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Physical Therapy Management of Myasthenia Gravis: A Case Study

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Abstract

Purpose: Myasthenia gravis (MG) is an autoimmune disease that involves dysfunction of the neuromuscular junction, and commonly involves fluctuating muscle weakness and central fatigue. Current literature lacks consensus on the benefit of exercise in addressing central fatigue in this population. This case report explores the role of physical therapy in an individual with MG for whom fatigue is a primary concern. **Methods:** This case study describes the physical therapy management of a 62-year-old Caucasian male recently diagnosed with myasthenia gravis. Physical therapy intervention focused on strength and balance training as well as patient education on energy conservation and activity pacing. Diaphragmatic breathing and coordination of interdisciplinary referrals were also incorporated. **Results:** The patient demonstrated improved functional strength per the 5 Times Sit to Stand, and improved standing balance per the Modified Clinical Test of Sensory Interaction in Balance. The patient's 6 Minute Walk Test did not indicate improved endurance. Subjectively the patient mentioned ongoing fatigue, and although his MFIS and FSS scores improved, these measures do not have established MDC or MCID values for the MG population. **Conclusion:** The results of this case are consistent with current literature, suggesting that physical therapy interventions can improve strength and balance in patients with MG, but not necessarily fatigue. Further research is needed to determine optimal management of fatigue in MG.

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ABSTRACT

Purpose: Myasthenia gravis (MG) is an autoimmune disease that involves dysfunction of the neuromuscular junction, and commonly involves fluctuating muscle weakness and central fatigue. Current literature lacks consensus on the benefit of exercise in addressing central fatigue in this population. This case report explores the role of physical therapy in an individual with MG for whom fatigue is a primary concern. **Methods:** This case study describes the physical therapy management of a 62-year-old Caucasian male recently diagnosed with myasthenia gravis. Physical therapy intervention focused on strength and balance training as well as patient education on energy conservation and activity pacing. Diaphragmatic breathing and coordination of interdisciplinary referrals were also incorporated. **Results:** The patient demonstrated improved functional strength per the 5 Times Sit to Stand, and improved standing balance per the Modified Clinical Test of Sensory Interaction in Balance. The patient's 6 Minute Walk Test did not indicate improved endurance. Subjectively the patient mentioned ongoing fatigue, and although his Modified Fatigue Impact Scale (MFIS) and Fatigue Severity Scale (FSS) scores improved, these measures do not have established MDC or MCID values for the MG population. **Conclusion:** The results of this case are consistent with current literature, suggesting that physical therapy interventions can improve strength and balance in patients with MG, but not necessarily fatigue. Further research is needed to determine optimal management of fatigue in MG.

Keywords: physical therapy, rehabilitation, myasthenia gravis

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disease that involves dysfunction of the neuromuscular junction with associated muscle weakness. Its prevalence is 150 to 250 cases per 1 million persons.[1] MG typically presents in women under age 40 and men over age 60, but can occur at any age.[2] The hallmark symptom of MG is fluctuating weakness of striated muscles, which commonly presents initially as asymmetric ptosis with or without diplopia.[3] Most patients then develop generalized weakness involving the facial, bulbar, neck, axial, and limb muscles, typically within two years of disease onset.[4] The upper limbs are generally more affected than the lower limbs.[5] As a result of this weakness, common symptoms include breathing difficulties, ptosis, diplopia, hypomimia, problems with chewing, dysphagia, and dysarthria.[2]

Fatigue is a primary complaint and significantly impedes function in about 80% of patients with MG at some point of the disease.[5] While fatigue is a difficult concept to clearly define, it often involves a combination of central and peripheral fatigue factors. Furthermore, an individual with fatigue often experiences an increase in sedentary activity as a strategy to manage fatigue which ultimately leads to secondary deconditioning. This deconditioning adds to the burden of fatigue an individual manages day to day. Given the fluctuating weakness that is a hallmark of MG, physical fatigue due to repeated use is a key symptom. Furthermore, individuals can also experience central fatigue; central fatigue is defined as a lack of physical and/or mental energy - is also a common complaint that is separate from muscle fatigue and is not related to weakness or pain.[6] Both types of fatigue can impact a patient's ability to perform activities of daily living and to exercise, as well as participation in their work, family, and social lives.[5] The pathophysiology of central fatigue is largely unknown, but it has been associated with depression, female gender, disease severity, and lower quality of life.[3] It is also important to note that although depression is a covariate, central fatigue is not simply psychological but is an effect of the disease process of MG.[5]

