrome: Heritable(congenital) disorders of postsynaptic neuromuscular junction transmission, however it is not directly inherited nor it is contagious [27].

Epidemiology

- The annual incidence of MG is 8-10 cases per 1 million persons and its prevalence is 150-250 cases per 1 million persons [3].
- Age and sex appears to influence the occurrence of myasthenia gravis. Below 40years of age male: female ratio is 1:3 but over 50years it mainly decrease in male [10].
- MG can affect people of any age, typically starting in women under 40 and men over 60. Muscle specific kinase myasthenia gravis (MuSK-MG) is a rare subgroup of MG affecting mainly women during childbearing years [22].
- Its prevalence has been increasing over the past several decades secondary to better awareness, recognition, and increased survival, it's not a linear increase, the age of onset is characterized by a bimodal distribution with an early incidence peak in the 2nd to 3rd decades affecting young women and a late peak in the 6^{th} to 8^{th} decades that is primarily seen in men [13,15].

Classification

According to Foundation of America Clinical Classification, Myasthenia gravis has been classified as follows [29].

Class: Description

- I: Any eye muscle weakness, possible ptosis, no other evidence of muscle weakness elsewhere
- II: Eye muscle weakness of any severity, mild weakness of other muscles
- IIa: Predominantly limb or axial muscles
- IIb: Predominantly bulbar and/or respiratory muscles
- III: Eye muscle weakness of any severity, moderate weakness of other muscles
- IIIa: Predominantly limb or axial muscles
- IIIb: Predominantly bulbar and/or respiratory muscles
- IV: Eye muscle weakness of any severity, severe weakness of other muscles
- IVa: Predominantly limb or axial muscles
- IVb: Predominantly bulbar and/or respiratory muscles
- V: Intubation needed to maintain airway.

Subtypes of Myaesthenia Gravis are broadly classified as follows: [2]

- Early-onset Myaesthenia Gravis: Age at onset <50 years. Thymic hyperplasia, usual females.
- Late-onset Myasthenia Gravis: Age at onset >50 years. Thymic atrophy, mainly males.
- Thymoma-associated Myasthenia Gravis (10%-15%)
- Myasthenia gravis with anti-MUSK antibodies.
- Ocular Myasthenia Gravis (oMG): Symptoms only affecting extraocular muscles.
- Myasthenia Gravis with no detectable AChR and muscle-specific tyrosine kinase (MuSK) antibodies.

Clinical features

The usual primal illness is a specific muscle weakness instead generalized weakness - repeatedly ocular (eye) symptoms. Extraocular muscle weakness or ptosis is present initially in 50% of patients and happens along the course of illness in 90% of patients. Patients also repeadtedly report diplopia (double vision).

In myasthenia gravis ocular weakness solely occur in 10 - 40% of patients. It has been observed that in some patients, having generalised weakness there is no ocular muscle weakness. Eye muscle weakness are often asymmetrical and variable.

Bulbar muscle weakness is also common, fascial muscle weakness can result in, trouble smiling or trouble whistling. Weakness tends to spread from the ocular to facial to bulbar muscles and then to truncal and limb muscles. With the weakness of neck flexors more common and neck extensor weakness is rare to present. Limb weakness may be more severe proximally than distally. Isolated limb muscle weakness is the presenting symptom in fewer than 10% of patients. Weakness is typically least severe in the morning and worsens as the day progresses. Weakness is increased by exertion and alleviated by rest. Weakness progresses from mild to more severe over weeks or months, with exacerbations and remissions.

Approximately 87% of patients have generlised disease within 13 months after onset, and about 75% will have generalized weakness within the first 2 to 3 years. Less often, symptoms may remain limited to the extra-ocular and eyelid muscles for many years. Respiratory muscle weakness develop in up to 40% of patients and myaesthenic crisis(respiratory failure) present in about 15% - 20% of patients with MG [11].

In about two-thirds of individuals, the introductory symptom of MG is related to the muscles around the eye. Eyelid drooping (ptosis may occur due to weakness of m. levator palpebrae superioris) [16] and double vision (diplopia, due to weakness of the extraocular muscles) [23].

Eye symptoms tend to get poorer when watching television, reading, or driving, individyally in bright conditions. Consequently, some affected individuals choose to wear sunglasses [7].

Weakness of the muscles responsible for speaking may lead to dysarthria and hypophonia.

Due to weakness of the muscles of facial expression and muscles of mastication, patients become unable to hold the mouth closed.

Diagnosis:- The following tests are applicable in the diagnosis of myasthenia gravis:-

Edrophonium (Tensilon) test

Edrophonium is an AChE inhibitor that works within a few seconds (30 seconds) and the effect lasts for a few minutes (about five minutes) [14,17].

It goes intravenously. It is likable to use a placebo injection (for example, normal saline) prior to the edrophonium injection. There should be a observable weakness of the part (for example, ptosis or slurred speech or inability to sustain a posture of the outstretched arm) to monitor the response. A fractionated dose is usually given where initially 1-2 mg of the drug is administered and remaining 8-9 mg is given only if there is no response until 60 seconds after the first dose.

