Exercise prescription in the physiotherapeutic management of Myasthenia Gravis: a case report

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Abstract
This paper reports on the use of an exercise-based programme in the management of a person with Myasthenia Gravis. This programme was based on current literature pertaining to the therapeutic management of Myasthenia Gravis and other chronic progressive neuromuscular disorders. Although the patient showed moderate gains in clinical measurements of muscle strength and endurance, the effectiveness of the exercise programme was mainly demonstrated by the patient’s decreased levels of fatigue and in the achievement of his stated goals. Davidson L*, Hale L, Mulligan H (2005). Exercise prescription in the physiotherapeutic management of Myasthenia Gravis: a case report. New Zealand Journal of Physiotherapy 33(1) 13-18.

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INTRODUCTION
Myasthenia Gravis (MG), a slowly progressive neuromuscular disorder, can be classified as either ocular or generalised. MG affects between 5 – 12 people per 100,000 (Muscular Dystrophy Association, 2004). Ocular involvement is often the first sign of MG with patients complaining of ptosis and diplopia. Seventy-five to ninety percent of patients with ocular involvement then progress to having generalised MG (Kernich and Kaminski 1995; Evoli et al., 1996). Muscle weakness and fatigue are significant problems for patients, with proximal muscles frequently more affected than distal muscles (Walton, 1989).

The specific role of exercise prescription in the management of MG has not yet been established; however some research has been conducted into the effects of exercise prescription in other slowly progressive neuromuscular disorders (NMD) having similar symptomatology. These conditions include myotonic muscular dystrophy, limb-girdle syndrome and fascioscapulohumeral dystrophy, and other conditions where fatigue is an important or primary symptom, such as multiple sclerosis and chronic fatigue syndrome (Aitkens et al., 1993; Petajan et al., 1996; Wright et al., 1996; Fulcher and White, 1997; Whiting et al., 2001).

This case report discusses exercise prescription for people with MG and the implementation and outcome of a specific exercise programme prescribed to a patient with MG.

Management of Myasthenia Gravis
MG is thought to be initiated by an auto-immune response which ultimately disrupts transmission at the neuromuscular junction (Lindstrom, 2000). In an unaffected individual, action potentials from the motor neuron set in motion a series of events that eventually lead to the release of the neurotransmitter acetylcholine (ACH) from the pre-synaptic membrane. ACH then binds to ACH receptors (ACHr) on the post-synaptic (skeletal muscle cell) membrane, opening specific ion channels and causing depolarisation of the muscle cell which ultimately may lead to a muscle contraction. In MG, however, the auto-immune response causes excessive production of certain auto-antibodies, with the following effects:

1) Auto-antibodies directly block ACHr (Lindstrom, 2000).
2) Auto-antibodies cause an increased turnover of ACHr through endocytosis. Normally, the average life of an ACHr is seven days, whereas in patients with MG it is only one day (Havard and Fonsega, 1990).
3) Auto-antibodies cause damage to the post-synaptic muscle membrane, altering the ACHr shape, thus inhibiting ACH binding and disrupting synaptic transmission (Lindstrom, 2000).

Consequently there are fewer viable ACHr at the neuromuscular junction, which results in less muscle cell depolarisation and weaker
muscle contractions particularly with repetitive stimulation.

Drug management is aimed at minimising the autoimmune response and maximising the amount of ACH available for uptake. Corticosteroids are often the first line of treatment and are effective in up to 80% of patients; they work to decrease autoantibody synthesis (Evoli et al., 1996, Newsom-Davis, 2003). Anticholinesterases are also widely used. These drugs act to minimise the hydrolysis of ACH (degradation) thus enhancing the availability of ACH for reception. This intervention does not affect the underlying disease process but helps to reduce symptoms (Evoli et al., 1996). Corticosteroids and anticholinesterases are the most commonly used drug management strategies for MG (Havard and Fonseca, 1990; Evoli et al., 1996).

The principles behind exercise prescription in the management of NMD include maintenance of muscle strength within the limitations of the disease process, thus minimising atrophy (Vignos, 1983). Research suggests that resisted exercise is beneficial in slowly progressive NMD (Vignos, 1983; Milner-Brown and Miller, 1988a and b; Aitkens et al., 1993; Forrest and Qian, 1999). Milner-Brown and Miller (1988a) investigated the effects of a high resistance strengthening programme conducted over a 6-12 month period, focusing on elbow flexors/extensors and knee extensors, with ten people with NMD. In this study, patients with 25-75% of normal strength showed significant strength and endurance improvements, while patients with less than 10% of normal muscle strength did not. The knee extensors showed the greatest improvement. Comparable results were reported in a similar study using a low resistance muscle strengthening programme and electrical stimulation (Milner-Brown and Miller, 1988b).

