Implementation of tailored exercise programs for MG patients in a gym setting: a pragmatic feasibility case study

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A B S T R A C T

Although supervised aerobic and resistance training in a hospital setting was proven safe and beneficial for well-controlled myasthenia gravis (MG) patients, implementation of similar programs in the community has not been studied. We conducted a pragmatic open-label study at a large gym in Uppsala, Sweden. Seven patients with generalized MG were recruited to participate in an individualized, tailored exercise program, based on individual baseline status and personal goals, with a personal trainer. All patients completed the entire training period. The individually tailored exercise program was implemented safely and effectively, with all patients improving in aerobic capacity, muscle strength, and balance. Our pragmatic open-label case study suggests that well-controlled patients with generalized MG can extend their physical exercise to personal training in the gym. This is an essential step towards reducing the barriers to implementing exercise protocols and increasing the availability of these interventions to MG patients.

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1. Introduction

Myasthenia gravis (MG) is an autoimmune disorder where abnormal neuromuscular transmission results in fluctuating skeletal muscle weakness and fatigue, which can be worsened by physical exercise. However, based on several recent studies, it is safe for clinically stable MG patients to follow supervised or home-based exercise programmes [1–4], and muscle strength and functional capacity improve upon physical exercise [2–4]. In order to go beyond the general recommendation of the minimum recommended international guidelines on exercise for healthy adults, i.e., at least 150 min of moderate-intensity exercise a week [5], evidence of tolerance to individualized training regimens outside of the hospital setting is needed. Therefore, this study aimed to evaluate whether MG patients can follow a more long-term individually tailored exercise program at the gym over six months. The idea came from MG patients that participated in a previous supervised physical exercise study in a hospital setting [4]. We hypothesized that the gym intervention would improve MG patients’ functional performance over time without interfering with the disease activity. All subjects provided oral and written informed consent to participate in the study before enrolling, which was approved by the Regional Ethical Review Board (Dnr 2016/144/1), Uppsala, Sweden.

2.1. Case study design

This was a prospective unblinded case series study wherein each patient served as his/her control. The inclusion criteria were adults with a diagnosis of mild to moderate generalized MG (MGFA class II-III), followed at the outpatient Neurology clinic of Uppsala University Hospital, Sweden. In total, 13 MG patients were invited to participate in the study, mainly recruited from a previous training intervention study at Uppsala University Hospital [4]. Subjective muscle strength assessment (patient) and objective assessment using photo and video documentation of movements were performed at baseline, at 3 months, and 6 months after initiation of the training regimen. The activity level at baseline was evaluated by a validated questionnaire on physical activity habits [6]. The questionnaire contains two questions: (1) How much time do you devote to physical exercise that increases your pulse on a regular week, for example, running, football, etc.? (2) How much time per week do you devote to everyday activities involving motion that last at least 10 min, for example, walking, cycling, and gardening? Health-related disease-specific quality of life and fatigue were assessed through two questionnaires, the Myasthenia gravis Quality of Life 15 (MG-QoL15) [7] and the Fatigue Severity
Score (FSS) [8] at baseline and then monthly. The level of exertion during physical activity was subjectively assessed by each patient at every gym training occasion using the Borg Rating of Perceived Exertion (RPE) scale [9]. Participants’ exercise programs and weekly diaries provided information regarding duration and adherence to the intervention components and any occurring MG symptoms by participants. Each participant could report on adverse events in a free text question in daily and weekly questionnaires or directly to a team member. Nutritional counseling was not provided.

2.2. Individually tailored exercise programs and comparisons over time

The exercise regimen was tailored to each MG patient based on their wishes and prior training experience by a certified personal trainer (PT; Anna Modig) at ACTIC Centralbadet gym, Uppsala, with a duration of 6 months. Each training program contained the elements of aerobic exercise, resistance training, and balance training. Exercises were adjusted to the individual based on a pragmatic assessment of physical function on-site in the gym, e.g., the PT introduced each exercise and estimated submaximal loading and weights to secure a safe and slow introduction. Sessions were scheduled twice a week, with each session lasting 60 min and at least one per week with the PT present. The sessions included functional muscle training with a whole-body approach, focusing on the main muscle areas such as the back, shoulder, abdominal, hip, leg, and pelvic floor muscles. Exercises using gym equipment included bicycling, rowing, knee bending (TRX), abdominal muscle resistance exercises, reverse Pec-deck, chest press, leg kick, leg curl, leg press, and resistance rubber band exercises. Data were not normally distributed according to D’Agostino Pearson’s test (too few observations). Paired analyses between baseline and 3 or 6 months were done using the Wilcoxon matched-pairs signed rank test. A p-value < 0.05 was considered significant.

