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High-intensity inspiratory muscle training in COPD

K. Hill*,#,f, S.C. Jenkins#,¶,f, D.L. Philippe*, N. Cecins#,¶,f, K.L. Shepherd*, D.J. Green+, D.R. Hillman* and P.R. Eastwood*,§,f

ABSTRACT: The aim of the present study was to investigate the effects of an interval-based high-intensity inspiratory muscle training (H-IMT) programme on inspiratory muscle function, exercise capacity, dyspnoea and health-related quality of life (QoL) in subjects with chronic obstructive pulmonary disease.

A double-blind randomised controlled trial was performed. Sixteen subjects (11 males, mean forced expiratory volume in one second (FEV_1) 37.4±12.5%) underwent H-IMT performed at the highest tolerable inspiratory threshold load (increasing to 101% of baseline maximum inspiratory pressure). Seventeen subjects (11 males, mean FEV_1 36.5±11.5%) underwent sham inspiratory muscle training (S-IMT) at 10% of maximum inspiratory pressure. Training took place three times a week for 8 weeks and was fully supervised. Pre- and post-training measurements of lung function, maximum inspiratory pressure, maximum threshold pressure, exercise capacity, dyspnoea and QoL (Chronic Respiratory Disease Questionnaire; CRDQ) were obtained.

H-IMT increased maximum inspiratory pressure by 29%, maximum threshold pressure by 56%, 6-min walk distance by 27 m, and improved dyspnoea and fatigue (CRDQ) by 1.4 and 0.9 points per item, respectively. These changes were significantly greater than any seen following S-IMT.

In conclusion, high-intensity inspiratory muscle training improves inspiratory muscle function in subjects with moderate-to-severe chronic obstructive pulmonary disease, yielding meaningful reductions in dyspnoea and fatigue.

KEYWORDS: Chronic obstructive pulmonary disease, inspiratory muscle training

Several studies have investigated the effects of inspiratory muscle training (IMT) on pulmonary function, inspiratory muscle function, exercise capacity, dyspnoea and health-related quality of life (QoL) in subjects with chronic obstructive pulmonary disease (COPD) [1–9]. However, results have been mixed due to differences in study designs, subject selection, assessment tools and training protocols. A recent meta-analysis of randomised controlled trials of IMT in COPD concluded that improvements in inspiratory muscle function and dyspnoea occur following such training. However, the effects on exercise capacity and QoL remain unclear [7] and, subsequently, debate still exists on the role, if any, IMT may play in the rehabilitation of COPD subjects. Currently, IMT is not recommended as a standard component of a pulmonary rehabilitation programme [10–12].

An optimal IMT protocol for COPD subjects has yet to be defined. To date, most studies have applied training programmes characterised by repeated inspiratory efforts against sub-maximal workloads, prolonged training periods and slow progression of training loads [13, 14]. Most IMT studies achieve loads equivalent to <75% of the baseline maximum inspiratory pressure [1, 3, 4, 8, 15–20]. Attaining greater loads may be beneficial as it appears improvements in inspiratory muscle function are dependent on the magnitude of the inspiratory load, with more substantial gains achieved in subjects training at higher loads [15, 21]. Furthermore, greater improvements in dyspnoea and exercise capacity may be possible following IMT programmes that achieve larger gains in inspiratory muscle function [14, 15]. In COPD subjects, achieving very high training loads is difficult with continuous-based training programmes, probably due to the onset of intolerable dyspnoea [22]. In contrast, interval-based training programmes offer the opportunity for COPD subjects to potentially achieve very high training loads with less dyspnoea [23]. The current authors recently demonstrated the feasibility of interval-based high-intensity IMT (H-IMT) in subjects with moderate-to-severe COPD [24].

The primary objective of the current study was to determine the effect of H-IMT on inspiratory

AFFILIATIONS
Depts of *Pulmonary Physiology and, #Physiotherapy, Sir Charles Gairdner Hospital, and ¶Asthma and Allergy Research Institute, and +School of Human Movement and Exercise Science, and, §School of Anatomy and Human Biology, University of Western Australia, Nedlands, and fSchool of Physiotherapy, Curtin University of Australia, Bentley, Australia.

CORRESPONDENCE
P.R. Eastwood
Dept of Pulmonary Physiology
Sir Charles Gairdner Hospital
Hospital Avenue
Nedlands
Western Australia
6009 Australia
Fax: 61 893462034
E-mail: peter.eastwood@health.wa.gov.au

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muscle function, exercise capacity, dyspnoea and QoL in a COPD population. It was hypothesised that H-IMT would allow a very high training load to be tolerated, yielding rapid, pronounced gains in inspiratory muscle strength and endurance, reductions in dyspnoea and improvements in exercise capacity and QoL in subjects with moderate-to-severe COPD.

METHODS

Subjects

Subjects who had a diagnosis of COPD, a smoking history >10 pack-yrs and a forced expiratory volume in one second (FEV_1) ranging 15–70% of predicted normal were recruited. Exclusion criteria included: 1) comorbid conditions likely to reduce exercise capacity (*e.g.* symptomatic ischaemic heart disease, body mass index (BMI) >35 $kg \cdot m^{-2}$); 2) previous lung surgery; 3) use of long-term oxygen therapy; and 4) weaning doses of oral corticosteroids. The study was approved by the appropriate ethics committees and informed consent was obtained. Subjects were recruited from referrals to pulmonary rehabilitation programmes and in response to local advertising.

