Myasthenia Gravis

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Contributor: Benedetto Giardulli

Myasthenia gravis (MG) is an autoimmune disorder characterized by muscle weakness and fatigue. The cause is a postsynaptic defect of neuromuscular transmission, which brings, in the majority of patients, to develop autoantibodies directed against the postsynaptic nicotinic acetylcholine receptor (AChR).

Keywords: congenital myasthenic syndromes ; muscle weakness ; myasthenia gravis ; neuromuscular junction ; physical therapy modalities ; rehabilitation ; neurology

1. Introduction

The annual incidence of MG is 8–10 cases per 1 million persons and its prevalence is 150–250 cases per 1 million persons [1]. 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 [2].

2. Clinical Manifestation

The clinical manifestation of MG is weakness of skeletal muscles, which increases with fatigue and during the day, often with nearly normal muscle strength in the morning. The muscular weakness can be localized or generalized, and usually is more proximal than distal [3]. Eye and oropharyngeal muscles are often affected, but the distribution of muscle weakness is highly variable [4]. Muscle weakness causes common symptoms of MG that include: fatigue, breathing difficulties, ptosis, diplopia, hypomimia, problems with chewing and swallowing, and dysarthria. Myasthenic crisis is a complication of MG characterized by worsening of muscle weakness, resulting in respiratory failure that requires intubation and mechanical ventilation. MG and thymic neoplasms are frequently associated; one half of cortical thymoma patients develop MG, while 15% of MG patients have thymomas [5][6]. MG has an extensive impact on physical, psychological, and social wellbeing of the patients, causing a reduced health related quality of life (HRQoL): the more severe muscle symptoms and disability, the lower the physical components of the outcome [7][8][9][10].

3. Diagnosis

The diagnostic approach to MG can be difficult and is focused on confirming the clinical diagnosis established by the history and typical examination findings. Point-of-care tests (the ice pack test, alone or combined with sustained upgaze, and the edrophonium test) are sensitive, but they have major limitations due to concerns about excess false-positive results [11]. The most reliable laboratory methods that aid in the confirmation are serologic tests for autoantibodies and electrophysiological studies (repetitive nerve stimulation—RNS, and single-fiber electromyography—SFEMG). MG can be classified in the following main subgroups defined on the basis of clinical, antibody, and thymic features: late onset, early onset, ocular, seronegative, thymoma, lipoprotein receptor–related protein 4 (LRP4), and MuSK [12]. According to the Osserman and Genkins classification, the clinical severity of MG is graded in five stages (I, ocular signs only; IIA, generalized mild muscle weakness; IIB, generalized moderate weakness and/or bulbar dysfunction; III, acute fulminating presentation and/or respiratory dysfunction; IV, late generalized weakness) [13].

4. Medical Treatment and Rehabilitation

Treatment of MG includes acetylcholinesterase inhibitors (e.g., pyridostigmine, edrophonium, and ephedrine), thymectomy, immunosuppressive agents (e.g., prednisone, azathioprine, rituximab, tocilizumab, and mycophenolate mofetil), and short-term immunomodulation with plasma-exchange and intravenous immunoglobulin (IVIG) [14][15][16][17][18].

Rehabilitation is defined as “a set of measures that assist individuals who experience disability to achieve and maintain optimal physical, sensory, intellectual, psychological and social functioning in interaction with their environment” (World Health Organization. World Report on Disability. Geneva, Switzerland: WHO; 2011). It is a complex process of delivering a

coordinated interdisciplinary care program, comprising a series of individualized and goal-oriented therapies tailored for specific patient needs. The goal of rehabilitation is to improve functional independence and enhance participation with emphasis on patient education and self-management. In neuromuscular disorders, an effective rehabilitation program can help maximize the patient's physical and psychosocial functions as well as maintain a patient's quality of life [19][20][21][22]. Furthermore, an effective rehabilitation program can minimize secondary medical comorbidities, prevent or limit physical deformities, and allow the patient to integrate into society [23][24][25][26].

According to experts' recommendations, rehabilitation is essential in the management of possible MG complications such as contractures and respiratory failure [27]. However, it is well known that typical MG weakness increases with exercise and repetitive muscle use [28]. It follows that it is not clear whether exercise is beneficial or harmful for patients with MG. Therefore, the role of exercise in the management of these patients remains controversial [29][30]. Because muscle weakness is the main problem, muscular exercise would be valuable if it helped to counteract the loss of muscle tissue and strength.

Respiratory training has proven to be a very effective approach in the management of fatigable weakness and respiratory failure, both of which strongly limit the performance of daily activities in people with MG[13][31][32][33][34][35][36][37][38]. The benefits of respiratory training included not only a measurable improvement in respiratory muscle strength, in respiratory endurance, and in physical performance [31][32][33][39][40], but also a reduction in the incidence of several MG complications, like dyspnea [41]. Furthermore, sustained hyperpnea training was considered a more appropriate approach than respiratory strength training in people with MG, because it reduced significantly diaphragm and abdominal muscles fatigue [40]. In addition, respiratory training improved MG subjective symptoms, like fatigability. The effects of respiratory training can be explained by the fact that a long-term respiratory muscle endurance training reduces the patient's respiratory rate. As a consequence, the work of breathing decreases the breathing reserve during physical activity and improves overall physical fitness. Respiratory training could be also practiced at home under the supervision of clinicians in order to enhance the conventional pharmaceutical therapy [40].

Balance training consists of exercises that target the sensorimotor system in order to improve function and reduce the risk of falls [42]. Additionally, balance training could also increase bone density, which can be reduced due to the sedentary lifestyle caused by muscle weakness and fatigue [43]. The positive effect of balance exercises on symptoms might be explained by an increase in the number of mitochondria within muscles, by the musculoskeletal mass building, and by the impulse to lactate degradation [44]. Consequently, this would lead to more efficient neuromuscular transmission, to the increase ability of muscles to cope with fatigue, and to improved strength and endurance [45]. Moreover, the increased visual-vestibular integration would lead to a better balance, since vestibular input has been suggested to play a key role in balance control [46][47].

Eventually, psychotherapy in combination with physical training (aerobic, stretching, and breathing strategies) could improve patient's fatigue more than physical training alone [48]. Moreover, group therapy could modify a MG patient's lifestyle since it helps to manage anxiety, depression, and social isolation [48].

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