Ice pack test

This test can be performed when ptosis is present. The application of an ice pack to lids of the affected eyes improved ptosis due to myasthenia gravis in 80% of cases but it did not improve in ptosis due to other aetiologies [9,24].

Anti-MuSK antibodies test

It is well known that about 10%-20% of patients do not have anti-AChR antibodies in their sera (sero-negative myasthenia gravis). Although, focuses for antibody attack other than the AChR were not known until recently. It was a collaboration between Vincent., *et al*. in UK and a German scientist (Hoch) that led to the recognition of a new target for antibody attack in myasthenia gravis [12].

Electrophysiological tests

Electrophysiological tests consists repetitive nerve stimulation test and single fibre electromyography. The repetitive nerve stimulation test reflects progressive reduction in the ampilitude of the compound muscle action potential from the fourth stimulation when a nerve is subjected to repetititve supramaximal electrical stimulations at a frequency of 3 Hz. In normal subjects also the fourth evoked response may be slightly smaller than the first one, but the reduction is not more than 7%. If the decrease in amplitude of the compound muscle action potential is $\geqslant$10%, the test is called positive (a decremental response). The test is more likely to be positive on testing several muscles or when a weak muscle is tested [18].

Imaging

A chest X-ray may reflect widening of the mediastinum suggestive of thymoma, but computed tomography or magnetic resonance imaging (MRI) are more susceptive ways to identify thymomas and are generally done for this reason [6].

MRI of the cranium and orbits may also be performed to exclude compressive and inflammatory lesions of the cranial nerves and ocular muscles [1].

Management

There are two approaches for the management of myasthenia gravis based on the pattern of pathophysiology of disease, the first is by the increasing the amount of acetylcholine that is available to bind with post synaptic receptor using an acetylcholinestrase inhibitor agent such as pyridostigmine and the second is by using immunosuppressing drug that decreases the binding of the acetylcholine receptors by antibody.

Thymectomy (removal of thymus gland) is used as a surgical approach to reduce the symptoms of myasthenia gravis and it may improve the condition of the patient suffering from myasthenia gravis [30]. It has been observed that surgical management of thymus may give better result suffering from Surgical management like thymectomy so better result [4].

Physiotherapeutic management

Physiotherapeutic approach is concerned with identifying and maximising quality of life and movement potential within the spheres of pronotion, prevention, treatment/intervention, habilitation and rehabilitation. It is science -based commited to extending, applying, evaluating and reviewing the evidence that under pin sand inform its practice and delivery.

Aims for physiotherapeutic management

The aim to control myasthenia gravis after diagnosis should be prompt symptomatic control and the induction of remission or minimal modification.

- To provide psychological support to the patient.
- To prevent respiratory complications.
- To improve the vital capacity of the patients.
- To avoid undue fatigue in the muscles.
- To train for oromotor control.
- To advise for assisstive devices.
- To maintain normal muscles properties such as strengthening and extensibility.
- To improve functional capacity of the patient [20].

Plans for physiotherapeutic management

Patient must be inspired to move his limbs actively with or without assistance. If required, passive movements are given by the therapist. Passive stretching plays a vital role to maintain normal length of soft tissues. Certain corrective splints are provide to maintain the stretch. Aerobic exercises in the form of deep breathing like diaphragmatic and pranayama are made to practice by the patient to prevent respiratory complications [31]. Postural drainage, coughing, huffing are done to remove the secretions and maintain good bronchial hygiene.

All precautionary measures should be taken to prevent pressure sores;

- Frequent change in position.
- Good skin hygiene is maintained.
- Prevent creases over bed
- Waterbed or air bed is advised
- Care of the bladder is very important.

To maintain functional independence the following exercises is employed:

- Mat exercises
- Strengthening exercises
- Weight bearing exercises
- Gait training
- Transfer techniques.

Skeie., *et al.* (2010) reported physical exercise is well tolerated in patients with well-regulated Myasthenia Gravis and practice under limited training intensity. Aerobic exercise, respiratory muscle training and mild strength training can be advised and should be supervised [31].

Balance strategy training maybe helpful in improving balance, improve the vestibular function through targeting sensorimotor system to improve balance and decrease falling risk, moreover more research into this domain has to be done [25].

Gradual resisted training exercises

Respiratory muscle training believed to be effective in management of fatigue, weakness and respiratory failure specially with moderate cases that hinder normal activities of daily living (ADL) [4]. Rassler., *et al.* 2007 observe effect of respiratory muscles endurance training patients with myasthenia gravis gives better result.

In people with generalized MG, some evidence indicates a partial home program including training in diaphragmatic breathing, pursed-lip breathing, and interval-based muscle therapy may improve respiratory muscle strength, chest wall mobility, respiratory pattern, and respiratory endurance [5].

Conclusion

Myasthenia gravis is an autoimmune neuromuscular disorder, which can be diagnosed with various test mentioned above in the text. Patient should be treated according to the symptoms in patients. The combinations of various therapy and rehabilitation may improve the condition of patients suffering from myasthenia gravis.

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