In total, 55 subjects (34 males) were screened for suitability to participate in the study. Of these, 17 were excluded during the ''screening and familiarisation'' phase: nine could not complete the assessments due to comorbid conditions or intercurrent illness; six did not meet inclusion criteria based on formal lung function testing; and two had a BMI >35 $kg \cdot m^{-2}$. Three subjects withdrew of their own accord during the screening and familiarisation phase. The majority of those who were excluded or withdrew during the screening and familiarisation phase were recruited from the general community in response to local advertisements and were not under the care of a respiratory physician. A total of 35 subjects were randomised to receive either H-IMT or sham IMT (S-IMT).

Study design

A prospective, double-blind, randomised, controlled design was used with a treatment group undergoing 8 weeks of H-IMT and a control group undergoing 8 weeks of S-IMT (fig. 1). Prior to randomisation, all subjects entered a 2-week screening and familiarisation phase, during which time baseline measurements were recorded: 1) resting lung function; 2) inspiratory muscle strength and endurance; 3) exercise capacity; 4) dyspnoea; and 5) QoL. To account for any improvements due to familiarisation [26], assessments of inspiratory muscle strength and endurance were performed on four separate occasions (>24 h apart) with the best test result recorded as the baseline measure. Subjects were allocated to H-IMT or S-IMT groups according to a computer-generated, random number sequence with randomisation stratified for sex and severity of airflow obstruction. On completion of the 8-week training period, measurements were repeated in both groups.

Blinding

Neither the investigator responsible for the collecting the pre- and post-training data nor the subjects were aware of whether an individual had been allocated to the H-IMT or S-IMT group. Blinding of subjects was maintained throughout the study by ensuring H-IMT and S-IMT groups trained at different times. Subject training and assessments were performed by different investigators.

Training device and protocols

Subjects attended supervised training sessions three times per week for 8 weeks. Each session lasted 21 min and comprised seven cycles of 2 min of breathing on an inspiratory threshold loading device (Threshold IMT; Respironics, Cedar Grove, NJ, USA) followed by 1 min of rest. The threshold training device was modified to allow imposition of loads as large as -103 cmH_2O (for H-IMT) and as small as -3 cmH_2O (for S-IMT; fig. 2). H-IMT was performed at the maximum load tolerable for each 2-min work interval and was progressively increased over the training period [24]. S-IMT was prescribed at 10% of baseline maximum peak inspiratory mouth pressure ($P_{I,max}$), and remained at this level during all training sessions. Throughout training, subjects were permitted to choose their own breathing pattern. Inspiratory mouth pressure was continuously recorded (PowerLab/8sp; ADInstruments Pty Ltd, Castle Hill, NSW, Australia) and the pressure–time integral (area subtended by the pressure–time curve; $\int Pdt$) [27] was calculated for every training session in each subject.

Measurements

Resting lung function

Measurements of the following were obtained: 1) lung volumes (Medgraphics Elite Series DX plethysmograph; Medical Graphics Corporation, St Paul, MN, USA); 2) FEV_1, forced vital capacity (digital pneumotachograph, Vertek Series; Hewlett-Packard, Palo Alto, CA, USA); and 3) single-breath diffusing capacity for carbon monoxide (P.K. Morgan Ltd, Chatham, UK).

Inspiratory muscle strength

The $P_{I,max}$ generated against an occluded airway (differential pressure transducer; Honeywell, Morristown, NJ, USA) was measured from functional residual capacity (FRC) [27]. Upon each testing occasion, the highest $P_{I,max}$ within 5% of two others was recorded.

Care was taken to ensure that measurements of $P_{I,max}$ were taken at similar end-expiratory lung volumes. In addition to the measurement of FRC before and after the training period (see Resting lung function), end-expiratory lung volumes were monitored *via* measurements of inspiratory capacity [28] and *via* respiratory inductance pneumography (Respitrace Corporation, Ardsley, NY, USA) [25, 29] during both the fourth pre-training and the post-training assessment sessions. Only $P_{I,max}$ measures collected during these assessment sessions were included in the analyses.