While current literature suggests that exercise is safe in patients with MG, there is a lack of specific exercise guidelines for this population. In general, moderate intensity exercise (including strength and balance training) can improve symptoms, functional outcomes, for MG patients.[6] The role of exercise in improving quality of life is mixed.[7,8] The role of exercise in managing central fatigue, however, is unclear - some studies have noted that physical training programs do not necessarily improve an individual's perception of (central) fatigue, but others suggest that patients with central fatigue may benefit from psychological or physical training programs.[3,6] While no adverse effects have been observed in prior studies of the impact of moderate exercise in MG, patients with only mild to moderate symptoms have been the focus of this research.[2] A 2020 narrative review by O'Connor et al had similar findings, and suggested that it is reasonable to follow the minimum recommended guidelines for healthy adults of 150 minutes of moderate intensity exercise per week.[9] It is important to note, however, that these recommendations are based on level III to IV evidence comprised of feasibility, pilot, and case studies. Farrugia and Goodfellow's 2020 narrative review advised that the mode and intensity of exercise should be adapted for patients when MG is more symptomatic. For example, high intensity aerobic exercise may not be ideal during periods of increased fatigue, but stretching and Tai Chi may be more appropriate at these times.[5] Overall, few studies have explored the knowledge translation of these recommendations into patient care, as well as their clinical application considering the fatigue that many MG patients experience. Therefore, the purpose of this case study was to explore the role of physical therapy in managing central fatigue in a patient with myasthenia gravis.

CASE DESCRIPTION

The patient was a 62-year-old male diagnosed with seropositive myasthenia gravis (AChR+ generalized MG). Onset of symptoms in 2017 started as difficulty speaking and swallowing, with occasional blurry vision. The patient stated that he had been feeling off balance for the past 2.5 years and that his blurry vision started worsening in late 2022.

At evaluation, he was taking two pharmacological treatments for MG including 1 gram of mycophenolate mofetil twice daily, and 180 milligrams of pyridostigmine sustained release twice daily. The patient was previously treated with IVIG infusions of immune globulin human (IgG) at a dose of 1 gram per kilogram but stopped as they seemed to cause muscle cramps. He sought physical therapy due to worsening balance and history of falls with blurry vision and muscle weakness. His medical history included obesity, type 2 diabetes with hyperlipidemia and bilateral mild non-proliferative retinopathy, gout, diabetic peripheral neuropathy, and sleep apnea. He reported fatigue as a primary concern, as it impacted his ability with walking, stairs, showering, and dressing, along with imbalance. He had no known history of anemia or thyroid problems that could contribute to fatigue. Sleep apnea was treated with nightly CPAP and diabetes was managed with medication.

The patient was able to walk independently, typically without an assistive device, but reported difficulty navigating uneven surfaces and had multiple prior falls. He also noted unsteadiness and intermittent dizziness that would occur if making quick movements. He reported sensations of overheating, imbalance, and tiredness increased activity but noted that symptoms improved after 10 to 15 minutes of seated rest. The symptoms he experienced were worse later in the day.

At the time of the evaluation, the patient lived independently and was retired. Prior to retirement, he worked as an estimator developing floor plans. However he retired within the past few years, as MG-related vision problems contributed to difficulty focusing on the computer, impeding his work. During the day his physical activity involved a goal of walking 4000 steps daily which he tracked with a pedometer. His ability to exceed this goal was limited by a sense of his legs being too fatigued to continue and worsening imbalance. The patient's primary goals were to learn how to exercise considering his condition and be able to lose weight.

Tests and Measures

Primary outcome measures were the Five Times Sit to Stand Test10, the 6 Minute Walk Test[11], the modified Clinical Test of Sensory Interaction on Balance (CTSIB), the Fatigue Severity Scale, and the Modified Fatigue Impact Scale.

