BRONCHIECTASIS

Exercise training and inspiratory muscle training in patients with bronchiectasis

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Background: Bronchiectasis is a chronic suppurative lung disease often characterised by airflow obstruction and hyperinflation, and leading to decreased exercise tolerance and reduced health status. The role of pulmonary rehabilitation (PR) and inspiratory muscle training (IMT) has not been investigated in this group of patients.

Methods: Thirty two patients with idiopathic bronchiectasis were randomly allocated to one of three groups: PR plus sham IMT (PR-SHAM), PR plus targeted IMT (PR-IMT), or control. All patients (except the control group) underwent an 8 week training programme of either PR or PR plus targeted IMT. Exercise training during PR was performed three times weekly at 80% of the peak heart rate. IMT was performed at home for 15 minutes twice daily over the 8 week period.

Results: PR-SHAM and PR-IMT resulted in significant increases in the incremental shuttle walking test of 96.7 metres (95% confidence interval (CI) 59.6 to 133.7) and 124.5 metres (95% CI 63.2 to 185.9), respectively, and in endurance exercise capacity of 174.9% (95% CI 34.7 to 426.1) and 205.7% (95% CI 31.6 to 310.6). There were no statistically significant differences in the improvements in exercise between the two groups. Significant improvements in inspiratory muscle strength were also observed both in the PR-IMT group (21.4 cm H_2O increase, 95% CI 9.3 to 33.4; p = 0.008) and the PR-SHAM group (12.0 cm H_2O increase, 95% CI 1.1 to 22.9; p = 0.04), the magnitude of which were also similar (p = 0.220). Improvements in exercise capacity were maintained in the PR-IMT group 3 months after training, but not in the PR-SHAM group.

Conclusion: PR is effective in improving exercise tolerance in bronchiectasis but there is no additional advantage of simultaneous IMT. IMT may, however, be important in the longevity of the training effects.

Pulmonary rehabilitation is a multidisciplinary approach to treating patients with chronic lung disease and is advocated in American,[1] British[2] and European[3] guidelines on the management of chronic obstructive pulmonary disease (COPD) as an important component of medical care. Since pulmonary rehabilitation has traditionally focused on patients with COPD, its effectiveness in other chronic lung diseases has received little attention, although it has been implemented with clinical success in patients with cystic fibrosis[4] and in those with restrictive pulmonary defects.[5]

Bronchiectasis is a chronic (often suppurative) lung disease not traditionally included in the definition of COPD, but also characterised by airflow obstruction and symptoms including cough, sputum production, wheeze, dyspnoea, and decreased exercise tolerance.[6][7] The causes of dyspnoea and the reduced exercise capacity are multifactorial and include altered pulmonary mechanics, inefficient gas exchange, decreased muscle mass, and confounding psychological morbidity, all of which lead to a progressive detraining effect.[8] Theoretically, one would therefore expect pulmonary rehabilitation to be as effective in bronchiectasis as it is in COPD, but to date only one study has been performed which included only seven patients with the disease.[9]

The reduced exercise capacity and increased dyspnoea in patients with COPD is partly attributable to expiratory flow limitation resulting in dynamic hyperinflation and increased intrinsic positive end expiratory pressure, exacerbated by a reduction in inspiratory muscle force. Recently, Koulouris *et al*[10] demonstrated the presence of tidal expiratory flow limitation in patients with bronchiectasis, related to an increase in dyspnoea and a reduced exercise tolerance. This was also postulated to be a result of dynamic hyperinflation and consequent inspiratory muscle loading.

Inspiratory muscle training (IMT) has been shown to be an important adjunct to pulmonary rehabilitation in COPD patients with reduced respiratory muscle strength, resulting in greater improvements in exercise capacity than with exercise training alone.[11][12] This improvement in exercise capacity may be due to a reduction in the perception of dyspnoea during exercise, or it may be a result of the increase in inspiratory muscle strength at the end of the training programme.[13] The effect of IMT in conjunction with exercise training in patients with bronchiectasis has not been investigated previously. However, the demonstration of inspiratory muscle loading during exercise[10] suggests that IMT may also be beneficial in this group of patients.