Inspiratory muscle endurance

Inspiratory muscle endurance was assessed *via* a progressive loading protocol [30], which required subjects to breathe against threshold loads [31, 32] that were increased each minute by 10% of baseline $P_{I,max}$ until voluntary task failure. Standard verbal encouragement was provided throughout. Inspiratory muscle endurance was defined as the maximum threshold pressure ($P_{th,max}$) sustained for a minimum of 30 s [25]. Subjects were seated, wore a nose-clip, and were permitted to choose their own breathing pattern. Mouth pressure (differential pressure transducer; Honeywell), inspiratory flow and volume (Fleisch 2 pneumotachograph and differential pressure transducer; Validyne Engineering,

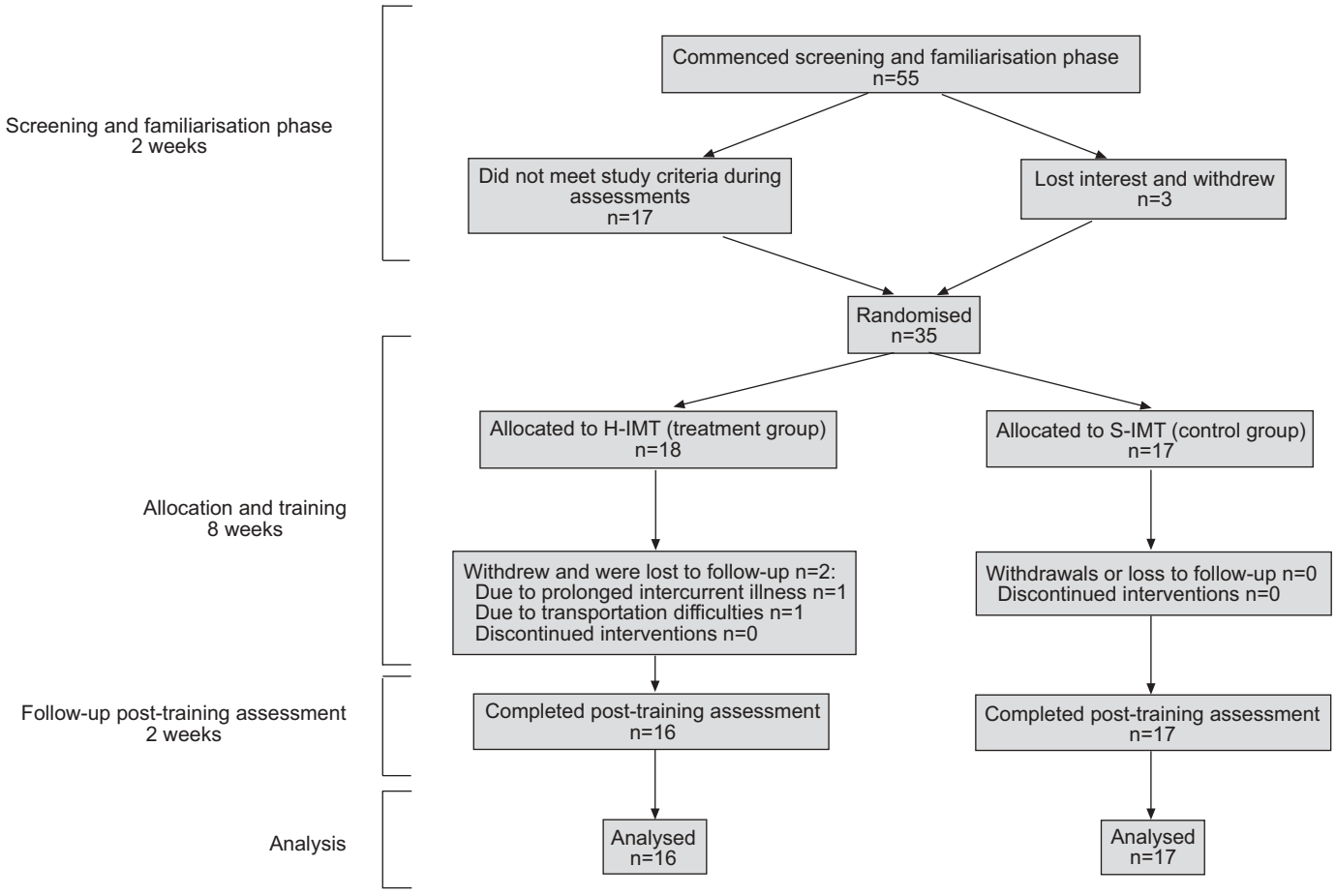

FIGURE 1. Study design and allocation of subjects according to the Consolidated Standards of Reporting Trials guidelines [25]. H-IMT: high-intensity inspiratory muscle training; S-IMT: sham inspiratory muscle training.

Northridge CA, USA) were continually recorded (Powerlab/16s; ADInstruments Pty Ltd). Dyspnoea and respiratory effort scores (modified Borg category ratio scale) were recorded on completion of the test [33].

Whole-body exercise capacity

Exercise capacity was assessed *via* a cycle ergometry test and 6-min walk test (6MWT). Scores for dyspnoea were recorded every minute throughout both tests. On completion of each test, scores for dyspnoea and leg fatigue were obtained [33].

The symptom-limited cycle ergometry test was performed on an electronically braked bicycle ergometer (ER 900; Jaeger, Hoechberg, Germany). Work rate was increased by 10 $W \cdot min^{-1}$ until voluntary cessation. Throughout the test, breath-by-breath measurements of ventilation, breathing pattern and gas exchange were collected using an automated exercise metabolic system (Medgraphics CardiO2; Medical Graphics Corporation).

