

A randomized controlled trial of inspiratory muscle training in stable chronic heart failure

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Aims To assess whether a domiciliary programme of specific inspiratory muscle training in stable chronic heart failure results in improvements in exercise tolerance or quality of life.

Methods and Results We conducted a randomized controlled trial of 8 weeks of inspiratory muscle training in 18 patients with stable chronic heart failure, using the Threshold[®] trainer. Patients were randomized either to a training group inspiring for 30 min daily at 30% of maximum inspiratory mouth pressure, or to a control group of 'sham' training at 15% of maximum inspiratory mouth pressure. Sixteen of the 18 patients completed the study. Maximum inspiratory mouth pressure improved significantly in the training group compared with controls, by a

mean (SD) of 25.4 (11.2) cmH₂O ($P=0.04$). There were, however, no significant improvements in treadmill exercise time, corridor walk test time or quality of life scores in the trained group compared with controls.

Conclusion Despite achieving a significant increase in inspiratory muscle strength, this trial of simple domiciliary inspiratory muscle training using threshold loading at 30% of maximum inspiratory mouth pressure did not result in significant improvements in exercise tolerance or quality of life in patients with chronic heart failure.

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Key Words: Chronic heart failure, inspiratory muscle training, threshold loading.

Introduction

A reduction in inspiratory muscle strength is a well-established finding in chronic heart failure^[1–8] although the precise reasons for this are poorly understood. Dyspnoea is a prominent symptom in chronic heart failure and persists after patients have been established on optimal drug therapy. There is evidence suggesting that this relative inspiratory muscle weakness is part of the cause of dyspnoea on exertion in chronic heart failure. Mancini *et al.*^[3] measured the tension-time index of the diaphragm as a measure of the 'work' of breathing and Borg dyspnoea scores during cycle ergometer exercise in patients with chronic heart failure and controls. The tension-time index was found to be increased in patients with chronic heart failure and significantly correlated with dyspnoea scores. In normal subjects, experiments with inspiratory resistive loading have shown that dyspnoea is proportional to load, and at any

given load is worse in subjects with a low maximal inspiratory mouth pressure^[9].

Specific inspiratory muscle training has been shown to increase indices of inspiratory muscle strength in normal subjects^[10–12] and is now widely used as part of pulmonary rehabilitation programmes for patients with chronic obstructive pulmonary disease. There are varying reports of the success of inspiratory muscle training in reducing exertional dyspnoea and improving exercise tolerance in chronic obstructive pulmonary disease, some show no significant benefit^[13,14] and others show significant benefits^[15–17].

There is to date only one published study of inspiratory muscle training in chronic heart failure^[18] which showed significant benefit in terms of improved 6 min walk test time, and an increase in peak oxygen uptake on exercise. The 'drop-out' rate in this trial was high owing to the intensity and time commitment of the training programme. The trial was also not properly controlled, with those subjects failing to complete the training programme serving as a 'comparison' group. We have therefore conducted a randomized controlled trial of simple domiciliary inspiratory muscle training using the Threshold[®] trainer (Healthscan Products Inc., New Jersey, U.S.A.) in patients with stable chronic heart failure.

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Methods

Patient population

Eighteen patients (three female) with stable chronic heart failure were recruited into the study. All were taking loop diuretics and angiotensin converting enzyme inhibitors, and had been clinically stable for at least 2 months prior to enrolment in the study. All had normal serum potassium levels at the start of the study: mean (SD) concentration was 4.5 (0.6) mmol.l⁻¹. Mean (SD) age was 66.5 (5.6) years. Twelve subjects were in New York Heart Association (NYHA) functional class 2 and six were in class 3. All had echocardiographic evidence of left ventricular dysfunction. The mean (SD) left ventricular diastolic diameter was 6.1 (0.7) cm. The aetiology of chronic heart failure was ischaemic in 16 cases, hypertensive heart disease in one case and atrial septal defect in one case. Five subjects had undergone previous coronary artery bypass grafting and one subject had well controlled non-insulin dependent diabetes. None had evidence of chronic obstructive pulmonary disease either clinically or on pulmonary function testing, none were current smokers and eight were ex-smokers.

All subjects gave written informed consent to the study, and ethical approval was obtained from the University Hospital of Nottingham Ethics Committee.

Baseline investigations

The following investigations were performed within one week before starting inspiratory muscle training.