One of the hallmark symptoms of patients with bronchiectasis is the chronic production of purulent sputum, the clearance of which may be improved by physiotherapy,[14] antibiotic treatment[15] and, in patients with cystic fibrosis, by exercise training.[16] Repeated inspiratory manoeuvres performed during specific IMT may potentially have a beneficial effect on ease of expectoration in patients with bronchiectasis, but this has not been investigated.

The aims of this study were therefore to compare the effects of pulmonary rehabilitation together with either targeted or sham IMT in patients with bronchiectasis. We assessed a range of outcome measures including respiratory

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muscle function, lung function, exercise capacity, sputum clearance, and health status.

METHODS

Subjects

Thirty two patients (six men) with bronchiectasis confirmed by high resolution computed tomography (HRCT) were allocated randomly (using a computer generated random number sequence) to one of three groups: (1) pulmonary rehabilitation plus sham IMT (PR-SHAM, n = 11); (2) pulmonary rehabilitation plus targeted IMT (PR-IMT, n = 12); and (3) a control group with no intervention (n = 9). In 18 of the patients studied the disease was confined to one or two lobes within the lungs. The remaining 14 patients had widespread disease that was either varicose or cylindrical in nature. Patients with HRCT evidence of concomitant emphysema were excluded from the study. Seven patients had previously undergone a lobectomy for their disease (two in the PR-IMT group, three in the PR-SHAM group and two in the control group). In 23 patients the origin of the disease was unknown. In the remaining nine the disease was attributed to a past childhood illness including pneumonia (n = 5) and whooping cough (n = 4).

During the training programme one patient withdrew from the PR-SHAM group and one from the PR-IMT group due to an exacerbation of the disease. During the subsequent follow up period a further two patients withdrew from each of the training groups, two for personal reasons and two because of an exacerbation of their disease.

Patients were excluded if they had evidence of endocrine, orthopaedic, or primary cardiac disorders, coronary artery disease, hypertension or cor pulmonale. Patients were also excluded if they had experienced an acute exacerbation within the previous 6 weeks or were receiving long term oral corticosteroid treatment. All other medications were permitted for use during the study. All patients were observed over a 4 week run-in period when their regular treatment was maintained, to verify stability in their clinical and functional status. The study protocol was approved by the South Birmingham Health Authority research ethical committee.

Measurements

In the PR-IMT and PR-SHAM groups measurements were performed at the start and the end of the training programme (8 weeks) and 3 months after the programme had been completed. In the control group measurements were performed on two occasions 8 weeks apart. All patients attended the laboratory prior to these study visits in order to familiarise them with the measurement procedures and therefore minimise the effects of test habituation. On this occasion, measurements of respiratory muscle function were repeated until variability had decreased to less than 5% between manoeuvres and patients performed one test each of the maximal exercise test, endurance capacity test and the incremental shuttle walking test (ISWT). Lung function tests were not practised as all patients had previously performed these measurements on several occasions.

Lung function

Lung function testing was performed according to national guidelines[17] and included spirometric parameters, static lung volumes, and transfer factor. Results were compared with standard reference values.[18]

Respiratory muscle strength

Measurements were made according to the methods described by Black and Hyatt[19] using a handheld mouth pressure meter (Morgan Medical Ltd, Kent, UK). Maximal expiratory pressure (PEmax) was measured near total lung capacity after a maximal inspiration; maximal inspiratory pressure (PImax) was measured near residual volume after a maximal expiration. Pressures were maintained for at least 1 second and the highest of three technically satisfactory measurements (within 5%) was recorded.

Exercise testing

Exercise test conditions were standardised for time of day, medication administration, test instruction, and degree of coaching. The endurance exercise test was performed on the same day as the incremental exercise test with a rest period of 1 hour. The ISWT was performed on a separate day.

