Effects of Treatments Applied in Myasthenia Gravis on Gait: Review

Suzan AYDIN[*], Mustafa Oğuz KETHÜDAOĞLU[**], Hande Besna GÖÇEN[***], Havva Ezgi ALBAYRAK[****], Aygül KÖSEOĞLU KURT[*****], Mehmet Kaan ALTUNOK[******], Bülent Abut ÖZSEZİKLİ[*******]

Abstract

Myasthenia Gravis (MG) is an autoimmune disease in which neuromuscular transmission is blocked and neuromuscular junction physiology is affected. The main feature in MG is altered muscle weakness and fatigue of muscle groups that worsens with exercise and improves with rest. With the emergence of muscle weakness in the following periods, walking is affected in MG. This causes balance and walking problems. Most of the patients have complaints of falling and fear of falling. While applying MG treatment, myasthenic symptoms should be reduced and a stable clinical picture should be obtained in which the daily activities of the person are relieved. The aim of this study is to understand the effect of rehabilitation practices on gait in MG and to determine which exercises are effective. As a result, physiotherapy and rehabilitation approaches can provide solutions to patients' complaints, albeit symptomatically. Active resistance exercises, aerobic exercises, balance strategy training, endurance exercises, posture exercises, stretching exercises and active–passive range of motion exercises should be performed in an exercise program. In addition, rhythmic auditory stimulation and pre-surgical respiratory physiotherapy also have positive effects on walking.

Keywords: Autoimmune, balance, gait, myasthenia gravis.

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[*] MSc. Pt. PhD (c), Bahçeşehir University, Graduate Education Institute Physiotherapy and Rehabilitation Department, İstanbul, Türkiye ; Lecturer İstanbul Gelişim University, Vocational School of Health Services Physiotherapy Department, İstanbul, Türkiye. E-mail: suzanaltnkeser@gmail.com ORCID https://orcid.org/0000-0002-8470-9425
[**] MSc. Pt. PhD (c), Bahçeşehir University, Graduate Education Institute Physiotherapy and Rehabilitation Department, İstanbul, Türkiye ; Lecturer Cumhuriyet University, Health Sciences Faculty Physiotherapy and Rehabilitation Department, Sivas, Türkiye. E-mail: mustafaoguzkethudaoglu@gmail.com ORCID https://orcid.org/0000-0001-9723-9680
[***] MSc. Pt. PhD (c), Bahçeşehir University Graduate Education Institute Physiotherapy and Rehabilitation Department, İstanbul, Türkiye ; Lecturer İstanbul Gelişim University Vocational School of Health Services Physiotherapy Department, İstanbul, Türkiye. E-mail: handegocen@outlook.com ORCID https://orcid.org/0000-0002-4208-0366
[****] MSc. Pt. PhD (c), Bahçeşehir University, Graduate Education Institute Physiotherapy and Rehabilitation Department, İstanbul, Türkiye ; Lecturer Avrasya University, Vocational School of Health Services Occupational Therapy Department, Trabzon, Türkiye. E-mail: ezgii.karas@gmail.com ORCID https://orcid.org/0000-0002-4595-2043
[*****] MSc. Pt. PhD (c), Bahçeşehir University, Graduate Education Institute Physiotherapy and Rehabilitation Department, İstanbul, Türkiye ; MSc. Pt. Uropelvic Solutions, İstanbul, Türkiye. E-mail: aygulkoseoglu@gmail.com ORCID https://orcid.org/0000-0001-7180-3693
[******] MSc. Pt. PhD (c), Bahçeşehir University, Graduate Education Institute Physiotherapy and Rehabilitation Department, İstanbul, Türkiye ; Lecturer Selçuk University, Health Sciences Faculty Physiotherapy and Rehabilitation Department, Konya, Türkiye. E-mail: mehmetkaan.altunok@selcuk.edu.tr ORCID https://orcid.org/0000-0002-3851-0685
[*******] Asst. Prof., Bahçeşehir University, Graduate Education Institute Physiotherapy and Rehabilitation Department, İstanbul, Türkiye. E-mail: bulent@ozsezikli.com ORCID https://orcid.org/0000-0003-0805-8146