Pulmonary function tests. Spirometry was performed using a dry bellows Spirometer (Vitalograph, Buckingham, U.K.) and lung volumes were measured using the helium dilution method (P. K. Morgan, Kent, U.K.). Reference values approved by the European Respiratory Society were used^[19].

Maximum inspiratory mouth pressure. Using the portable PImax analyser[®] device (P. K. Morgan, Kent, U.K.) subjects were seated wearing a noseclip and breathing through a flanged mouthpiece. Repeated maximal inspiratory manoeuvres at functional residual capacity were made until two maximal values were obtained within 10% of one another.

Treadmill exercise test. Subjects walked on a treadmill according to a modified Bruce protocol. The speed and slope of the treadmill was increased at intervals of 3 min in the following stages: stage 1, 2.7 km . h⁻¹, 0°; stage 2, 2.7 km . h⁻¹, 1.3°; stage 3, 2.7 km . h⁻¹, 2.6°; stage 4, 2.7 km . h⁻¹, 4.3°; stage 5, 4.0 km . h⁻¹, 5.4°; stage 6, 5.4 km . h⁻¹, 6.3°. Test duration was measured in seconds. Blood pressure was measured using cuff sphygmomanometry during each stage and electrocardiographic monitoring was continuous throughout the test.

All subjects had previously had experience of walking on a treadmill and were familiar with the protocol.

Corridor walk test. Subjects walked a flat 100 m course according to the protocol described and validated by Bassey *et al.*^[20]. Subjects walk the course at three self-selected speeds; slowly, normal walking pace and hurrying but without overexerting. At the end of each 100 m walk the time to complete the walk is measured in seconds and dyspnoea is assessed according to the scale of Borg^[21].

Quality of life score. Subjects completed a disease-specific questionnaire developed for use in chronic heart failure and validated previously by our group^[22]. The questionnaire consists of 16 questions about the potential impact of chronic heart failure in five areas: mobility, home management, social activities, emotional state and general symptoms. Each question has seven graded responses (1=severe impact, 7=no impact) and the result can either be expressed as a total score, or (if patients have left questions unanswered) as a mean score per question.

Inspiratory muscle training protocol

The commercially available portable Threshold[®] trainer was used for inspiratory muscle training. The device contains a spring-loaded valve, attached to a mouthpiece through which subjects inspire while wearing a noseclip. The threshold opening pressure of the valve can be increased or decreased by compressing or decompressing the spring, respectively. A scale of threshold pressure in cmH₂O is marked on the device. This device has been validated both by our group^[23] and others^[24] is widely used for inspiratory muscle training in chronic obstructive pulmonary disease. Subjects are instructed to inspire for 15 min twice daily through the device, at a threshold pressure which is set under medical supervision. It has been shown elsewhere^[15,16] that the threshold pressure must be set at 30% of maximal inspiratory mouth pressure or higher for individual subjects to achieve significant improvements in inspiratory muscle strength.

All subjects had a one-week run-in period with the trainers set at the lowest level possible to accustom themselves to the device, and were then randomized either to a training group with their trainers set at 30% maximal inspiratory mouth pressure, or to a control 'sham' training group with their trainers set at 15% maximal inspiratory mouth pressure. The trial was single-blind with patients unaware of which group they were in.

Both groups inhaled through their Threshold[®] trainers for 15 min twice daily for at least 8 weeks, and kept a diary card. All were reviewed at weekly intervals by one investigator (P.H.J.) who checked the diary card and measured their maximal inspiratory mouth pressure each time. In the training group, some subjects were

unable to manage the required pressure in the first week and their threshold pressure levels were adjusted upwards in increments to achieve at least 30% maximal inspiratory mouth pressure. All subjects in the training group then trained at the full 30% for at least 6 weeks. As their maximal inspiratory mouth pressure rose during the duration of the trial, the threshold pressure was also raised to ensure that it stayed at 30% maximal inspiratory mouth pressure. In the control group the threshold pressure was set at 15% maximal inspiratory mouth pressure at the start of the trial and not raised.

Statistical analysis

Results obtained before and after the training period in the training and control groups were compared using Wilcoxon's rank sum tests. The level of statistical significance was taken as $P < 0.05$.