The Five Times Sit to Stand Test measures functional lower extremity strength and mobility. In a study of community dwelling older adults above the age of 60, estimated values for normal performance in 60- to 69-year-olds was 11.4 seconds.[8] Higher values indicate poorer lower extremity strength.

The Six Minute Walk Test measures aerobic endurance and exercise capacity and has excellent test-retest reliability and moderate construct validity to measure functional exercise capacity in patients with MG.[11] Mean distance in meters for community-dwelling adult males between 60-69 years old is 572 meters.[12] The minimal detectable change for older adults is 58.21 meters.[12]

ThemCTSIB assesses standing postural control under different sensory conditions, including altered somatosensory inputs and elimination of vision. While it has not been studied in patients with myasthenia gravis and lacks specific cut-off scores, it was chosen given the patient's reports of difficulty navigating uneven surfaces and history of peripheral neuropathy.

Standards for measurement of fatigue have not been validated for the MG population. However, prior studies have utilized both the Fatigue Severity Scale (FSS) and the Modified Fatigue Impact Scale (MFIS). In patients with multiple sclerosis (MS) a neuromuscular disease that also presents with a primary complaint of fatigue, the MFIS and FSS both showed acceptable reliability over 6 months.[14] The minimum clinically important differences of these two measures in patients with MS were 0.45 points on the FSS and 4 points on the MFIS.[14]

Examination Findings

Upon initial assessment, the patient presented walking independently with wide based gait, decreased left arm swing, and without an assistive device. He was overweight with a Body Mass Index of 40.43. His speech and cognition were intact, but he spoke with a slight nasal tone. The patient's visual fields were intact bilaterally. Oculomotor exam revealed trailing of the left eye with left gaze during smooth pursuits; he also reported intermittent blurred vision. The cover-uncover test showed medial shift of both eyes, but this was within acceptable limits. Sensation was intact to light touch in bilateral upper and lower extremities and functional lower extremity proprioception was impaired as noted by a positive Romberg balance test.

Range of motion was within functional limits in bilateral lower extremities. Upper extremity strength was grossly 4+/5 throughout. Lower extremity MMT was ⅘ for right hip flexion and right ankle dorsiflexion compared to 4+/5 on the left. Bilateral hip extension, abduction, and knee extension were within functional limits, however, functional weakness occurred as these muscles were observed to fatigue with repeated activities within a therapy session.

The patient's 5 Times Sit to Stand (assessed without upper extremity support) score of 29.45 seconds is associated with increased disability and morbidity. On the modified Clinical Test of Sensory Interaction on Balance; he maintained balance for 30 seconds on all conditions except for eyes closed on firm and foam.

The patient's self-selected gait speed without an assistive device was 0.88 meters per second and fast pace was 1.02 meters per second. His initial Functional Gait Assessment score of 20/30, also performed without an assistive device, confirmed his risk of falls. Figure 1 summarizes the patient's clinical presentation and subjective history according to the World Health Organization's International Classification of Functioning, Disability and Health (ICF). (Insert Figure 1 here)

Figure 1. WHO International Classification of Functioning, Disability, and Health

BODY STRUCTURES / FUNCTION (IMPAIRMENTS)	ACTIVITY (TASKS)		PARTICIPATION	
	Abilities	Limitations	Abilities	Restrictions
- Vision - Strength - Somatosensation - Static and dynamic standing balance - Endurance	- Ambulates independently without device	- Stairs - Showering - Dressing - Walking on uneven surfaces - Tolerance to overall physical activity is limited by fatigue, dizziness, balance	- Able to drive - Continues to exercise (walking dogs, shopping)	- Muscle cramps with driving - Had to retire from work as an estimator due to visual deficits

ENVIRONMENTAL			
Internal		External	
+	-	+	-
Motivated to stay active	Higher BMI - increased work required for daily activities	Family support (son and wife) - son had been helping him out	- 2 steps to enter house

INTERVENTION

The patient was scheduled for follow up rehabilitation sessions in clinic every 3 weeks for 12 weeks. His prognosis towards his goals was fair, given that his need for energy conservation and pacing would likely limit his exercise tolerance and subsequently weight loss. The waxing and waning nature of his condition was also an important consideration, as it would determine symptom severity and consequently the impact on daily life. Positive prognostic factors included the patient's good motivation to participate in therapy, both in the clinic and on his own.