The 6MWT was performed in accordance with current recommendations [34], but modified to include the following throughout: 1) standardised encouragement every 15 s during rest periods to continue walking when able; and 2) monitoring of arterial oxygen saturation by pulse oximetry (S_{p,O_2}; Ohmeda 3700; GE Healthcare, Louisville, CO, USA) and heart rate (Polar a1 heart rate monitor; Polar Electro Oy, Kempele, Finland). On each occasion, two tests were performed, separated by 30 min, with the greatest 6-min walk distance (6MWD) recorded. In the event that S_{p,O_2} decreased to <80% during a test, the investigator instructed the subject to rest until S_{p,O_2} had increased to >80%. The test was then continued. Data from tests obtained in subjects demonstrating arterial oxygen desaturation <80% were excluded from subsequent analyses.

Health-related QoL

This was assessed *via* the Chronic Respiratory Disease Questionnaire (CRDQ), which was administered *via* interview [35]. The CRDQ assessed four domains: 1) dyspnoea during activities of daily living (ADL); 2) fatigue; 3) mastery; and 4) emotional function. Subjects were required to answer between four and seven questions (items) within each domain. Overall QoL score was defined as the average score from all items. Domain-specific scores were defined as the average score from all items within that domain. During post-training interviews, subjects were informed of their pre-training responses [36].

Statistical analyses

Baseline measurements were compared between groups using unpaired t-tests or Chi-squared tests. Pre- and post-training differences between H-IMT and S-IMT groups were analysed

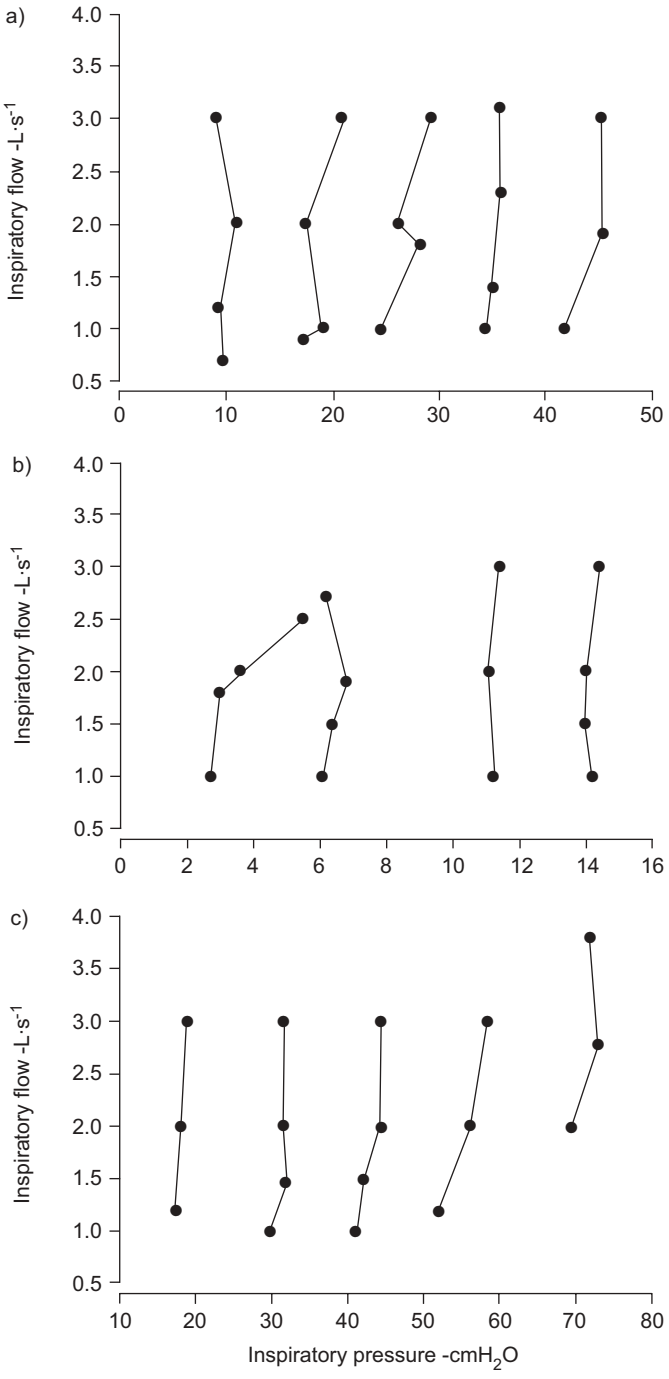

FIGURE 2. Pressure–flow characteristics of the inspiratory muscle training device using a) the manufacturer's spring, b) a spring of weaker tension than that supplied by the manufacturer, and c) a spring of heavier tension than that supplied by the manufacturer. Only at very low inspiratory pressures (<-4 cmH_2O) was pressure and flow dependence noted, *i.e.* at inspiratory flow rates >1.7 $L \cdot s^{-1}$.

using two-way repeated measures of ANOVA. Pre- and post-training differences within H-IMT and S-IMT groups were analysed using paired t-tests. A p-value $\leqslant 0.05$ was considered significant. Initial analyses for sample size and statistical power were based on the results from the pulmonary rehabilitation programme conducted at Sir Charles Gairdner Hospital (Nedlands, WA, Australia), pilot studies and data available in the literature.