2.3. Cases and adherence to the program

Seven individuals with generalized MG, all with MGFA class II decided to participate (Table 1) and six patients did not participate, mainly due to lack of time. Self-reported time devoted to strenuous exercise during a typical week ranged from 0 to >120 min/week (median: <30 min/week). Self-reported time devoted to physical activity not regarded as exercise during a typical week ranged from 30 min/week to >300 min/week (median: 150–300 min/week). The FSS and MG-QoL15 scores varied greatly in-between patients and between timelines (Fig. 1). All seven patients completed the individual training regimen programs for six months. The participation rate (measured as attended times of maximal 48 occasions) ranged from 83.5% to 98% (median: 93±5%). Resistance weights at strength-training exercises for arm-, back-, and leg muscles could be increased in all patients during the training period. A trend toward lower scores was seen on FSS and MG-QoL15 throughout the process (p>0.05; Fig. 1A and B). All patients could complete the program regardless of their initial or subsequent scores. Patients significantly improved their rowing distance improved from baseline (median: 661 m; 95% CI:470–843 m) to 3 months (median: 821 m; 95% CI: 550–1000 m; p = 0.016) and from 3 months to 6 months (median: 835 m; 95% CI: 655–943 m; p = 0.016) respectively. The resistance training weights at rowing also significantly improved from baseline (median: 23 kg; 95% CI: 16–43 kg) to 3 months (median: 36.5 kg; 95% CI: 18.3–54.4 kg; p = 0.03) but not from 3 to 6 months (median: 40.5 kg; 95% CI: 27–57 kg) respectively (p = 0.63; Fig. 1C). Further, the resistance weight at chest press improved over time in all subjects from baseline (median: 18 kg; 95% CI: 16–20 kg) to 3 months (median: 20 kg; 95% CI: 18–36 kg) and from 3 to 6 months (median: 30.5 kg; 95% CI: 18–41 kg). The participants’ subjective thoughts indicated stronger back and leg muscles (see case descriptions 2.4 and table 2). All seven patients participated in the 6-month program and adhered to their individualized exercise programs.

2.4. Individual cases

2.4.1. Case 1

A 32-year-old female with AChR+ MG for four years and only symptomatic medication with pyridostigmine bromide (Mestinon®), which remained unchanged during the intervention. The main complaints initially were poor core strength, restricted thoracic flexibility and weak buttock muscles. Her personal goal with the PT was to restore her balance by improving the mobility of the thoracic spine and strengthening the core muscles, buttocks, and thigh muscles. Between baseline and two months, she experienced temporary neck muscle fatigue, which improved between after two months of the intervention. At three months, she felt much stronger in her upper and lower back and leg muscles. She experienced temporarily exaggerated weakness in her neck extensor muscles, but that was quickly recovered. At six months, the core muscles were also markedly stronger. Her FSS score reduced from 31 at baseline to 13 at six months, and MG-QoL15 changed from 1 to 2.

2.4.2. Case 2

A 71-year-old female with AChR+ MG for five years, medication with Mestinon® and prednisone 10 mg, and concomitant disorders of asthma and hypertension. At baseline, she experienced proximal leg muscle weakness, which limited ADL; for example, she had to plan her walking distance. She desired to be more active, but

### Table 1

<table>
<thead>
<tr>
<th>PAT #</th>
<th>Sex/age</th>
<th>Dur (Y)</th>
<th>WEIGHT/BMI</th>
<th>MGFA class</th>
<th>Antibody subtype</th>
<th>MG Medications</th>
<th>Concomitant disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F/32</td>
<td>4</td>
<td>59/19.7</td>
<td>IIB</td>
<td>AChR+</td>
<td>Mestinon</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>F/71</td>
<td>5</td>
<td>67/25.2</td>
<td>IIA</td>
<td>AChR+</td>
<td>Mestinon</td>
<td>Hypertension, asthma</td>
</tr>
<tr>
<td>3</td>
<td>M/84</td>
<td>22</td>
<td>85/26.5</td>
<td>IIA</td>
<td>AChR+</td>
<td>Prednisolone 10 mg</td>
<td>Spinal stenosis, cardiovascular disease</td>
</tr>
<tr>
<td>4</td>
<td>M/76</td>
<td>34</td>
<td>77/24.3</td>
<td>IIA</td>
<td>AChR+</td>
<td>Prednisolone 10 mg</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>5</td>
<td>F/58</td>
<td>12</td>
<td>87/30.8</td>
<td>IIA</td>
<td>MuSK+</td>
<td>Rituximab</td>
<td>Diabetes type II</td>
</tr>
<tr>
<td>6</td>
<td>F/34</td>
<td>15</td>
<td>64/21.9</td>
<td>IIB</td>
<td>AChR+</td>
<td>Prednisolone 5 mg</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>F/34</td>
<td>8</td>
<td>80/26.7</td>
<td>IIA</td>
<td>AChR+</td>
<td>Prednisolone 5 mg</td>
<td>None</td>
</tr>
</tbody>
</table>
Fig. 1. Development over time of the outcome parameters. (A) rowing capacity, distance (meters), (B) FSS score and (C) MG-QoL15 score. FSS, fatigue severity scale; MGQoL15, Myasthenia Gravis Quality of Life 15 questions. Right panel: Illustration of physical performance before and after the intervention. Upper right panel: at baseline, case 4 was not able to perform lunges due to proximal buttock and leg muscle weakness. Lower right panel: At 3 months, he was able to perform full lunges.