Results

Sixteen of the 18 patients completed the study. One patient in the control group died suddenly at home 2 days after randomization, and one patient in the training group was withdrawn 6 weeks after randomization due to the development of musculoskeletal chest pain when inhaling through the Threshold[®] trainer. No changes to medication were required during the trial in any of the patients. Two patients (one in the training group and one control) developed upper respiratory tract infections during the course of the trial necessitating a break from inspiratory muscle training and prolongation of their training period by 2 weeks.

Table 1 shows patient details and baseline values in the training and control groups. None of the differences in mean values between the groups are statistically significant when compared using Wilcoxon's rank sum tests. Table 2 shows the mean changes in treadmill exercise time, quality of life scores, corridor walk test times with Borg dyspnoea scores and maximal inspiratory mouth pressure in each group. Maximal inspiratory mouth pressure increased significantly in the trained group compared with the control group (by 25.4 cmH₂O against 12.3 cmH₂O, $P = 0.04$). Figure 1 shows the change in treadmill exercise time plotted against the increase in maximal inspiratory mouth pressure for all 16 patients who completed the study. There is no difference between the trained and control groups and no correlation, with an r value of 0.37 for the trained group and 0.36 for controls.

Discussion

This randomized controlled trial of inspiratory muscle training in stable chronic heart failure showed no signifi-

Table 1 Baseline values in the training and control groups. Values are shown as means (SD)

Parameter	Training group (n=9)	Control group (n=9)
Age (years)	70.0 (4.6)	63.4 (4.5)
LVDd (cm)	6.01 (0.69)	6.10 (0.77)
FEV ₁ (percent predicted)	101 (20)	91 (21)
FER (%)	74 (10)	73 (9)
TLC (percent predicted)	94 (12)	88 (10)
ETT (s)	542 (383)	543 (287)
QoL score	5.3 (0.9)	4.6 (0.8)
CWT: slow speed (s)	93.5 (16.4)	96.5 (25.7)
Borg dyspnoea score	8.9 (1.9)	8.8 (1.9)
CWT: normal speed (s)	79.8 (12.3)	76.1 (11.2)
Borg dyspnoea score	10.7 (1.9)	10.4 (1.8)
CWT: fast speed (s)	66.1 (11.5)	66.8 (20.2)
Borg dyspnoea score	12.8 (2.3)	13.1 (2.4)
MIP (cmH ₂ O)	70 (33)	84 (18)

LVDd=left ventricular diastolic diameter; FEV₁=forced expiratory volume in one second; FER=forced expiratory ratio (i.e. ratio of FEV₁: forced vital capacity); TLC=total lung capacity; ETT=exercise tolerance test measured using modified (Bruce) treadmill protocol; QoL=quality of life. Result is expressed as a mean score per question from 16 questions, as described in the Methods section; CWT=corridor walk test: time in seconds to walk 100 m; MIP=maximum inspiratory mouth pressure.

cant improvements in exercise tolerance or quality of life after a supervised 8-week domiciliary inspiratory muscle training programme.

Our results are not in agreement with those of Mancini *et al.*^[18], although there are important differences between the two studies which may explain this. Firstly it is possible that our inspiratory muscle training programme was not intensive enough. The training load of 30% maximal inspiratory mouth pressure was ascertained in patients with chronic obstructive pulmonary disease^[15,16], and it may be that a higher percentage than this is required for patients with chronic heart failure. Mancini *et al.*^[18] trained their subjects using three different types of inspiratory muscle training exercises. The regime was, however, hospital-based and six out of 14 subjects did not complete the programme. We chose a training load of 30% of maximal inspiratory mouth pressure for several reasons. The 30% level has been validated in breathless patients^[15,16] and is a realistic target for patients to achieve. In addition it was the level chosen by Mancini *et al.*^[18] for threshold loading in their inspiratory muscle training protocol. Another factor to consider is that although the starting maximal inspiratory mouth pressure values between the two groups did not differ significantly, the mean starting maximal inspiratory mouth pressure in the trained group was lower than controls and the final (post-training) maximal inspiratory mouth pressure between the two groups was therefore similar. This may also account for a lack of significant improvement in symptoms in the training group. Some of our subjects did not have a particularly low initial maximal inspiratory mouth pressure and a

Table 2 Mean (SD) changes from baseline values in training and control groups at the end of an eight-week inspiratory muscle training programme, for the eight patients in each group who completed the training programme