Myastenia Gravis'te Uygulanan Tedavilerin Yürümeye Etkisi: Derleme

Öz

Miyastenia Gravis (MG), nöromusküler iletimin bloke olduğu ve nöromusküler kavşak fizyolojisinin etkilendiği otoimmün bir hastalıktır. MG'de temel özellik, egzersizle kötüleşen ve dinlenme ile iyileşen kas gruplarının değişen kas güçsüzlüğü ve yorgunluğudur. İlerleyen dönemlerde kas zayıflıklarının ortaya çıkmasıyla MG'de yürüme etkilenmektedir. Bu durum denge ve yürüme problemlerine neden olur. Hastaların çoğunda düşme ve düşme korkusu şikâyetleri vardır. MG tedavisi uygulanırken miyastenik belirtileri azaltılıp kişinin günlük yaşam aktivitelerinin rahatladığı stabil klinik tablo elde edilmelidir. Bu çalışmanın amacı MG'de rehabilitasyon uygulamalarının yürümeye etkisinin anlaşılması ve hangi egzersizlerin etkili olduğunu belirlemektir. Sonuç olarak fizyoterapi ve rehabilitasyon yaklaşımları, hastaların şikayetlerine semptomatik de olsa çözüm getirebilir. Egzersiz programında aktif dirençli egzersizler, aerobik egzersizler, denge strateji eğitimleri, endurans egzersizleri, postür egzersizleri, germe egzersizleri ve aktif–pasif eklem hareket açıklığı egzersizleri yapılmalıdır. Ayrıca ritmik işitsel stimülasyonun ve cerrahi öncesi respiratuar fizyoterapinin de yürümeye olumlu etkileri vardır.

Anahtar Sözcükler: Otoimmün, denge, yürüme, miyastenia gravis.

Introduction

Myasthenia Gravis (MG) is the most common neuromuscular junction disease. It is an autoimmune disease in which neuromuscular transmission is blocked and neuromuscular junction physiology is affected, causing weakness, especially in the ocular, extremity and bulbar muscles[1-3]. The pathophysiology of MG is well-defined. The main problem is the creation of antibodies against nicotinic acetylcholine receptors (AChR). Anti-ACrH antibodies damage the postsynaptic membrane, and this causes clinical weakness and fatigue in general or certain muscle groups due to insufficient neuromuscular transmission[4,5].

MG is an uncommon disease with a prevalence of approximately 150-300 per million and an incidence of 10 per million in the general population[6]. Although the etiology is not fully known, genetic risk factors and the role of thymic pathologies are emphasized. It is thought that possible neoplastic, inflammatory and age-related changes, especially in the thymus tissue, play a role in the immunopathogenesis of MG[7,8]. 60-75% of MG patients have thymic hyperplasia and 20-25% have thymoma[9].

The main clinical characteristics of MG are altered muscle weakness and fatigue of muscle groups that worsen with exercise and enhance with rest. This symptom usually presents initially as ptosis or diplopia and is prominent in the ocular muscles. In most patients, within the first two years after the onset of the disease, it is observed that the

muscle weakness becomes generalized with the involvement of the extremity muscles, as well as the bulbar muscles, which result in difficulty in speaking, chewing and swallowing, difficulty in closing the jaw, and loss of facial expression[5]. Respiratory muscle weakness develops in approximately 40% of patients with MG, and myasthenic crisis occurs in approximately 15-20%. Muscle weakness spreads to the ocular muscles, facial muscles, bulbar muscles, trunk, arm and leg muscles, respectively. However, muscle weakness is typically minimal in the morning and worsens over time during the day[10].

As in all neuromuscular junction diseases, progressive loss of muscle strength, fatigue, decrease in exercise capacity, difficulty in transfer activities, pain and weight problems are observed in MG[11]. Physiotherapy and rehabilitation approaches in MG are the most important treatments that can provide solutions to the complaints of patients, even if they are symptomatic. Tovazhnyanska et al. conducted a study to determine the role of rehabilitation in the treatment algorithm of patients with MG and the components of post-surgical treatment-rehabilitation. In this study, they mentioned that rehabilitation for MG patients is not the main part of the patient's treatment algorithm, but a very important part[12]. The aims of the rehabilitation program in MG are to maximize functional capacity, maintain independence in daily life and transfer activities, limit the progression of the disease, prevent physical deformities, increase the quality of life of patients and support their participation in society[1].

