Randomised controlled trial of weightlifting exercise in patients with chronic airflow limitation

K Simpson, K Killian, N McCartney, D G Stubbing, N L Jones

Abstract

Background Patients with chronic airflow obstruction are often limited by muscle fatigue and weakness. As exercise rehabilitation programmes have produced modest improvements at best a study was designed to determine whether specific muscle training techniques are helpful.

Methods Thirty four patients with chronic airflow limitation (forced expiratory volume in one second (FEV₁) 38% of predicted values) were stratified for FEV₁, to vital capacity (VC) ratio <40% and arterial oxygen desaturation during exercise and randomised to a control or weightlifting training group. In the experimental group training was prescribed for upper and lower limb muscles as a percentage of the maximum weight that could be lifted once only. It was carried out three times a week for eight weeks.

Results Three subjects dropped out of each group; results in the remaining 14 patients in each group were analysed. Adherence in the training group was 90%. In the trained subjects muscle strength and endurance time during cycling at 80% of maximum power output increased by 73% from 518 (SE 69) to 898 (95) s, with control subjects showing no change (506 (86) s before training and 479 (89) s after training). No significant changes in maximum cycle ergometer exercise capacity or distance walked in six minutes were found in either group. Responses to a chronic respiratory questionnaire showed significant improvements in dyspnoea and mastery of daily living activities in the trained group.

Conclusions Weightlifting training may be successfully used in patients with chronic airflow limitation, with benefits in muscle strength, exercise endurance, and subjective responses to some of the demands of daily living.

Severe chronic airflow limitation is associated with chronic disability and handicap. Functional exercise capacity is generally thought to be curtailed by the limited breathing capacity and impaired gas exchange, but as these are accompanied by a reduction in daily activities muscle function is reduced concomitantly, which may eventually become limiting. In a recent study examining symptom intensity at maximal exercise capacity muscle fatigue was identified as the limiting symptom in a third of patients.¹ In a later study measurements of isometric strength of quadriceps muscles, handgrip, and respiratory muscles indicated that reductions in skeletal muscle strength paralleled reductions in ventilatory capacity and contributed independently to reductions in exercise capacity.² Thus the most impaired exercise capacity was found in patients with the most severe airflow obstruction and greatest reduction in indices of skeletal muscle strength.

Exercise rehabilitation programmes have been investigated in the hope that improvements in exercise capacity might be achieved, despite the absence of any expected effect on pulmonary function variables, but the results have been variable, with only modest improvements in aerobic function being found.³⁻⁴ The ventilatory limitation to exercise may, however, preclude patients with severe airflow limitation from achieving an exercise training intensity high enough to improve aerobic capacity.⁵ Belman and Kendregan⁶ used needle muscle biopsy specimens to show that the increase in mitochondrial enzyme activity that normally accompanies an exercise training programme was not seen in patients with chronic airflow limitation who underwent exercise training. Although aerobic endurance training exercise is often accompanied by severe dyspnoea, patients might be able to undertake high intensity short term exercise, as is used in a weightlifting training programme, to improve muscle strength and exercise capacity. This type of training can improve muscle strength and endurance in elderly subjects⁷⁻¹³ and in patients with cardiac¹⁴ and neuromuscular disorders.¹⁵

We applied a weight training regimen previously shown to be effective in patients with coronary artery disease¹⁶ to patients with chronic airflow limitation, with random stratified assignment to an experimental and a control group. Outcome was assessed with a newly developed instrument to measure quality of life,¹⁷ ¹⁸ and several methods were used to assess muscle and exercise function.

Methods We recruited 34 subjects, 19 men and 15 women, aged 58–80 from a pool of about 100 patients attending a respiratory outpatient clinic. Subjects were in a clinically stable state, with no recent infective exacerbation, and drug management was considered to be optimal. Entry criteria included a ratio of forced

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Randomised controlled trial of weightlifting exercise in patients with chronic airflow limitation

expiratory volume in one second (FEV₁) to vital capacity (VC) of less than 0.7, a body weight within 30% of the predicted ideal body weight, the absence of other disorders likely to affect exercise, and the capacity to take part in the training programme. Thirty six patients originally agreed to enter the study (the most common reasons for refusal were travelling distance and the time commitment required); two patients were excluded before randomisation, one because of a serious arrhythmia during exercise and one because of an exacerbation of bronchitis. Written informed consent was obtained and the study was approved by the institution’s ethics committee.