RESULTS

In total, 35 subjects were randomised to H-IMT or S-IMT. Two subjects (allocated to the H-IMT group) withdrew during the study (one due to prolonged intercurrent illness and one to transportation difficulties). Results are presented for the 33 subjects (22 males) who completed the study.

Baseline characteristics

There were no significant differences between the H-IMT and S-IMT groups in baseline measures of resting lung function, inspiratory muscle function, exercise capacity, dyspnoea and QoL (tables 1–3).

Familiarisation

With H-IMT and S-IMT groups considered together, during the screening and familiarisation phase, $P_{I,max}$ and $P_{th,max}$ increased by 22% ($p<0.001$) and 56% ($p<0.001$), respectively. $P_{I,max}$ expressed as a percentage of the predicted normal value [41] increased from 65±20 to 81±26% ($p<0.001$). $P_{th,max}$ expressed as a proportion of $P_{I,max}$ ($P_{th,max}/P_{I,max}$) increased from 49±22 to 61±17% ($p=0.001$).

Training load

Over the 8-week period, the training load for the H-IMT group increased from 45±13% (session 1) to 101±26% (session 24) of baseline $P_{I,max}$ ($p<0.001$; fig. 3). When expressed in terms of the $\int Pdt$ during each training session, training load increased from 8,265±3,218 to 11,432±5,291 $cmH_2O \times s$ ($p=0.037$).

In the S-IMT group, the inspiratory load remained unchanged over the 8-week training period, being 14±4% (session 1) and 11±3% (session 24) of baseline $P_{I,max}$. The $\int Pdt$ during the S-IMT decreased over the training period from 2,420±786 to 2,017±624 $cmH_2O \cdot s$ ($p=0.035$).

Training effects

Measurements obtained before and after training in the H-IMT and S-IMT groups are presented in tables 1–3 and summarised as follows.

Resting lung function

With the exception of a 90-mL decrease in FEV_1 in the S-IMT group ($p=0.023$), no changes were observed in any measure of pulmonary function. Inspiratory capacity was unchanged over the 8-week training period in both groups.

Inspiratory muscle strength and endurance

In the H-IMT group, $P_{I,max}$ and $P_{th,max}$ increased by 29% ($p<0.001$) and 56% ($p<0.001$), respectively. $P_{th,max}/P_{I,max}$ increased from 63 to 75% ($p=0.01$). Following S-IMT, $P_{I,max}$ increased by 8% ($p=0.023$), while $P_{th,max}$ and $P_{th,max}/P_{I,max}$ remained unchanged.

Notably, the magnitude of the observed increases in $P_{I,max}$ ($p=0.002$), $P_{th,max}$ ($p<0.001$) and $P_{th,max}/P_{I,max}$ ($p=0.012$) were greater in the H-IMT group when compared with changes seen following S-IMT.

TABLE 1 Subject anthropometrics and the effects of training on resting lung function

	H-IMT		S-IMT	
	Baseline	Post-training	Baseline	Post-training
Anthropometrics				
Male/female n	11/5		11/6	
Age yrs	69.4±7.2		66.6±9.8	
BMI kg·m^{-2}	24.9±4.3		24.1±3.7	
Current smokers n	4		3	
Resting lung function				
FEV_1 L	1.0±0.4	1.0±0.4	1.1±0.5	1.0±0.4*
FEV_1 % pred^{+}	37.4±12.5	35.7±12.7	36.5±11.5	32.6±9.2*
FEV_1/FVC	38.7±9.3	38.1±9.3	37.2±10.4	37.5±12.8
FVC L	2.7±0.7	2.6±0.7	2.8±0.9	2.6±0.9
FVC % pred$^{\#}$	71.1±15.3	69.0±16.4	73.9±15.6	66.8±15.6
FRC L	4.9±1.3	4.7±0.9	5.3±1.4	5.2±1.3
FRC % pred$^{\#}$	151.4±42.4	144.6±30.1	158.6±30.3	156.2±27.4
TLC L	7.2±1.3	7.0±1.1	7.4±1.8	7.2±2.2
TLC % pred	117.8±19.3	116.0±17.7	118.1±16.2	114.9±23.6
RV L	4.2±1.2	4.1±0.9	4.2±1.3	4.3±1.3
RV % pred$^{\#}$	179.0±60.9	174.0±46.7	178.7±48.2	183.6±46.8
$D_{L,CO}$ mL·min^{-1}·mmHg^{-1}	9.2±3.3	9.2±3.6	10.5±3.5	10.0±3.4
$D_{L,CO}$ % pred$^{\#}$	33.5±12.1	33.4±12.7	36.3±8.6	34.3±7.9

Data are presented as mean±SD, unless otherwise stated. H-IMT: high-intensity inspiratory muscle training; S-IMT: sham inspiratory muscle training; BMI: body mass index; FEV_1: forced expiratory volume in one second; % pred: per cent of predicted; FVC: forced vital capacity; FRC: functional residual capacity; TLC: total lung capacity; RV: residual volume; $D_{L,CO}$: single-breath diffusing capacity for carbon monoxide. $^{\#}$: predicted normal values derived from [37–39]. *: $p<0.05$ compared with baseline measures. 1 mmHg=0.133 kPa.