Maximal incremental treadmill test

Progressive exercise testing was performed on a treadmill (Morgan Medical Ltd) using a modification of the Balke protocol.[20] After initial recording of resting measurements (2 min) the grade increased from an initial zero grade by a gradient of 1% each minute. During the test, continuous measurements were made of inspired ventilation, oxygen uptake and carbon dioxide output and averaged over 30 second intervals. Ventilation (l/min) was measured by integration of the flow signal via a pressure transducer (Morgan Medical Ltd) from a Fleisch pneumotachograph placed at the inspiratory port of a two-way non-rebreathable valve (Hans Rudolf, Cranlea, Birmingham, UK). Expired gas passed via a mixing chamber (Morgan Medical Ltd) through oxygen (Zirconia Cell Analyser, Morgan Medical Ltd) and carbon dioxide (Infrared Analyser, Morgan Medical Ltd) analysers, respectively. Heart rate and oxygen saturation were monitored throughout the test via a pulse oximeter (Ohmeda Biox 2700, Ohmeda, Herts, UK). At the termination of the test, end of exercise dyspnoea was rated using a modified Borg scale;[21] peak oxygen uptake was recorded in ml/min/kg and compared with predicted values.[22]

Submaximal exercise test

Endurance exercise capacity was measured on a treadmill (Morgan Medical Ltd) at 85% of the peak oxygen uptake achieved on the baseline incremental test. Patients exercised to volitional fatigue and the total distance walked in metres was recorded. Throughout the test, heart rate and oxygen saturation were continuously monitored via a pulse oximeter (Ohmeda Biox, Ohmeda). The intensity of the endurance test was the same at the start and end of the training programme.

Incremental shuttle walking test (ISWT)

Patients walked at an increasing speed up and down a 10 m course delineated by two cones according to the methods of Singh et al.[23] The test was terminated when the patient was no longer able to maintain the required speed or became too breathless to continue, at which time the distance walked in metres was recorded.

Health status

Patients completed the St George's Respiratory Questionnaire (SGRQ)[24] which included assessment in the three domains of symptoms, activities and impacts. Patients were blinded to their responses on previous visits to minimise bias after the training programme.

24 hour sputum volume

Patients began collection at a set time on the day preceding the scheduled visit and completed the collection period 24 hours later. They were encouraged to collect all expectorated sputum into preweighed containers and the volume collected was determined by weight, assuming 1 g = 1 ml of sputum.[25]

Pulmonary rehabilitation programme

Exercise training

Patients in the PR-SHAM and PR-IMT groups completed an 8 week hospital based outpatient programme of high intensity exercise training. Exercise training sessions were performed three times weekly and consisted of two sessions within the hospital and one further session at home. The duration of each exercise training session was 45 minutes and patients were required to exercise at 80% of the peak heart rate achieved on the initial maximal incremental exercise test targeted using the Borg rating scale for dyspnoea.[23] Exercise training within the hospital consisted of treadmill walking (15 minutes), cycle ergometry (15 minutes), and stair climbing (15 minutes). The home exercise programme consisted of a 45 minute period of walking (with the intensity targeted using the Borg rating scale) recorded in a diary card that was reviewed weekly in order to monitor compliance. No formal maintenance training sessions were offered at the end of the 8 week programme and patients only attended the hospital during this time as part of their routine clinical management. All patients were advised, however, on the importance of continuing with the exercises at home in order to maintain the benefits obtained at the end of the programme.

All groups received an 8 week programme of educational sessions which included disease pathology, rationale for training, medication, coping strategies, relaxation, nutritional advice, physiotherapy, and smoking cessation (where appropriate).

Inspiratory muscle training (IMT) programme

Training was performed using a pressure threshold device[26] at an individually programmed intensity. In the PR-IMT group, training started at 30% PImax and increased by 5% each week until a training intensity of 60% PImax was achieved. In the PR-SHAM group training was performed at a very low load (fixed at 7 cm H_2O) which has previously been shown to have no effect on the inspiratory muscles in patients with COPD.[27][28]

IMT was performed using an identical technique for both groups. Patients were instructed to insert the mouthpiece and exhale gently as far as possible to residual volume. Following this, they were instructed to take a rapid breath inwards to total lung capacity. Patients were advised that inspiration should last for approximately 2 seconds and expiration for 6 seconds, so that the breathing frequency was approximately 8 breaths/min. This breathing pattern has previously been shown to improve inspiratory muscle function during IMT in patients with COPD.[28]

IMT was performed for 15 minutes twice daily at home for 8 weeks. Patients were instructed in the use of the device and maintained a training diary. Training progression was monitored by weekly re-evaluation of PImax in both training groups and training intensity was adjusted by altering the spring tension within the device. This was performed weekly by the investigator using a pressure transducer to record the inspiratory pressure developed during inspiratory manoeuvres. Patients in the control group did not undergo inspiratory muscle training.