Because the severity of airflow limitation and impaired pulmonary gas exchange may vary considerably between patients and contribute to exercise limitation, subjects were stratified according to FEV₁ (percentage of predicted values) and arterial oxygen saturation during maximal exercise testing into two groups: (a) subjects who developed an arterial oxygen saturation below 90% at rest or on exercise or had an FEV₁ to VC ratio of less than 40% of predicted values and (b) subjects whose FEV₁ to VC ratio was greater than 0.4 and who did not show oxygen desaturation during exercise. Subjects in the two groups were then sequentially assigned by tossing a coin to either a weightlifting programme or a control group.

The subjects underwent a series of tests, which were carried out on three non-consecutive days to avoid the effect of fatigue. All subjects had undergone pulmonary function and exercise studies on one or more occasions before. On the first day subjects underwent spirometry, measurement of total lung capacity and lung volume subdivisions, single breath carbon monoxide uptake (TLCO), mixed venous carbon dioxide tension by rebreathing, and maximum expiratory and inspiratory pressures. Isometric force during flexion and extension of the quadriceps muscle and handgrip strength were measured. An incremental progressive exercise test to a symptom limited maximum was performed. Predicted values were taken from Crapo et al for spirometry and lung volumes, Crapo and Morris for TLCO, and Jones et al for exercise capacity.

Quadriceps strength was measured with the knee flexed (in the 90° position) and tension was measured with a Lafayette 32528 tensiometer; handgrip strength was measured with a hand held dynamometer (Lafayette 32528 HD).

The progressive exercise test was performed on a calibrated electrically braked cycle ergometer (Siemens Elema 370). The power output initially was 8.2 W (50 kpm/min) and was increased at the end of each minute by 8.2 W. Subjects breathed through a high velocity, low resistance one way valve (Hans Rudolph), and expired air was sampled and analysed for oxygen and carbon dioxide tension by an exercise testing system (Sensor Medics Horizon). Arterial oxygen saturation was measured by ear oximetry (Ohmeda Biox 3700) and heart rate by electrocardiography (Hewlett Packard 1515). Perceived exertion for leg effort and for breathlessness was scored with a Borg category ratio scale (0-10), which was presented within easy vision of the the subject. The scale has valid ratio properties and also qualities related to absolute symptom intensity, allowing the score to be treated as a parametric variable for statistical purposes.

A trained interviewer administered a questionnaire designed for chronic respiratory disease, which has specific questions about physical and emotional topics considered to be important in chronic respiratory disease. The responses to questions about discomfort during everyday activities were scored with a seven point Likert scale in which 1 = extreme shortness of breath and 7 = no shortness of breath. The interviewer was blinded to the allocation of the patient to the training or control group. When the questionnaire was administered again at the end of the study subjects were informed of their previous answers; this reduces variability and increases the validity of the responses.

The tests carried out on the second and third days were randomly varied. On one day the following measurements were carried out: one repetition maximum for single arm curl, single knee extension, and single leg press; peak force of right elbow flexors with interpolated twitch; a submaximal cycling exercise endurance test; and a six minute walking test. One repetition maximum was defined as the weight that the subject could lift only once, with three minutes of rest between lifts and resistance increased by increments of 1.25 kg for leg lifts and 0.25 kg for elbow flexors. On the other day one repetition maximum arm curl, knee extension, and leg press; distance walked in six minutes; and peak force of elbow flexors were repeatedly measured. This testing protocol was used to exclude an element of habituation for the six minute walking test and muscle strength studies; results obtained on the second day were used in the analysis of results.

Single knee extension and single leg press exercise were carried out on a Global Gym apparatus. Motor unit activation was assessed by the interpolated twitch technique applied to the elbow flexors, with the elbow joint at an angle of 110°. Muscle stimuli consisting of voltage pulses of 50 μs and voltage increasing from 40 to 100 V were delivered to rubber electrodes taped to the biceps by a Devices stimulator; they were increased until there were no further increases in torque production with increases in stimulus intensity. The lack of increase in torque with increasing stimulus was taken to indicate that all motor units were recruited and firing at optimal frequencies for tension development.

The six minute walking test had a standardised protocol to ensure consistency in encouraging one way valve (Hans Rudolph), and expired air was sampled and analysed for oxygen and carbon dioxide tension by an exercise testing system (Sensor Medics Horizon). Arterial oxygen saturation was measured by ear oximetry (Ohmeda Biox 3700) and heart rate by electrocardiography (Hewlett Packard 1515). Perceived exertion for leg effort and breathlessness on the Borg scale.