In two studies investigating moderate resistance exercise programmes for participants with slowly progressive NMD, strength in the exercised muscles increased relative to that of muscles which did not receive exercise. This increase was especially noticeable in the lower limb muscles (Aitkens et al., 1993; Lindeman, 1995).

There has been limited research on the effects of muscle strengthening using resistance for patients with MG. Lohi et al (1993) conducted a strength-training programme (knee extension and elbow flexion/extension) for 10 weeks in 11 volunteers (aged 25-50 years) with mild or moderate MG. Isometric dynamometry was used as the primary outcome measure. Participants were randomised into two groups for dynamic strength training of both their right arm and left leg, or vice versa, with the contralateral extremity acting as a control. The supervised training sessions consisted of 10 repetitions per set, and weights were progressed from 25% to 45% of maximal force. Results showed that maximal muscle force for knee extension improved by 23% on the trained limb, compared to 4% on the untrained limb. Only minimal changes, however occurred in elbow flexion and extension strength, perhaps because many participants were unable to complete the number of repetitions or increase the amount of resistance used as prescribed in the study. There were a number of potential difficulties with this study. For instance, the use of volunteers may have resulted in selection bias. In addition, medication strategies were not discussed; individual results were not included; and the definition of mild or moderate MG was not given.

Engaging in physical activity maybe of benefit in reducing the fatigue felt by people with MG. Grohar-Murray et al. (1998) investigated the personal strategies utilised by people with MG to manage their disease in a postal survey (n=550, response rate 46%). Although 90% of respondents reported that they had changed their lifestyle, for example they had given up social activities and work, 59% stated that they now engaged in as much physical activity as possible. Low impact aerobic exercise, such as swimming, walking, and running, was used by 20% of respondents. Two-thirds of respondents who engaged in physical activity felt that the activity helped to relieve fatigue.

Exercise has proven to be an effective management strategy for generalised fatigue in both multiple sclerosis and chronic fatigue syndrome (Petajan et al., 1996; Whiting, 2002). Petajan et al (1996) investigated the effects of a 15 week aerobic training programme for people with MS (n=54) in a randomised controlled trial, which resulted in a non-significant reduction in fatigue, measured by the Fatigue Severity Scale. In addition there was a significant reduction in psychological variables, such as anger, depression, fatigue, vigour, tension and confusion, as measured by the Profile of Mood States.

Research investigating the benefits of exercise for people with MG and progressive NMD is limited. The few studies reported suggest that lower limb strengthening and low impact aerobic exercise programmes may be beneficial to people with mild to moderate MG or NMD.

The following case report illustrates the management of a patient with MG using an exercise programme based on lower limb muscle endurance training and low impact aerobic exercises.

Case Report

History

A 78 year old retired male presented to the neurology wards with a six-month history of double vision, ptosis and balance difficulties. A provisional diagnosis of MG was given to the patient and this was later confirmed through a positive tension test and a positive blood test for ACH antibodies. The patient was discharged to his home after drug therapy had been initiated and tolerated. Drug therapy consisted of Prednisone (60 mg daily) and Mestinon (60 mg 4 x daily) (anticholinesterase). He was also referred to neurology physiotherapy
outpatients for further advice on management of his disease.

At the initial physiotherapy assessment the patient reported feeling generally weak and fatigued. He was unable to lift his arms above his head or walk further than 200 metres. The patient’s voice was noted to be hoarse and got progressively quieter during the examination. He reported having a six-month history of increasing shortness of breath. He was an ex-smoker and spirometry testing as an inpatient had confirmed a diagnosis of mild chronic obstructive airways disease.

Signed consent for the publication of this case report was obtained from the patient concerned.

**Baseline Evaluation**

Testing was completed over two days to limit the effect of fatigue on the results. On subjective evaluation, the patient’s primary complaints were a lack of muscle strength, fatigue, and unsteadiness during walking. Objective examination comprised muscle strength testing (see Table 1) and outcome measures to evaluate balance (Berg Balance Scale), gait (Rivermead Mobility Index, 10 metre walk test, 6-minute walk test) and fatigue (10-point single item fatigue scale) (see Table 2).