Statistical analysis

Baseline characteristics are reported as mean (SD) with changes from baseline given as mean and the 95% confidence interval (CI). Comparisons of the changes between groups were performed using a one way ANOVA with significant differences being further investigated using unpaired t tests with adjustment for multiple comparisons (Bonferroni). Baseline and post training data were compared within groups using a paired t test.

The study was powered to detect a mean (SD) difference of 20 (15) cm H_2O in PImax between the groups with 80% power and a significance level of 0.05. This indicated 10 patients in each group would be required. A difference in walking distance of 50 m (using the ISWT) between the groups (assuming a SD of 40 m) would require 11 patients per treatment group.

RESULTS

There were no significant differences between the groups at baseline (table 1) and no changes in lung function throughout the study. No changes were observed in the control group in any of the parameters measured over the 8 week period.

At baseline, all three patient groups demonstrated a reduction in PEmax (table 1) compared with the predicted value, which remained unchanged throughout the period of study (data not shown). The groups displayed a wide range of

Table 1 Mean (SD) baseline physiological characteristics of patients who completed the study (n = 32)

Parameter	PR-SHAM	PR-IMT	Control
M/F	4/7	2/10	0/9
Smoking status	4 EX/7 NS	2 EX/10 NS	2 EX/7 NS
Age (years)	63.1 (3.5)	57.3 (2.4)	62.9 (3.9)
FEV$_1$ (l)	1.44 (0.77)	1.23 (0.74)	1.49 (0.61)
FEV$_1$ (% predicted)	64	54	69
FEV$_1$/VC%	57.0 (0.20)	54.1 (0.20)	66.2 (0.09)
RV (l)	2.14 (0.97)	2.51 (0.95)	1.83 (0.87)
RV (% predicted)	111	133	99
TLC (l)	5.04 (1.68)	4.92 (1.10)	4.26 (1.37)
TLC (% predicted)	97	98	88
TLCO (mmol/min/kPa)	6.32 (2.07)	5.88 (1.61)	5.92 (2.13)
TLCO (% predicted)	79	76	76
KCO (mmol/min/kPa/l)	1.65 (0.44)	1.63 (0.29)	1.66 (0.35)
KCO (% predicted)	86	82	82
PImax (cm H_2O)	66.4 (22.0)	78.0 (17.7)	77.2 (24.7)
PImax (% predicted)	87	98	103
PEmax (cm H_2O)	97.3 (37.5)	75.8 (28.5)	87.4 (22.9)
PEmax (% predicted)	66	53	63
Peak $\dot{V}O_2$ (ml/min/kg)	15.6 (6.2)	19.8 (8.3)	19.0 (5.0)
Peak $\dot{V}O_2$ (% predicted)	77	88	92

EX, ex-smoker; NS, never smoked; FEV$_1$, forced expiratory volume in 1 second; VC, vital capacity; TLC, total lung capacity; RV, residual volume; TLCO, lung carbon monoxide transfer factor; KCO, carbon monoxide transfer coefficient; PImax, PEmax, maximum inspiratory and expiratory pressures; $\dot{V}O_2$, oxygen consumption.
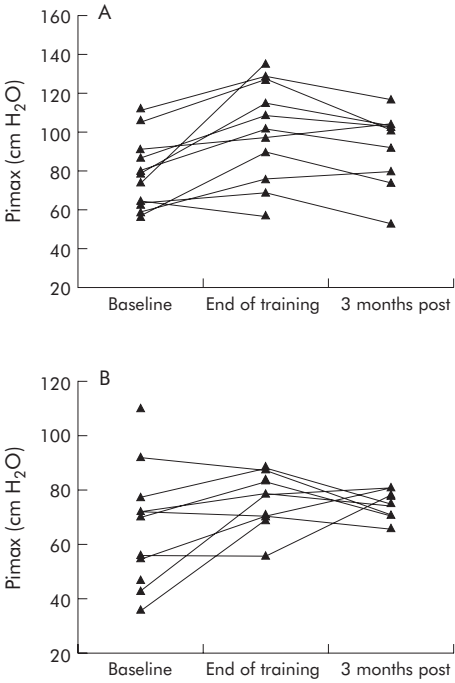
Figure 1 Individual changes in Pımax during training in (A) the PR-IMT group and (B) the PR-SHAM group. Individual values for Pımax during training are shown. The lines join data for individual patients.