A submaximal endurance cycling test was...
carried out on a calibrated cycle ergometer (Monark 868) at 80% of the maximum power output achieved during the incremental exercise test; the test was continued until the subject could no longer maintain the desired pedalling frequency of 60 revolutions/minute.

Training sessions were held three times a week for eight weeks. Weight lifting consisted of 10 repetitions of single arm curl, single leg extension, and single leg press exercise, which were repeated three times. The resistance was increased progressively from 50% of one repetition maximum during the first week to 85% during the final week of training. The one repetition maximum for all the exercises was re-evaluated every sixth session and a constant relative training stimulus was ensured by adjusting the resistance in terms of the most recent maximum. Subjects were coached and observed to obtain a slow smooth movement with normal breathing control during the lifting phase of the exercise. There was an initial warm up period of five minutes of low resistance cycling and two minutes of low resistance arm exercise on an arm crank ergometer. The control group attended only for testing at the beginning and end of the study.

STATISTICAL METHODS

Two way analysis of variance with repeated measurements was used to establish the significant effects of time, treatment, and their interaction. The Tukey post-F test was used to determine the location of significance when it was implied by the F ratio. The level of significance was taken, as $p = 0.05$. Data obtained in subjects who did not return for testing after training were excluded from the comparison analysis.

Results

Stratification and random assignment yielded two groups of 17 subjects with similar anthropometric and pulmonary function measurements, but there were more women in the experimental group (table 1). Before the end of the eight week training programme three subjects dropped out of the study, one because of a chest infection and two because of changes in their treatment; in the remaining subjects, attendance at the training sessions averaged 90% (SD 10·6) of the scheduled occasions. Three subjects in the control group also failed to return after the eight weeks of the study, leaving 14 subjects in each group for statistical analysis; the two groups remained comparable in terms of the variables presented in tables 1 and 2, and outcome measures were not statistically affected by the inclusion of the data from the subjects who dropped out. All subjects had severe airflow limitation; in 21 of the 28 subjects TLCO was below 80% of predicted values; 12 were hypercapnic, with a mixed venous carbon dioxide tension above 7·3 kPa (above 8·7 kPa in one); 10 had a reduction in arterial oxygen saturation of more than 5% during exercise. There were no significant differences between the two groups in the muscle strength variables before training, maximum exercise capacity, distance walked in six minutes, endurance time at 80% of maximum exercise capacity (table 2), and the responses to the questionnaire (figure).

EFFECT OF WEIGHT LIFTING

Results are presented for the 28 subjects who completed the tests after the study period. Eight weeks of weightlifting were significantly associated with increases in muscle strength ($p < 0·01$); one repetition maximum increased by 33% for arm curl, by 44% for leg extension, and by 16% for the leg press (table 2). No changes were seen in the same variables in the control group. Mean (SE) maximum isometric force in the quadriceps muscle increased from 240 (23·6) N to 301 (25·3) N ($p < 0·01$), with no change being observed in control subjects. Similarly, there were increases in voluntary strength of the right elbow flexors, from 28 (2·6) N x m to 33 (3·2) N x m ($p < 0·01$), with no changes observed in the control group. The extent of voluntary motor unit activation increased from 90% (1·8%) to 97% (0·4%) in the experimental group and from 86% (3·1%) to 90% (3·2%) in control subjects, before and after training respectively; two way analysis of variance showed a significant effect of time but no effect of treatment or any interaction between time and treatment.

After training there were no significant changes in spirometric variables: FEV1 was 0·88 (0·11) (40% (5·0%) of predicted values) before training and 0·94 (0·16) (44% (6·7%) predicted values) afterwards; in the control group the values were 1·04 (0·14) (39% (5·7%)) and 0·93 (0·13) (35% (5·0%)) respectively. Two way analysis of variance showed no significant effect of time or treatment in vital capacity and variables derived from the inspiratory and expiratory cycle. Maximum static inspiratory and expiratory pressures were similarly unchanged. Maximum inspiratory pressure was 36 (5·2) cm H2O before training and 40 (3·4) cm H2O afterwards (48 (6·3) cm H2O respectively.