The patient was at risk of falls due to unpredictable dizziness, impaired vision, and lower extremity dysfunction, so initial intervention included issuing a single point cane for household and community distances. He was trained in appropriate sequencing with the cane for both level surfaces and steps and was also educated on pacing of activity and parameters for walking. His initial home exercise program targeted his balance and strength deficits through sit to stand, tandem stance, and half tandem stance with head rotation. All exercises were to be performed 1 to 2 times daily. To accommodate his fluctuating fatigue and perceptions of weakness, the patient was instructed to complete 2 sets of 5 to 10 repetitions sit to stand, except for 2 to 3 reps of 10 to 20 second hold for tandem stance depending on his fatigue and activity tolerance (rate of perceived exertion moderate to severe).

To ensure the patient's impairments were addressed holistically, other healthcare providers were contacted. The patient's neurologist was contacted regarding potential solutions for his blurry vision; unfortunately, the patient would not be a good candidate for prisms, as the vision changes in MG are dynamic and prisms are intended to assist with static ocular misalignment. Additionally, occupational therapy expertise was added given the patient's difficulty with showering and dressing.

On visit 2 (3 weeks after initial evaluation), the patient reported that using the cane was helpful with his stability during transfers and stairs. He had successfully increased his daily physical activity level to 5000 steps without a change in his global fatigue or imbalance. Given his persistent fatigue we reviewed energy conservation principles and advised using shorter during, higher frequency walking intervals for exercise, taking seated breaks when shopping, and doing more activity in the morning. To improve

his balance on various surfaces, his home exercise program was progressed to performing half tandem stance with head rotation on a foam pad and performing tandem walking for more dynamic balance training.

On visit 3 (6 weeks after initial evaluation), the importance of activity pacing was reviewed. Leg muscle fatigue and respiratory fatigue occurred when attempting to walk 6000 steps. His home exercise program intervention progressed with the addition of a 5-pound weight to the sit to stand for a functional strength and balance challenge, as his 5 Times Sit to Stand performance had been improving. Additionally, diaphragmatic breathing exercises during seated rests were added this session to address potential respiratory muscle fatigue and improve aerobic capacity given his challenges with tolerating bouts of exercise to help his cardiorespiratory fatigue, though there is little evidence that diaphragmatic breathing may improve exercise capacity and respiratory function.[14]

On visit 4 (9 weeks after initial evaluation) the patient stated he would be starting Rituximab therapy within the next month after consultation of his neurologist to help address his persistent symptoms. He continued walking an average of 5,000 steps per day and his home balance training was progressed to decrease the base of support via tandem stance on foam pad and tandem walk with 1 hand to 2 finger support to address his postural instability in tight spaces. A nutrition consult was also recommended to address his current dietary needs, as one of his primary goals was to lose weight, but his overall exercise tolerance was limited. Weight control would also alleviate load to neuromuscular junction and decrease overall energy cost to daily living.

RESULTS

All appointments were completed mid-morning to standardize the patient's performance and fatigue levels between therapy visits. The patient's 5 Times Sit to Stand and mCTSIB tests showed overall improvement during his course of treatment. His 5 Times Sit to Stand performance improved from 29.45 seconds at visit 1 to 21.31 seconds on visit 4 (Table 1).

Table 1. Five Times Sit to Stand. Surface height: 19" standard height chair,without use of upper extremities

Date:	Visit 1	Visit 2	Visit 3	Visit 4
Time Completed:	29.45 seconds	27.41 seconds	17.99 seconds	21.31 seconds

On the mCTSIB, at evaluation he could maintain balance with eyes closed on foam for 16 seconds. By visit 4 he maintained balance for 30 seconds on all 4 conditions (Table 2).