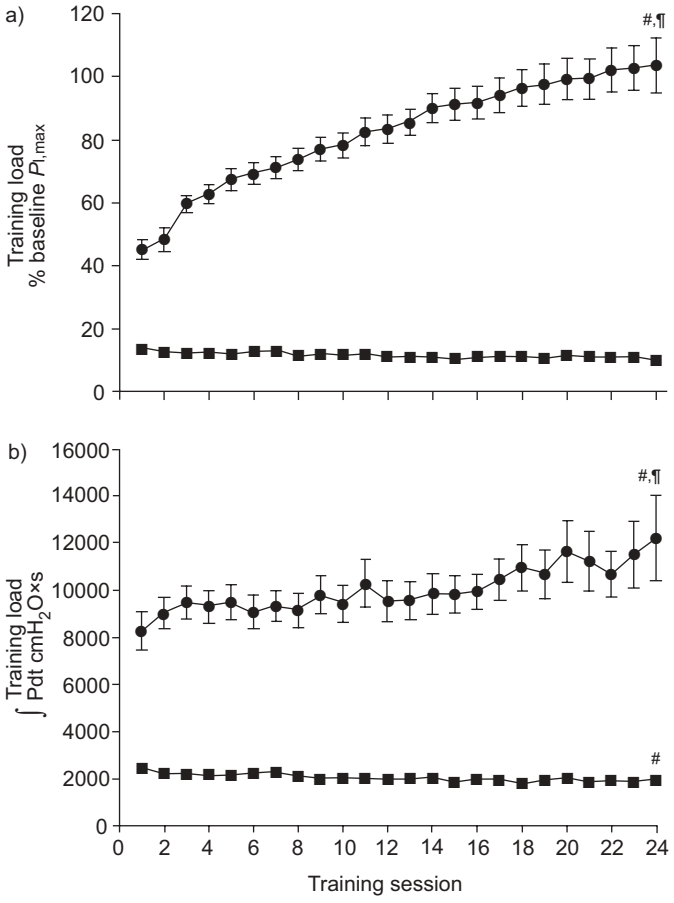

FIGURE 3. Change in inspiratory threshold training load (mean±SEM). Training load expressed as a percentage of the baseline maximum inspiratory pressure (a) and pressure–time integral ($\int$Pdt) (b) over 24 training sessions. $P_{I,max}$: peak inspiratory mouth pressure. ●: high-intensity inspiratory muscle training; ■: sham inspiratory muscle training (S-IMT). $^{\#}$: $p<0.05$ *versus* training session 1; ¶: $p<0.05$ *versus* S-IMT.

Exercise capacity

The maximum work rate achieved during cycle ergometry testing remained unchanged in both groups. No between-group differences were observed in any cardiopulmonary measure collected at maximum work rate.

Sub-maximal cardiopulmonary responses were compared between pre- and post-training cycle ergometry tests at 50% of the maximum work rate achieved during the baseline assessment. No significant differences between the groups were observed in any cardiopulmonary measure.

Data from three subjects randomised to the H-IMT group and one to the S-IMT group were excluded from the 6MWD analyses due to arterial oxygen desaturation. In the remaining subjects, 6MWD increased by 27 m in the H-IMT group ($p<0.001$) and was unchanged in the S-IMT group. Compared with S-IMT, the magnitude of the change in 6MWD was greater following H-IMT ($p=0.018$).

Health-related QoL

Overall QoL scores improved by 0.8 and 0.4 points per item in the H-IMT group and the S-IMT group, respectively (table 2). The magnitude of change was not different between the groups. Following H-IMT, improvements were seen in all four domains of the CRDQ ($p<0.02$). Following S-IMT, improvements were seen in dyspnoea during ADL ($p<0.001$) and mastery ($p=0.043$). Compared with S-IMT, the magnitude of the improvement in dyspnoea during ADL ($p=0.026$) and fatigue ($p=0.01$) was greater following H-IMT.

DISCUSSION

The present study has demonstrated that in subjects with moderate-to-severe COPD, 8 weeks of interval-based H-IMT yields significant improvements in inspiratory muscle strength, inspiratory muscle endurance, dyspnoea during ADL and fatigue, with modest gains in functional exercise capacity. When compared with previous studies of IMT in COPD, this study has employed a novel, particularly rigorous methodology. First, the study was double-blind, adequately powered to detect changes in inspiratory muscle function, dyspnoea and 6MWD, with well-matched treatment and control groups. Secondly, great care was taken to ensure familiarisation with assessments of inspiratory muscle function and the 6MWT prior to initiating training. Thirdly, the training programme was fully supervised, thereby ensuring compliance and employed regular increases in training load. Fourthly, the length of each training session (21 min), and

TABLE 2 The effects of training on inspiratory muscle function and health-related quality of life