**Table 1** Data on subjects in weight training and control groups. Values are means (SD)

<table>
<thead>
<tr>
<th>Training group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>(nine women, five men)</td>
<td>(four women, ten men)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>73 (4·8)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>159 (8·1)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>65 (10·4)</td>
</tr>
<tr>
<td>FEV1, % predicted</td>
<td>95 (18·6)</td>
</tr>
<tr>
<td>FEV1/VC (%)</td>
<td>49·7 (12·9)</td>
</tr>
<tr>
<td>Tlco (ml/min/mmHg)*</td>
<td>1·96 (6·81)</td>
</tr>
<tr>
<td>Alveolar ventilation (l)</td>
<td>4·15 (1·121)</td>
</tr>
<tr>
<td>MEP (cm H2O)</td>
<td>59 (9·7)</td>
</tr>
<tr>
<td>MEP (cm H2O)</td>
<td>66 (23·5)</td>
</tr>
<tr>
<td>D after oxygen saturation (%) rest</td>
<td>94 (3·3)</td>
</tr>
<tr>
<td>D after maximal exercise</td>
<td>91 (0·2)</td>
</tr>
</tbody>
</table>

MIP = maximum inspiratory pressure; MEP = maximum expiratory pressure.

*To convert to ml/min/kPa divide by 2·99.

**Table 2** Maximum (one repetition maximum) weight lifted before and after training period. Values are means (SE)

<table>
<thead>
<tr>
<th>Training group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>Single arm curl (kg)</td>
<td>12·1 (1·22)</td>
</tr>
<tr>
<td>Single knee extension (kg)</td>
<td>17·2 (2·84)</td>
</tr>
<tr>
<td>Single leg press (kg)</td>
<td>106·5 (5·13)</td>
</tr>
</tbody>
</table>
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Summary of responses to chronic respiratory questionnaire.* * * p < 0-05, ***p < 0-01.
Categories were not comparable across the scale; in each category symptom responses were scaled 1–7 for each of several activities or feelings, with 1 representing extreme disability and 7 none. Four activities were assessed for dyspnoea, fatigue, and mastery, yielding a maximum score of 28 and a minimum of 4; seven questions were used to assess emotional responses, yielding a maximum score of 49 and a minimum of 7.

49 (5-5) respectively in control subjects). Maximum inspiratory pressure was 64 (6-3) cm H₂O before training and 80 (4-4) cm H₂O afterwards (81 (10-9) and 85 (8-2) cm H₂O respectively in control subjects).

Maximal incremental exercise capacity was 40% (6-0%) of predicted values before training and 48% (8-2%) afterwards (43% (7-6%) and 45% (7-8%) respectively in control subjects); these changes were not significant in either group. Maximal oxygen intake was 0-63 (0-06) l/min before and 0-74 (0-06) after training (0-70 (0-09) and 0-82 (0-08) respectively in control subjects); none of these changes was significant. Other measurements made at maximum exercise (carbon dioxide production, minute ventilation, tidal volume, breathing frequency, and oxygen saturation) were also unaffected. The Borg scale ratings of perceived effort and dyspnoea during the test were not significantly changed. Similarly, performance assessed by the six minute walking test was unchanged at the end of the study in both groups. There was a positive trend towards a treatment effect on the distance walked, from 391 (22-5) m before and 427 (27-2) m after training (p = 0-1); in the control group the respective distances were 369 (32-0) m and 376 (32-1) m.

In contrast to maximum exercise capacity and performance in the six minute walking test, endurance to fatigue during cycling at 80% of maximum exercise capacity improved significantly from 518 (69) s to 898 (95) s (p < 0-01) but was unchanged in control subjects (506 (86) s before and 479 (89) s after). Rating of leg effort and dyspnoea on the Borg scale at the end of the test were similar in both groups before and after training.

Responses to the questionnaire (figure) showed significant effects of treatment in the categories of dyspnoea and mastery (p < 0-01) and fatigue (p < 0-05) but no changes in emotional function. No changes were seen in any domain in the control group.

Discussion
The patients who took part in this study were typical of older patients who are handicapped by chronic airflow limitation. Pulmonary function was severely impaired, with ventilatory capacity, as expressed by FEV₁, only 39-5% of predicted values and gas exchange capacity, as reflected by TLCO, only 55% of predicted values. They were severely disabled; maximum cycle ergometer exercise capacity was only 42% of predicted values and they were able to walk only 380 m in six minutes, about half the distance achieved by the healthy subjects of a comparable age. The intensity of symptoms, as measured by the Borg scale, was considerably higher than expected in healthy subjects of comparable age; whereas healthy subjects rate leg effort and dyspnoea as 1 (very slight) at a relative power output of 40% of predicted maximum power, our subjects recorded an average rating of 5-5 (severe) for the effort in breathing and 4-5 for leg muscle effort. These findings are similar to those reported by Killian, who concluded that many subjects with chronic airflow limitation reach a limiting severity of leg muscle effort or fatigue before they are limited by dyspnoea during an incremental exercise test such as the one we used in this study. As suggested by several authors after studying the effects of aerobic exercise training, the severity of exercise induced symptoms makes it difficult for patients to achieve an adequate training stimulus, and it may lead to their dropping out of exercise programmes. Because of the generally disappointing results of previous exercise training studies, and because of the successful application of a weightlifting training programme in patients with coronary artery disease, we undertook this study to investigate the effects of a similar programme in patients with chronic airflow limitation. We expected the training to be better tolerated than comparable aerobic training, with improved compliance and efficacy. Ries et al reported a greater than 90% compliance with resistance training for upper body strength in patients with respiratory disease and noted that they preferred to increase resistance rather than increase the number of repetitions at the same resistance during the programme.