Figure 2 Individual changes in endurance capacity during training in (A) the PR-IMT group and (B) the PR-SHAM group. Individual data and changes in endurance capacity are shown before and after 8 weeks training.

measurements for Pımax (range 36–119 cm H_2O) with a significant degree of impairment being observed in some patients.

No changes in respiratory muscle function were observed in the control group over the 8 week period (77.2 (24.7) cm H_2O and 75.8 (8.5) cm H_2O at baseline and at the end of the 8 weeks, respectively). Pımax increased from 78.0 (17.7) cm H_2O at baseline to 100.5 (25.7) cm H_2O at the end of training (p = 0.003) in the PR-IMT group (fig 1A), with a similar increase in the PR-SHAM group (fig 1B). There was no significant difference in the magnitude of the increase in Pımax between the two training groups (p = 0.220; table 2). Similarly, there was no difference between the groups in the magnitude of the change between the end of training and 3 months after training (−9.7 cm H_2O (95% CI −17.5 to −1.8) in the PR-IMT group and (−1.9 cm H_2O (95% CI −12.7 to 9.0) in the PR-SHAM group; p = 0.186). We were unable to obtain data from two patients in each group at the 3 month follow up. Individual data obtained at this time are shown in figs 1A and B for the PR-IMT and PR-SHAM groups, respectively.

No changes in peak oxygen uptake were observed in any of the three groups at the end of the 8 week period (table 2). In contrast, th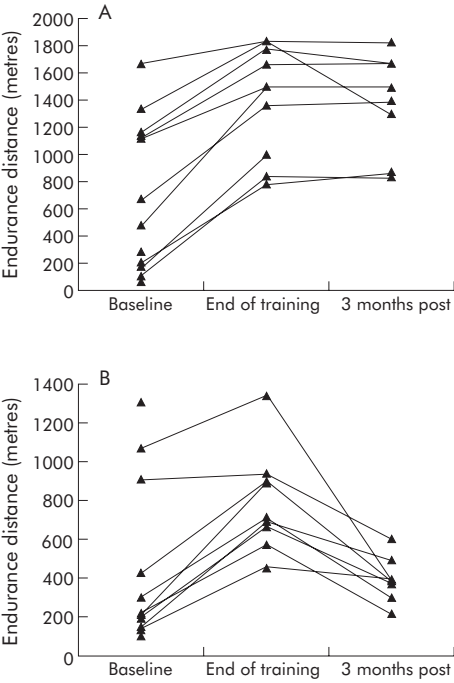ere were significant improvements in endurance exercise capacity in both the PR-IMT group (mean increase 607.3 metres, 95% CI 436.0 to 778.7) and the PR-SHAM group (mean increase 392.8 metres, 95% CI 251.7 to 534.0), the magnitude of which was similar between the groups. Individual patient data are shown in fig 2A and B, respectively.

Similarly, the percentage increase in walking distance was similar between the two training groups (mean change 205.7% (95% CI 34.7 to 426.1) in the PR-IMT group and 174.9% (95% CI 31.6 to 310.6) in the PR-SHAM group). No changes in endurance exercise capacity were observed in the control group (table 2).

Three months after the training programme had ended the improvement in endurance exercise capacity was maintained in the PR-IMT group (fig 2A) but not in the PR-SHAM group (fig 2B): 1394.7 (347.7) metres and 398.1 (114.2) metres in the PR-IMT and PR-SHAM groups, respectively (p<0.01). Furthermore, the change between the end of training and 3 months after training was significantly different between the groups (−60.8 metres (95% CI −203.4 to 81.7) in the PR-IMT group and −382.9 metres (95% CI −602.1 to 163.7) in the PR-SHAM group; p = 0.01).