	H-IMT[#]		S-IMT[¶]	
	Baseline	Post-training	Baseline	Post-training
Inspiratory muscle function				
$P_{I,max}$ -cmH_2O	62.7±16.5	80.7±17.8*,§	66.5±19.0	71.7±18.7*
$P_{I,max}$ % predicted	79.4±26.4	101.3±25.6*,§	83.4±26.6	89.7±24.7*
$P_{th,max}$ -cmH_2O	38.5±9.7	60.1±18.0*,§	40.5±18.3	42.8±18.6
$P_{th,max}/P_{I,max}$	62.9±13.4	75.0±15.5*,§	61.8±20.4	58.7±16.7
Dyspnoea at end of PTL	5.2±2.9	5.2±2.6	5.5±3.2	5.4±3.6
Respiratory effort at end of PTL	6.3±2.1	6.0±2.6	6.5±2.6	7.3±2.5*
Inspiratory capacity L	1.8±0.3	2.0±0.4	1.7±0.6	1.8±0.7
Health-related quality of life[+]				
Total score	4.5±0.9	5.3±0.7*	4.1±1.0	4.5±0.9*
Dyspnoea	3.4±1.1	4.9±0.7*,§	2.8±0.8	3.7±1.0*
Fatigue	3.9±0.9	4.8±0.8*,§	3.7±1.0	4.0±1.0
Emotional function	5.1±1.0	5.6±0.8*	4.6±1.2	4.9±1.2
Mastery	5.0±1.1	5.7±0.8*	4.8±1.5	5.3±1.3*

Data are presented as mean±SD. H-IMT: high-intensity inspiratory muscle training; S-IMT: sham inspiratory muscle training; $P_{I,max}$: maximum inspiratory pressure; $P_{th,max}$: maximum threshold pressure; PTL: progressive threshold loading test. [#]: n=16; [¶]: n=17; [+]: all results for health-related quality of life are presented as points per item. *: $p<0.05$ compared with baseline measures; [§]: $p<0.05$ *versus* change seen in S-IMT group.

frequency and duration of the training programme (three times per week for 8 weeks) falls within the current recommendations for outpatient whole-body exercise training programmes [11]. Therefore, it is more likely to be clinically feasible than other IMT protocols that have required prolonged training periods. Finally, outcome measures were selected that were both task specific (inspiratory muscle function) and non-task specific (exercise capacity and QoL), laboratory based (cycle ergometry testing) and field based (6MWT).

Training programme

An interval-based high-intensity protocol was used to maximise any potential training-related gains in inspiratory muscle strength and endurance. Consistent with the current authors' previous experience [24], H-IMT was well tolerated, with subjects achieving the highest training loads reported in any COPD population to date (101% of baseline $P_{I,max}$). The current authors attribute this to the characteristics of an interval-based training programme, with the frequent rest periods permitting relief of dyspnoea and local muscle fatigue, thereby allowing achievement of greater loads than would be possible when breathing against constant inspiratory loads with a continuous-based training protocol [24].

Training intensity, expressed as a percentage of baseline $P_{I,max}$, improved by 56% over the 8-week training period. The increase in $\int$Pdt, a measure of inspiratory muscle work independent of breathing pattern, was more modest (38%; fig. 3), suggesting that subjects altered their breathing pattern in a manner which lessened inspiratory muscle work. However, such a strategy could only partially compensate for the training load, which systematically increased over the 8-week period. Subjects undergoing S-IMT also appeared to adopt a strategy of manipulating breathing pattern to minimise inspiratory muscle work, as evidenced by a decrease in $\int$Pdt despite no change in training intensity.

Improvements in inspiratory muscle function

$P_{I,max}$ increased by 29% and $P_{th,max}$ by 56% following 8 weeks of H-IMT. The maximum load achieved during the progressive loading test, when expressed as a percentage of the maximum inspiratory pressure ($P_{th,max}/P_{I,max}$), also increased, suggesting that improvements in $P_{th,max}$ following H-IMT were not solely the result of gains in inspiratory muscle strength. These improvements in inspiratory muscle strength and endurance demonstrated following H-IMT are notable for three reasons. First, they are of similar or greater magnitude than the increases described in most studies published over the last 15 yrs, which have reported significant increases in inspiratory muscle strength (measured as $P_{I,max}$ [1–6, 8, 9]) and inspiratory muscle endurance (measured using progressive loading protocols [4, 8, 9, 17, 42, 43]). Secondly, the improvements in the current study were observed following a rigorous pre-training familiarisation period, during which time inspiratory muscle function improved substantially. It is possible that these improvements during the screening and familiarisation phase were the result of training-induced increases in inherent muscle contractility. However, the current authors believe this to be unlikely because changes that characterise neuromuscular adaptation with training, such as an increased number of motor units firing, appear to require a more intense training regimen over a longer period of time, being weeks rather than days [25, 44]. Muscle hypertrophy requires even longer training periods [44]. A more likely mechanism is neurosensory conditioning resulting from repeated exposures to the same task [25, 45]. Regardless of the precise mechanism, the current study demonstrated improvements in inspiratory muscle strength and endurance following H-IMT over and