The regimen of our present study was simple to prescribe individually and easy for the subjects to undertake without undue breathlessness; compliance with the study was good, with patients attending 90% of their scheduled sessions. The improvements in muscle strength were similar to those in comparable studies of healthy young and older subjects and patients with coronary artery disease and were not due to increases in motor unit activation. The impressive gain of 30% in overall strength of lower limb muscles was partially related to the initial extent of weakness but is likely to
translate into a significant improvement in the capacity to undertake everyday activities.

The study may be criticised on several grounds. Firstly, the random allocation of patients to the two groups was associated with a greater number of women in the experimental than in the control group. The initial disability and muscle weakness may thereby have been greater in the experimental group than in the control group; we believe that expressing results in terms of predicted values, in which the effects of sex are allowed for, should have counteracted this effect. Secondly, our patients were elderly and the results may not be generally applicable to patients with respiratory limitation: muscle strength declines disproportionately with age above 60. Thus, we may have seen a combination of the effects of inactivity and aging. Aniansson and Gustafsson reported appreciable improvement in muscle strength with training in elderly men.11

In common with some previous investigators12 we used several methods to assess exercise capacity. Changes in incremental cycle ergometry performance (8% increase) and the distance walked in six minutes (9% increase), though greater in the experimental group, showed no significant improvements. The extent of the changes is similar to those reported by McGavin et al after a programme of stair climbing at home.39 However, endurance during cycling improved substantially in the experimental subjects, who were able to exercise for longer before reaching the same limiting intensity of symptoms. We conclude from these findings that maximal exercise in our subjects was mainly limited by the constraints imposed by an extremely reduced ventilatory capacity; during cycle ergometry maximum ventilation was similar before and after training, and in the range expected for subjects with comparable airflow limitation.40 During submaximal exercise improved muscle strength allowed subjects to continue for longer before being limited by symptoms. The disproportionately large improvement in endurance compared with maximum exercise capacity in cycling and in the six minute walking test is probably more apparent than real. The relation between maximum power and endurance is not linear, and measures of endurance are more responsive to training. For example, in a study of weight training in patients with cardiac disease we found a 15% increase in aerobic power accompanied by a doubling of endurance;45 these figures are comparable with the findings in the present study. Similarly, the six minute walking test entails maximal effort. There are other possible reasons for not overemphasising the improved endurance. Levine et al carried out a careful study comparing ventilatory muscle endurance training with intermittent positive pressure breathing as a control measure; measurements were similar to ours and, in spite of improvements in respiratory muscle endurance, endurance training was associated with no greater improvement in exercise capacity than in control subjects, although both improved endurance during a treadmill exercise test.46 As the improvements were found in both experimental groups, Levine et al cautioned against ascribing improvements to any specific intervention in a hospital based programme.

The use of questionnaires to assess handicap in daily living activities and other subjective accompaniments of chronic airflow limitation has been emphasised by the findings of several groups. We used the questionnaire developed by Guyatt et al, in which the questions provide a rating of subjective dyspnoea, general fatigue, emotional distress (which expresses the subjective feeling of the patient's being in control). Though no changes were found in any category in the control group, significant improvements were recorded in the experimental group in the domains of dyspnoea and mastery. The importance of subjective improvements to the overall clinical state has been judged by Jaeschke et al to be clinically valuable if a minimum average change of 0·5 is obtained in the ratings for each question in a given domain.41 In our study the rating for dyspnoea improved by 1·3 per question, for fatigue by 1·0, and for mastery by 0·85 (figure). Whether improved exercise was effective in achieving a muscle training stimulus without distressing dyspnoea. It motivated patients to exercise as they could see the improvement in the weights they could lift, and it also increased patients' mastery over the demands of daily living. It seems to be a useful addition to an overall management programme for disabled patients with chronic airflow limitation.

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