There is no definitive treatment for MG, but in many cases, symptoms can be controlled with current treatments[13]. The main aim of treatment is to achieve remission with few or no myasthenic symptoms or to obtain a stable clinical picture with subjective and objective minimal symptoms that do not affect daily life[5]. Since autoantibodies cause MG, treatment should be based on reducing pathogenic antibodies in the immune system. It can be thought that prevention of antigenic modulation or complement activation, which has an important place in the pathogenesis of the disease, may also prevent neuromuscular junction damage[14]. For this purpose, various treatments such as removal of autoantibodies with immunosuppression and plasmapheresis, modulation of the immune system with intravenous IgG, and removal of the antibody-producing thymus are applied[5]. Although minimally invasive thymectomy methods are used, weakness occurs in respiratory and skeletal muscles due to stimulation of anesthetic agents, post-operative airway inflammation and increased autoantibody release. This weakness may result in difficulty in coughing and excreting, respiratory distress,

dyspnea, pneumonia, and atelectasis[3]. Chen et al. investigated the effects of pre-operative moderate-intensity respiratory muscle training and aerobic exercise on post-operative complications in surgically treated MG patients. It has been shown that pre-operative accelerated rehabilitation is safe in patients after thoracic surgery, it can have positive effects on post-operative complications and activities of daily living, and the length of hospital stay is reduced[15].

Physiotherapy and rehabilitation practices have a great impact on motor performance while helping to maintain and increase muscle strength, independence level in activities of daily living and quality of life of patients with MG. At the same time, effective rehabilitation can minimize the secondary health problems of the patient, reduce and prevent physical deformities and enable integration into social life[1].

Rehabilitation programs must be personalized. The patient and patient's family should be informed about the disease as soon as the diagnosis is made. In the next step, the expectations of the patient and the patient's family should be evaluated and a rehabilitation program should be planned accordingly. Depending on the potential of the patient, the rehabilitation program can be aimed at protecting, improving or slowing down. A good rehabilitation program should include exercise, nutritional counseling, psychosocial support and vocational counseling[16]. Farrugia et al. investigated whether a combination of 10 weeks of physical and psychological training could help relieve fatigue symptoms in 10 MG patients with stable disease and residual problematic fatigue. At the end of the program, there was a substantial improvement in the visual analog fatigue scale, but no significant improvement was observed in other scales (activities of daily living, quality of life, depression, etc.). In the follow-up evaluations after three months, it was observed that all fatigue scores regressed to the baseline[17]. Zhang et al., in their study, stated that the use of artificial intelligence in the treatment of MG might be beneficial in terms of the safe use and follow-up of immunosuppressive drugs, personal life guidance, development of a social platform for communication, rehabilitation and patient management[18].

With the emergence of muscle weakness in the following periods, gait is affected in MG and this causes balance and walking problems. Most of the patients have complaints of falling and fear of falling. Weakness in the upper extremity and trunk muscles causes trunk instability and an increase in lumbar lordosis, while the loss of strength in the hip abductors causes trendelenburg and waddling gait[1,19]. In addition, dorsiflexor weakness and overuse of the gastrosoleus muscle group stimulate toe walking. Weakness of the hip

flexors and extensors causes shortening of the steps, and the deformity of the appendix causes difficulty in keeping the foot in contact with the ground during the swing phase. Therefore, MG patients perform exaggerated hip and knee flexion to lift the foot off the ground during the swing phase (stepage gait). Stepage gait negatively affects patients both aesthetically and in terms of energy consumption. Considering all these, gait training has a great place in MG rehabilitation[1].

Myasthenia Gravis and Gait Training

Gait training includes increasing aerobic capacity, strengthening weak muscles, supporting them with assistive devices and selecting the appropriate walking aid. If the disease is in the initial stage or if there is a mild impact, aerobic exercises can positively affect walking time and energy consumption. After weakness develops, the use of assistive devices and orthoses can ensure efficient use of energy and smoothness of gait pattern. If orthotic support is required, the patient should be well evaluated in terms of function and compatibility with the device[1].