she felt limited by poor fitness, and therefore the goal included muscle strengthening of the entire body and fitness training. At 3 and 6 months, she experienced stronger proximal leg muscles and could walk longer without rest. Her FSS score reduced from 33 at baseline to 14 at six months, and MG-QoL15 improved from 18 to 2. Her MG medication remained unchanged.

2.4.3. Case 3
A 84-year-old man with AChR+ MG for 22 years, medication with Mestinon and concomitant disorders of lumbar spinal stenosis and cardiovascular disease. His main complaint at baseline was poor balance and the goal was to improve balance and leg muscle strength. At follow-ups at three and six months, he was stronger in squats and lunges. His FSS score reduced from 28 at baseline to 18 at 6 months and MG-QoL15 remained unchanged at 1. He did not experience any side effects apart from general training soreness, and his Mestinon dose remained unchanged.

2.4.4. Case 4
A 76-year-old man with seronegative MG for 34 years, medication with Prednisone 10 mg daily, and osteoporosis as the concomitant disease. His goal was to rebuild leg muscle strength due to the weak buttock and thigh muscles, mainly the quadriceps and hamstrings, and to counteract osteoporosis. His core- and leg muscles got considerably stronger, but he had to discontinue spinning class since this was too demanding on his body overall. His FSS score was 22 at baseline, then reduced to 18 every month but increased to 26 at six months and MG-QoL15 changed from 13 to 14. His MG medication remained unchanged.

2.4.5. Case 5
A 58-years-old woman with MuSK+ MG for 12 years, regular medication with Rituximab and prednisone 5 mg daily, concomitant disease of type II diabetes. Her initial complaints were mainly poor core strength, weak neck muscles, poor posture, and
poor balance rendering her to avoid walking stairs. Her goals with PT were to increase core stability and overall muscle strength and weight loss due to her comorbidity. At three months, her back and leg muscles were considerably stronger, poorer weaker in her neck for a few days, but then better. The FSS score was similar at baseline (15) and six months (17), whereas the MG-QoL15 improved from 5 to 3. Her MG medication remained unchanged.

### 2.4.6. Case 6

A 31-year-old female with AChR+ MG for 15 years with prednisone 10 mg daily and terbutaline, no concomitant disorders. She had been previously physically active at another gym. However, she experienced debilitating tiredness after strenuous resistance training programs that interfered with her ability to carry out ADLs for the remainder of the day. Her goal was to conduct resistance training with an overall lower intensity. Overall, muscle strengthening enabled her to train hard but still have strength left over for other activities, with a focus on a less strenuous strategy with fewer repetitions. She was able to increase resistance weights over time with fewer repetitions. However, at times she was limited by a flare of her MG, predominantly increased fatigue in her shoulder and arm muscles, which she explained as being due to high psychological stress during that period. Her FSS scores fluctuated from 23 at baseline to 49 at six months and MG-QoL15 from 5 to 42. Nevertheless, her MG medication remained unchanged.

### 2.4.7. Case 7

A 34-year-old female with AChR+ MG for eight years, no ongoing MG treatment, and no concomitant disorders. At baseline, she experienced weak core and back muscles following pregnancies and a period of sedentary behavior, and therefore the goal was mainly to strengthen core muscles. At 3 and 6 months, she experienced more muscular leg and core muscles. She had periods of weaker neck muscles, which could be corrected by limiting the types of exercises that involved neck extensor muscles. Her FSS score decreased from 14 at baseline to 9 at six months, and MG-QoL15 remained at 0. She did not experience any adverse effects and did not need to start MG medication during the intervention.