Muscle testing was measured using the Medical Research Council grades (Van der Ploeg et al., 1984), both with one repetition, and again after 10 repetitions to demonstrate fatigue. The patient demonstrated moderate hip and knee muscle weakness only after completing 10 repetitions (see Table 1.)

The Berg Balance Scale (BBS) (Berg et al., 1992) and Rivermead Mobility Index (Colleen et al., 1990) have proven reliability and validity, and are specific for the older population (Wade, 1992; Whitney et al., 1998). These tests were believed to be appropriate due to the patient’s complaint of unsteadiness during gait. The BBS was administered first and the patient only had difficulty achieving tandem stance and one-legged stand. The Rivermead Mobility Index was then administered as it comprises more dynamic activities to further challenge balance.

The 10 metre walk test is a measure of gait speed and the six-minute walk test of gait endurance, and both tests have been shown to be valid and reliable for older adults (Guyatt et al., 1988; Wade, 1992; Harade et al., 1999; Noonan and Dean, 2000).

The assessment of fatigue was important in this patient as this was one of his primary complaints. The patient was asked to rate his present level of general fatigue using the 10-point single-item fatigue scale (0 = “no fatigue” and 10 = “greatest possible fatigue”). The 10-point fatigue scale is a valid, efficient and clinically relevant means of assessing fatigue and monitoring responses to intervention in a clinical setting (Schwartz et al., 2002).

Quinn and Gordon (2003,p72) state: “standardised tests are important however these should never be used in place of an evaluation of specific activities pertinent to a patient”. In MG there is limited information and evidence on specific outcome measures and assessment tools. It was therefore considered relevant to include the achievement of patient-centred goals as an outcome measure for this patient. The patient reported that he been an active member of a golf club with a handicap of 12 eight months prior to the evaluation and was able to, at that time, walk to the shops (700 metres) daily. The patient’s goals were to return to these activities.

**Treatment**

Physiotherapy intervention focused on the patient’s goals of returning to golf and walking daily. Based on the few studies which have investigated the benefits of exercise for people with NMD or MG, a muscle endurance and aerobic training programme was prescribed for this patient. Although most studies have investigated programmes of 10 weeks or more in duration, due to physiotherapy service

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<td>Single maximal</td>
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<td>Tests</td>
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<td>Hip Extension</td>
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time constraints it was only possible to prescribe a 6 week programme for this patient, two weeks of which were based in the physiotherapy outpatients clinic, and four weeks as a home programme.

As lower limb weakness was most noticeable on repetitive testing of the hip and knee muscles, one exercise, which was considered by the author to be optimal in targeting all these muscles was prescribed, and progressed by increasing the number of repetitions. Gravity was utilised as the force which provided a resistance to the movement. The exercise chosen was hip and knee flexion and extension in the position of four-point kneeling. The exercise was repeated with each leg (see Table 3). After two weeks the patient was prescribed a generalised lower limb home exercise programme comprising the following exercises in supine lying: straight leg raises, “bridging” and hip abduction, and in standing: half-squats and calf raises. Table 3 shows the progression of these exercises over the subsequent four weeks.

To improve the patient’s aerobic capacity, a six week walking programme was prescribed. For the first two weeks treadmill training was used. Treadmill walking started at 6 minutes at 2.5kph and was progressed slowly, based on what the patient thought he could manage, over two weeks to 10 minutes walking at 3.0mph. A 2-minute warm-up and cool-down walk at 1.5 kpm were included at each session. The duration and speed of walking was specified by the patient. At the end of two weeks, a home walking programme was initiated in place of the treadmill walking. The patient indicated that he would like to walk to the library (500 metres) and back, three times a week. The home walking programme was progressed, based on the patient’s indication, to daily walks, and then extended to 1400 metres (to the shops and home), four times a week. The patient then began to cover this distance twice daily, four times a week. Finally the walking programme was extended to 1600 metres, four times a week (see Table 3). In addition, the patient was encouraged to practice golf in the park, starting in week three. The completed treatment programme is shown in table 3.

RESULTS
The patient made some important improvements from completing his exercise programme. The 10-point single-item fatigue scale showed the most clinically significant result with his self-rated general fatigue dropping from 8/10 in week one to 3-4/10 in week six. The 6-minute walk test improved in week three on retest to 530 metres, however in week six he only managed 480 metres (same as initial assessment). Manual muscle strength testing showed a moderate improvement in the hip extensors/ flexors (grade 4) and mild improvement in knee extensors (grade 5) after 10 repetitions (see Tables 1 and 2).