Table 2. Modified Clinical Test of Sensory Interaction on Balance

Activity	Visit 1	Visit 3
Eyes open on firm surface	30 seconds	30 seconds
Eyes closed on firm surface	30 seconds	30 seconds
Eyes open on foam	30 seconds	30 seconds
Eyes closed on foam	16 seconds	30 seconds

While distance covered on the 6 Minute Walk Test when tested did not improve overall, the patient's reported fatigue and perceived exertion did improve from 7/10 6/10 (Table 3).

Table 3. 6 Minute Walk Test

Date:	Visit 2	Visit 3	Visit 4
Distance walked	960.6 feet	777 feet	872 feet
Modified RPE	7/10	8-9/10	6/10

Clinically significant, however, was that the patient was observed to have improved his average daily walking distance from 4,000 to 5,000 steps -- an improvement of 25%. Finally, the Fatigue Severity Scale and Modified Fatigue Impact Scale both showed improved (decreased) scores at visit 4. Both changes met the established MCID for patients with multiple sclerosis (Table 4).

Table 4. Fatigue Severity Scale and Modified Fatigue Impact Scale

Date:	Visit 2	Visit 4
Fatigue Severity Scale total score	63	61
Modified Fatigue Impact Scale total score	61	56

At discharge, the patient had not yet decided if he wanted to see a nutritionist, but it was discussed that he could contact his primary care provider if he wanted to pursue this.

DISCUSSION

This case report describes a patient for whom fatigue and imbalance negatively affected his daily life and limited his ability with ADLs, household and community mobility, and exercise. With exercise training and education, the patient showed objective improvements in lower extremity strength and standing balance. However, he continued to have impaired aerobic endurance and significant fatigue, indicating limited carry-over of these clinical improvements into his daily life. The patient's decline in distance walked during the 6 Minute Walk Test illustrates his ongoing deficits in aerobic endurance. This deterioration could be related to his attempts to increase his overall daily activity and may highlight the importance of pacing and energy conservation.

While the patient's FSS and MFIS scores improved, subjectively he reported no significant change in his fatigue. Though the FSS and MFIS changes met MCID values for multiple sclerosis, specific MCID values for MG have not been established and thus may reflect that the measured changes are not clinically significant for this patient with myasthenia gravis.

The structure of therapy sessions was also adapted to account for the patient's fatigue. The patient preferred mid-morning appointments as his energy levels were optimal. Keeping consistent timing for sessions also reduced variability in measurement, since his activities earlier in the day would be similar at each visit. To prevent increased fatigue later in the day, not every outcome measure was performed each session. This also allowed for adequate energy reserve for the patient to participate in treatment and practice exercises to perform at home.

Our findings highlight the impact of fatigue on patients with MG, and the degree to which it can impact their progress towards their goals. While exercise has potential as an intervention, there are clearly limits. This is consistent with current literature that suggests physical training can improve functional strength and balance but does not improve fatigue.[6] The patient's increased weight may have also slowed his progress, as it can make activity more effortful and result in earlier fatigue. Upcoming adjustments to the patient's medication regime may allow physical therapy to have a greater effect, as pharmacological treatments have also been associated with improved fatigue.[3]

Prior studies have also indicated that physical and psychological training programs show promise in improving MG-related fatigue. While our interventions included patient education on fatigue management and energy conservation, establishing more a more structured plan for pacing and providing behavior change strategies may have been beneficial. The patient also noted that diaphragmatic breathing exercises felt helpful, so further assessment and intervention targeting his respiratory function may yield greater improvements in fatigue.

The findings of this study cannot be generalized as this is a report on a single participant. Larger scale studies can provide greater insight on potential correlations between various physical therapy interventions and their impact on fatigue in myasthenia gravis. The heterogenous nature of MG, however, creates challenges in establishing clear exercise guidelines as the interventions must be tailored to the specific patient and their point in the disease process. Similarly, educational strategies must be patient specific and cannot be applied in all cases of MG.

CONCLUSION

The results of this case are consistent with current literature and suggest that physical therapy can improve strength and balance in patients with MG, but not necessarily fatigue. Further research is needed to determine optimal management of fatigue in MG, though by nature of the condition it must be tailored to the patient's specific needs.

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