Table 2 Comparison of changes between the groups during the study

| Parameter | Change between baseline and end of training | | | |
	PR-SHAM	PR-IMT	Control	p value
Pımax (cm H_2O)	12.0* (1.1 to 22.9)	21.4†† (9.3 to 33.4)	−1.6 (−6.2 to 3.0 0)	0.003
V̇O_2 peak (ml/min/kg)	1.96 (−1.8 to 5.7)	0.35 (−2.4 to 3.1)	−1.91 (−4.6 to 0.8)	0.192
ISWT (m)	96.7** (59.6 to 133.7)	124.5†† (63.2 to 185.9)	11.0 (−16.9 to 38.9)	0.002
Endurance exercise (m)	392.8** (251.7 to 534.0)	607.3†† (436.0 to 778.7)	−112.6 (−518.7 to 293.4)	0.0001

Pımax, inspiratory oxygen pressure; V̇O_2 peak, peak oxygen uptake; ISWT, incremental shuttle walking test.
p values represent differences between the three groups (using ANOVA) at the time point shown. Numbers in parentheses are 95% confidence intervals.
*p<0.05, **p<0.01 control group v PR-SHAM.
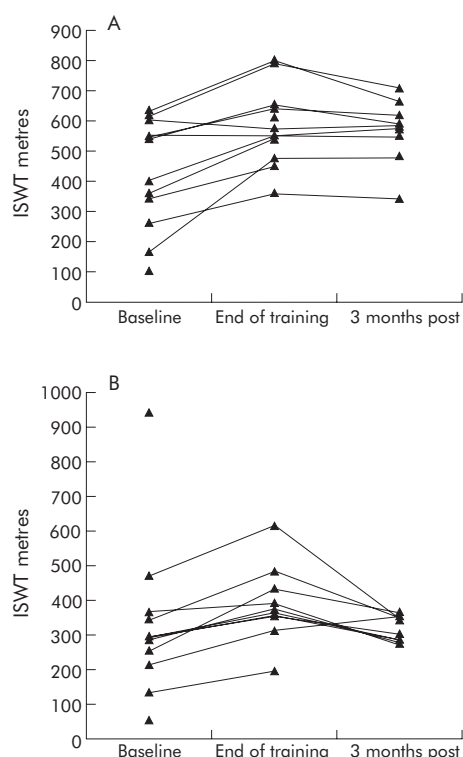††p<0.01 control group v PR-IMT.

Figure 3 Individual changes in ISWT during training in (A) the PR-IMT group and (B) the PR-SHAM group. Individual changes in ISWT at the start and end of the training programme are shown.

ISWT distance improved from a mean (SD) of 425.0 (182.9) metres to 579.1 (134.9) metres (p = 0.001) in the PR-IMT group (fig 3A) and from 328.2 (231.9) metres to 387.8 (115.8) metres (p = 0.0003) in the PR-SHAM group (fig 3B). There was no difference in the magnitude of the improvement between the two training groups (mean change 124.5 metres (95% CI 63.2 to 185.9) in the PR-IMT group and 96.7 metres (95% CI 59.6 to 133.7) in the PR-SHAM group). There were no significant changes in the ISWT in the control group (table 2). The improvement in ISWT was maintained 3 months after training in the PR-IMT group (579.1 (134.9) metres at the end of training and 568.8 (114.4) metres 3 months later; p = 0.121) but not in the PR-SHAM group (fig 3B). A comparison of the magnitude of the change between the end of training and 3 months after training in the two groups (−31.1 metres (95% CI −71.7 to 9.5) for the PR-IMT group and −96.3 metres (95% CI −169.4 to 23.1) for the PR-SHAM group; p = 0.07) just failed to reach statistical significance, which may be related to the fact that a further two patients withdrew from each group at this time and the sample size was thus reduced.