Parameter	Training group (n=8)	Control group (n=8)	P value
ETT (s)	+152 (144)	+82 (118)	ns
QoL score	+0.55 (0.48)	+0.06 (0.38)	ns
CWT: slow speed (s)	-3.8 (9.5)	-4.1 (16.3)	ns
Borg dyspnoea score	-1.2	+0.4	ns
CWT: normal speed (s)	-4.4	+1.5	ns
Borg dyspnoea score	-0.5	-0.1	ns
CWT: fast speed (s)	-6.3	-4.1	ns
Borg dyspnoea score	-1.3	+0.2	ns
MIP (cmH ₂ O)	+25.4 (11.2)	+12.3 (12.1)	0.04*

ETT=exercise tolerance test measured using modified (Bruce) treadmill protocol; QoL=quality of life. Result is expressed as a mean score per question from 16 questions, as described in the Methods section; CWT=corridor walk test: time to walk 100 m at three self-selected speeds, with Borg dyspnoea scores. MIP=maximum inspiratory mouth pressure. ns=non-significant ($P>0.05$). *=significant at $P<0.05$ level.

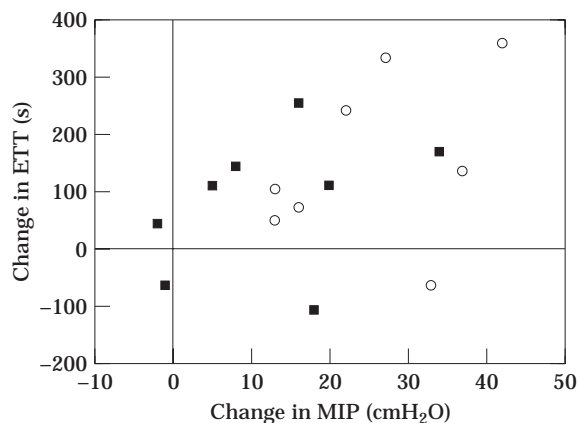


Figure 1 Graph showing change in exercise tolerance plotted against change in inspiratory muscle strength for all 16 subjects who completed the trial. ETT=exercise tolerance test. MIP=maximum inspiratory mouth pressure. Open circles=trained group. Closed squares=control group. For r values see text.

trial of inspiratory muscle training in a group with more severe inspiratory muscle weakness may be worthwhile.

Secondly it is possible that inspiratory muscle training in chronic heart failure is not an effective therapeutic measure. The lack of correlation in our study between increase in maximal inspiratory mouth pressure and change in treadmill exercise time would support this. While we documented some surprisingly large increases in treadmill exercise time in this study, there were no improvements in corridor walk test times or dyspnoea scores, which may be more relevant to patients in their activities of daily living. Our study had 80% power to show a 10% improvement in quality of life scores or corridor walk times. In chronic obstructive pulmonary disease, trials of inspiratory muscle training have produced varying results (as mentioned in the

Introduction section) but a meta-analysis^[25] of inspiratory muscle training in chronic obstructive pulmonary disease led the authors to conclude that there was 'little evidence of clinically important benefit to patients with chronic obstructive pulmonary disease'.

Thirdly we must consider the possibility that the sham training performed by our control group did in fact have a training effect, resulting in no significant differences between the training and control groups. We would regard this as unlikely as the increases in maximal inspiratory mouth pressure in the control group were varied and generally small, probably representing a learning effect. We used a sham training group as a control, rather than a control group in whom no action was taken because of the placebo effect of regular visits to a specialist centre while participating in clinical trials. Our trial was designed so that the only difference between the two groups was the training load. We assessed compliance with the training programme by means of diary cards: the significant rise in maximal inspiratory mouth pressure provides evidence of adequate adherence to the programme.

One further issue to address is that of blinding. The study was single blind but it is virtually impossible to blind patients completely during a form of exercise programme. Some patients in the control group may have realised that the intensity of their inspiratory muscle training was low.

A recent further report by Mancini's group^[26] sheds further light on the subject: diaphragm biopsies from transplant recipients (compared with previously healthy organ donors as controls) show biochemical and histochemical changes of increased oxidative metabolism, compatible with endurance changes. This would imply that the diaphragm may already be endurance trained in subjects with chronic heart failure, and that further training may therefore be fruitless, as borne out by our study.

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