The most important result was the achievement of the goals set by the patient of being able to return to walking to the shops and to playing golf. Although he was unable to play the amount of golf he had previously been able to, playing three holes of golf and being able to teach his grandson was a noteworthy improvement in participation.

DISCUSSION
Low impact aerobic exercise can help to manage symptoms of fatigue in patients with multiple sclerosis (Petajan et al., 1996) and chronic fatigue syndrome (Whiting, 2001), and it has also been used as an effective management strategy for some people with MG (Grohar-Murray et al., 1998). The prescription of walking was effective in this patient as it encouraged him to return to his previous activities and he reported a decrease in the level of fatigue experienced (as measured by the 10 point single-item fatigue score). Although it is difficult to say whether the patient was working at an aerobic capacity the benefits of achieving daily walking may have been similar to that hypothesised to occur in patients with MG (Grohar-Murray et al., 1998) and in the normal population (McDonald, 2002), such as improved body image, mood, and well-being. There may also have been physiological effects such as an increased number and density of mitochondria, increase in skeletal muscle mass and size of capillary beds, and improved lactate degradation (Grohar-Murray et al., 1998; McDonald, 2002). These effects may improve the muscles ability to cope with fatigue which is placed upon them due to the pathophysiological processes of MG.

Muscle weakness and fatigue appear to show an intimate relationship. The subjective feeling of muscle weakness that was not objectively demonstrated (single repetition) may occur due

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<th>Test</th>
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<td>Berg Balance Test</td>
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<tr>
<td>Rivermead Mobility Test</td>
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<td>10 metre walk</td>
<td>7 seconds (85.7m/minute)</td>
<td>6.8 seconds (88.34m/minute)</td>
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<td>6-minute walk test</td>
<td>480 metres</td>
<td>530 metres</td>
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<tr>
<td>10-point single item fatigue scale</td>
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to muscle fatigue that then limits the activity of the muscle. The patient was frequently unable to complete the prescribed amount of repetitions and this is consistent with findings by Lohi et al. (1993). This may indicate that it is difficult for patients with MG to complete high repetition exercise especially when completing other repetitive exercise such as a daily walking programme, due to muscular fatigue and the pathophysiological process of the disease.

Early deterioration and steroid induced weakness is common and generally occurs within two weeks of initiation of prednisone (Evoli et al., 1992; Hardy and Rittenberry, 1994; Kernich and Kaminski, 1995). The patient in this report demonstrated deterioration in the ability to carry out the prescribed exercises at the start of week three and this may have been due to the initiation of prednisone. By the end of week six the patient reported to be coping better with the prescribed exercise programme.

Quality of life is difficult to define. Wade (1992) reports that there are three things that contribute to quality of life. Firstly, the patient’s own wishes and expectations; secondly, the limitations there are on a patient’s ability to achieve his/her wishes, and lastly, the patient’s reactions to the limitations. In a study carried out by Abresh (as cited by McDonald, 2001) muscle weakness, fatigue, and difficulty getting exercise all significantly impact on quality of life. These three symptoms of neuromuscular disease can be affected through exercise prescription (Vignos, 1983; Milner-Brown and Miller, 1988; Aitkens et al., 1993; Lohi et al., 1993; Lindeman et al., 1995; Petajan et al., 1996; Wright et al., 1996; McDonald, 2001; Whiting, 2001). Exercise participation may specifically improve patients with MG ability to function more independently in the community as found by Grohar-Murray and associates (1998). The patient in this case study returned to previous activities, thus achieving the goals he set and possibly improving his quality of life. Specific quality of life measures such as the Medical Outcome Study Short-Form General Health Survey (SF-36) (Brazier et al., 1992) may have been an appropriate outcome measure to use in this case study to objectively assess the impact of exercise prescription on quality of life in patients with MG.

CONCLUSION

The prescription of exercises to increase endurance may have contributed to the improvement in the patient in this case report’s ability to participate in activities of choice and may be an effective ongoing management strategy for fatigue in patients with MG. However, some of the improvement may also be a result of the prescription of appropriate medication. Further research needs to investigate the effectiveness of low impact aerobic exercise in managing fatigue in MG and should incorporate quality of life measures.

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References


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