There were no significant differences in health status at baseline between any of the groups. Patients in the PR-IMT group had a significant improvement in the total SGRQ score (mean change −7.7 (95% CI −16.6 to 1.1)) compared with the control group (p = 0.05) that was greater than the minimum clinically important difference (4 points). Three months after the end of the programme the SGRQ score remained significantly improved compared with baseline (mean difference −10.0, 95% CI −21.3 to 1.3)). There were no significant changes in health status in the PR-SHAM group (mean change 2.3, 95% CI −2.9 to 7.4; p = 0.422 compared with the control group) at the end of the training programme despite improvements in exercise capacity.

At the end of the training programme there were no changes in 24 hour sputum volume in the PR-IMT group (mean (SD) 14.8 (12.1) ml at baseline and 10.6 (9.5) ml at the end of training; p = 0.424), the PR-SHAM group (12.4 (5.7) ml at baseline and 9.8 (6.1) ml at the end of training; p = 0.144) or in the control group (17.8 (10.1) ml at baseline and 16.9 (15.1) ml at the end of training; p = 0.386).

DISCUSSION

This is the first study to investigate the effects of exercise training in patients with bronchiectasis. It has shown that the improvements in exercise capacity are similar to those obtained after pulmonary rehabilitation in patients with COPD. Pulmonary rehabilitation, incorporating high intensity exercise training, was effective in improving both ISWT distance and endurance exercise capacity in patients with bronchiectasis. Targeted IMT resulted in significant improvements in respiratory muscle strength in the PR-IMT group but did not provide additional immediate benefit above the effects of exercise training.

The failure of IMT to enhance the magnitude of the improvements in exercise performance induced after high intensity exercise training is similar to the findings of both Berry et al[29] and Larson et al[30] in studies of patients with COPD, and may have occurred for several reasons. Firstly, the high intensity of the exercise training performed may have induced the maximum attainable benefits in exercise capacity in both the PR-IMT and PR-SHAM groups so that there was no further benefit with the addition of IMT. Indeed, the intensity of the exercise training was sufficient to induce a significant improvement in PImax even in the PR-SHAM group after training, despite there being no targeted IMT in this group. Secondly, patients had either normal or only mildly reduced inspiratory muscle strength at baseline, which suggests that functional weakness of the inspiratory muscles was not a major cause of dyspnoea. Indeed, in the study by Larson et al[30] in which no additional benefit of IMT was found in conjunction with exercise training, the baseline inspiratory muscle strength of the patients studied was also within normal limits. Finally, the low number of subjects studied may have been inadequate to demonstrate a small but significant difference between the groups. Indeed, to detect a statistically significant difference in the magnitude of the improvements in ISWT distance between PR-IMT and PR-SHAM groups would have required 59 patients in each patient group, based on the observed mean changes of 124.5 metres and 96.7 metres for the PR-IMT and PR-SHAM groups, respectively.

In the PR-IMT group the improvements in both exercise capacity and health status observed at the end of the training programme were maintained 3 months after the cessation of training, as shown previously in patients with COPD where improvements have been maintained for up to 11 months.[31–33] In contrast, the increase in exercise performance in the PR-SHAM group was not maintained, which could suggest an additive effect of IMT in the PR-IMT group. While this may relate to a decrease in the perception of dyspnoea during exercise after specific IMT,[13] this was not investigated during the present study.

We found no statistically significant changes in 24 hour sputum volume in any of the training groups, which suggests that neither exercise training nor IMT affected sputum clearance in this group of patients. While there have been no previous studies investigating the role of exercise training as an aid to sputum clearance in patients with bronchiectasis, these results are similar to those obtained by Salh et al[34] in adult patients with cystic fibrosis.

In summary, pulmonary rehabilitation resulted in improvements in health status and exercise capacity in

patients with bronchiectasis that were similar in magnitude to those in patients with COPD. IMT conferred no immediate additional benefits in terms of exercise performance but may influence the longevity of the observed training effects. These results highlight the potential role of pulmonary rehabilitation in patients with bronchiectasis, although further studies are necessary to identify the most eligible patients and to optimise the training programmes to maximise the training response and maintenance of the benefits.

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Competing interests: none.

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