The exercise program should include active-resistance exercises, aerobic exercises, endurance exercises, posture exercises, stretching exercises, and active-passive range of motion exercises[16]. Westerberg et al. examined functional skeletal muscle parameters (isometric muscle strength, muscle thickness, etc.), quality of life, and fatigue levels in 11 MG patients before and after applying a physiotherapy program including 12 weeks of supervised aerobic and resistance exercise. After the exercise program, improvements were observed in all measurements[20]. Wong et al., in their study with the hypothesis that balance strategy training would provide improvements in balance, strength and fitness levels, observed that balance strategy training provided significant improvements in all parameters of patients[21]. Rahbek et al. conducted a study to investigate whether progressive resistance exercises and aerobic exercises are applicable and efficient in MG. As a result of this study, while no change was observed in the aerobic exercise group, it was observed that the maximum strength and functional capacity increased in the resistance exercise group[22].

Andersen et al. examined whether rhythmic auditory stimulation improves walking distance and walking speed, on 48 patients with MG, and 6 Minutes Walk Test (6MWT) was applied under different conditions, including walking with rhythmic auditory stimulation at 100% of the fastest walking speed, walking with rhythmic auditory stimulation at 110% of the patient's fastest walking speed and walking silently. Those

who walked with auditory rhythmic stabilization at 110% of the patient's fastest walking speed increased walking distance by 8.3 meters in the 6MWT compared to those who walked silently but did not increase the mean walking heart rate or Borg scores. This result is theoretically important and has potential implications for planning a physical rehabilitation program for patients with MG[23].

Mohamed et al. investigated the effectiveness of treadmill training with partial body weight support on pulmonary functional tests, neuromuscular functions, and quality of life. Thirty children aged 13-16 were divided into 2 groups, and a designed physical therapy program was applied to both groups. In addition, partial body weight supported treadmill training was applied to Group A. The treatment was administered three times a week for 12 consecutive weeks. Pulmonary functional tests (FVC, FEV1, PEFR, and MVV), neuromuscular function tests (compound motor action potential, isometric muscle strength of biceps brachii and rectus femoris, balance, walking endurance, and fatigue) and quality of life, before and 12 weeks after treatment measured. A significant improvement was observed in both groups in all investigated variables. Both specific physical therapy and treadmill training with partial body weight support are effective in improving pulmonary functional tests, neuromuscular functions, and quality of life. Treadmill training with partial bodyweight support is an excellent adjunct to a physical therapy program[15].

Material and Methods

This study was prepared by examining Pubmed, ScienceDirect and Google Scholar databases between February and April 2023. The terms Autoimmune, balance, gait, and myasthenia gravis were used as keywords. Current studies on myasthenia gravis and physiotherapy and rehabilitation conducted in recent years are included.

Limitations

Our biggest limitation in writing this review is that there are few studies on myasthenia gravis. We attribute this to the small patient population.

Conclusion and Suggestions

MG is an autoimmune disease in which antibodies bind to AChR or functionally related molecules at the postsynaptic membrane of the neuromuscular junction, impairing neuromuscular transmission. Patients experience muscle weakness and fatigue, which increases with activity and decreases with rest. Muscle weakness in MG is generally

symmetrical, with the exception of the ocular muscles, and is more prominent in the proximal muscles[24].

Weakness of the ocular muscles is the most common initial symptom in MG. The involvement of these muscles causes ptosis, diplopia and sometimes blurred vision in patients. Involvement of the bulbar muscles can be seen in approximately 60% of patients. Difficulty may be experienced especially in chewing solid foods. Dysphagia and dysarthria occur as the initial symptoms of the disease in 15% of patients. Respiratory muscle weakness can also be seen in patients with bulbar involvement, which can cause life-threatening myasthenic crises. The symptoms are most severe in the first 2 years of the disease. Afterwards, the disease can usually be brought under control with current treatment approaches. The medical treatment of MG includes acetylcholinesterase inhibitors, immunosuppressive agents, plasmapheresis, intravenous immunoglobulin therapy, and thymectomy is performed[24].

A good rehabilitation program should include exercise, nutritional counseling, psychosocial support, and occupational counselling. Active-resistance exercises, aerobic exercises, endurance exercises, posture exercises, stretching exercises and active-passive range of motion exercises should be included in the exercise program. Gait training includes increasing aerobic capacity, strengthening weak muscles, supporting them with assistive devices and selecting the appropriate walking aid. If the disease is in the initial stage or if there is a mild impact, aerobic exercises can positively affect walking time and energy consumption. After weakness develops, the use of assistive devices and orthoses can ensure efficient use of energy and smoothness of gait pattern[24].

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