### Table 2

<table>
<thead>
<tr>
<th>Case</th>
<th>Baseline Subjective thoughts</th>
<th>Follow-up after 3 months Subjective thoughts</th>
<th>Follow-up after 6 months Subjective thoughts</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>“Stiff body, feeling old, pain in the upper and lower back, weak legs, difficulty taking deep breaths”</td>
<td>“The entire back region feels so much better. My neck worsened temporarily but then the issue resolved. Stronger legs and no problem with deep breathing”, “Legs are stronger and I can walk for longer without having to rest.”</td>
<td>“The entire back region still feels better. The neck feels good and strong, legs are stronger, no problem with deep breathing”.</td>
</tr>
<tr>
<td>2</td>
<td>“Cannot squat, difficult walking due to weak legs, weak arms”</td>
<td>“Leg muscles are stronger, easier to get up from sitting”</td>
<td>“Legs are still stronger and I can walk longer without having to rest. My family notices that I can do more”.</td>
</tr>
<tr>
<td>3</td>
<td>“My knees are weak, difficult to get up. My back feels stiff”</td>
<td>“My leg muscles are considerably stronger”. “Increasing my leg muscle strength allowed me to obtain higher working pulse in spinning class”</td>
<td>“My leg muscles are considerably stronger”.</td>
</tr>
<tr>
<td>4</td>
<td>“Leg muscles are very weak. Poor fitness, cannot get my pulse up”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>“Back pain, I avoid stairs due to weak legs. Weak arms”</td>
<td>“The back pain is almost gone. The neck got temporarily worse but is no longer a problem. My legs feel much stronger”.</td>
<td>“My back feels much stronger as do my legs”.</td>
</tr>
<tr>
<td>6</td>
<td>“Lower back pain sometimes, knee pain when running”</td>
<td>“No back problems”.</td>
<td>“My MG symptoms are worse when I increase my mental stress at work, not from performing physical activity”</td>
</tr>
<tr>
<td>7</td>
<td>“Problems with sciatica-pain from time to time, in my wrists”</td>
<td>“No back problems, wrists are OK”.</td>
<td>“No back problems”.</td>
</tr>
</tbody>
</table>

### 3. Discussion

This study aimed to evaluate whether MG patients can transfer their physical exercise regimen into an individually tailored exercise program in the community setting of a gym as opposed to supervised physical exercise at a hospital. The type of physical activity and the training protocol must be individualized to achieve long-lasting training regimens. In one previous study [4], patients expressed that they would like a PT to design their treatment intervention regimens; therefore, this study came about. Since MG patients, on average, perform less vigorous-intensity physical activity and spend more time on sedentary activities [10,11], it is crucial to encourage individualized training programs in MG patients with well-controlled disease. In this context, this study shows the importance of taking physical exercise protocols into the community setting of a gym in order to increase the availability of more MG patients. All patients in this study were well-controlled; however, case 6 had, towards the end of the PT program, a period of high psychological stress and a subsequent worsening in both FSS and MG-QoL15 parameters. Despite this obvious worsening in her MG status, she continued adhering to the exercise program. No patient had to take additional symptomatic medication (pyridostigmine) after the exercise or modify their MG treatment regimen. Adverse events consisted of slightly increased muscle fatigue, especially in the neck muscles, during the first two months in two patients, which subsided after that. No patient had respiratory symptoms that limited the exercise program.

Considering that physical exercise can help combat weight gain and secondary comorbidities from immunosuppression with corticosteroids and inactivity-induced muscle wasting [12], research is needed to understand what recommendations on exercise can be given to MG patients. In addition, other comorbidities and personal factors may affect the training regimen in MG, just like in other diseases. The PT in our study designed tailored training programs based on each patient’s previous physical activity and baseline fitness. The significant difference between different workout plans was how the PT targeted the exercise program focusing on different muscle groups and customizing the program to those the individual experienced as weak. The PT rotated exercises between large and small muscle groups, included variations in exercises, and avoided including the
same muscle group in two exercises in a row. The number of sets was initially lower to find the best level for the patient’s training/recovery, and the rest between each set depended on symptoms. The PT carefully tailored the exercises to allow patients to cope before and after training, thereby increasing strength and improving patients’ ability to carry out their ADLs. With this strategy, a PT program can be adhered to by patients with different forms of generalized MG, and subjective and objective improvement is seen based on the patients’ baseline status and goals for physical health. This unsupervised study aimed to minimize the number of follow-up visits to mimic a patient’s everyday setting in the community. Instead, the patients were encouraged to report adverse events and worsening of MG symptoms directly via email or phone. However, the low number of follow-up visits could be a limitation. Another limitation was that the MG-ADL, a common outcome parameter, was not assessed. Further, the disease duration was rather long; however, we hypothesize that a similar training approach can also be applied to patients with shorter disease duration as long as the MG status is stable.

4. Conclusion

Our pragmatic case series study suggests that well-controlled patients with generalized MG can extend their physical exercise to individualized personal training in the gym in a community setting. This enables MG patients with well-controlled disease, independent of their residence, to adhere to personal training regimens in the community setting, such as a public gym.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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References