TABLE 3 The effects of training on exercise capacity

	H-IMT[#]		S-IMT[¶]	
	Baseline	Post-training	Baseline	Post-training
6-min walk test				
Distance m	445.7±112.3	472.8±104.3*,§	508.0±87.6	513.2±82.6
Distance % predicted[+]	70.6±15.3	73.5±14.7*	80.3±15.8	81.3±15.6
Dyspnoea at end of test	5.5±2.6	5.1±2.5	4.9±2.5	5.0±2.4
Leg fatigue at end of test	2.8±2.5	2.8±2.6	2.5±2.7	2.8±3.1
Heart rate at end of test bpm	114.4±15.6	117.0±11.7	121.6±15.6	118.4±18.2
S_{p,O_2} at end of test %	87.5±2.2	87.8±3.8	87.6±3.3	86.6±4.6
Cycle ergometry variables collected at W_{max}				
Work rate W	64.4±15.9	64.4±14.6	65.9±17.0	70.0±22.6
V'_{O_2} mL·min^{-1}	876.4±216.5	867.8±219.1	888.4±197.7	912.8±301.4
V'_{O_2} mL·min^{-1}·kg^{-1}	12.4±2.6	12.1±2.3	13.0±3.1	12.9±2.7
V'_E L·min^{1}	39.4±13.2	39.4±14.2	37.0±10.1	36.1±11.0
t_I/t_{tot}	0.3±0.0	0.3±0.1	0.3±0.0	0.3±0.1
V_T mL	1114.4±284.5	1182.1±317.7	1174.3±499.4	1234.9±597.5
RR breaths·min^{-1}	35.2±6.8	33.1±7.1*	33.6±8.7	31.8±7.9
V'_E/MVV	97.5±14.8	94.9±13.5	100.8±20.9	94.9±17.4
Dyspnoea	6.1±1.6	5.8±2.3	6.1±2.0	6.6±2.6
Leg fatigue	5.0±2.4	5.0±2.9	5.8±3.0	6.6±3.3
Heart rate bpm	123.1±15.8	122.7±16.9	122.1±16.6	121.2±15.0
S_{p,O_2} %	91.2±4.2	92.5±4.1	92.7±4.9	93.7±3.3
Cycle ergometry variables at 50% W_{max}				
Work rate W	29.4±9.3	29.4±9.3	30.6±9.7	30.6±9.7
V'_{O_2} mL·min^{-1}	601.3±118.2	585.9±120.2	596.3±114.0	591.4±134.3
V'_{O_2} mL·min^{-1}·kg^{-1}	8.5±1.4	8.2±1.1	8.7±1.9	8.6±2.0
V'_E L·min^{-1}	23.6±5.2	22.6±5.5	24.1±6.6	21.9±5.6*
t_I/t_{tot}	0.4±0.0	0.4±0.0	0.4±0.0	0.4±0.0
V_T mL	1001.8±282.7	1083.4±354.2*	1026.1±345.8	1071.5±460.1
RR breaths·min^{-1}	24.7±5.8	21.6±4.6*	24.5±6.4	22.2±6.0*
Dyspnoea	1.1±1.0	0.8±0.6	1.5±0.9	1.5±1.2
Heart rate bpm	97.4±10.8	95.4±7.9	100.2±12.3	94.4±9.8*
S_{p,O_2} %	94.9±3.2	95.5±3.0	95.9±2.1	96.2±2.0

Data are expressed as mean±SD. H-IMT: high-intensity inspiratory muscle training; S-IMT: sham inspiratory muscle training; bpm: beats per minute; S_{p,O_2}: arterial oxygen saturation; Wmax: maximum work rate achieved during cycle ergometry test; V'_{O_2}: oxygen uptake; V'_E: minute ventilation; t_I/t_{tot}: duty cycle; V_T: tidal volume; RR: respiratory rate; MVV: maximal voluntary ventilation; 50% Wmax: work rate equivalent to 50% of maximum work rate achieved during baseline cycle ergometry test. [#]: n=16; [¶]: n=17; [+]: predicted normal values derived from [40]. *: $p<0.05$ compared with baseline measures; [§]: $p<0.05$ *versus* change seen in S-IMT group.

above any changes resulting from familiarisation. Thirdly, the improvements were achieved over a relatively brief total training period (see Training efficiency; fig. 4). Although the present study did not examine the length of time these gains were maintained after completing the H-IMT programme, a recent study has shown that training-related improvements in inspiratory muscle strength and endurance gradually decline over a 12-month period without adherence to a maintenance programme [46].

Only three previous studies have reported substantially greater increases in $P_{I,max}$ than observed in the current study (>40% improvement from baseline measures). However, each provided less rigorous familiarisation procedures for their assessments than the present study [17, 18, 42]; thus, some of the improvement ascribed to the training programmes may be attributable to familiarisation with the assessment procedures. Only one study has reported a substantially greater improvement in $P_{th,max}$ (143% improvement from baseline measures) [2], a finding which may be explained by differences in assessment protocol (*e.g.* increases in threshold pressure every 15 s *versus* 1 min in the present study) and possibly incomplete familiarisation to the task prior to initiating training.

Training efficiency

The interval-based nature of the H-IMT programme optimised the time spent breathing against an inspiratory load for any given increase in $P_{I,max}$ (*i.e.* training efficiency). Figure 4 compares training efficiency of the current H-IMT programme to that calculated for previous randomised controlled trials of

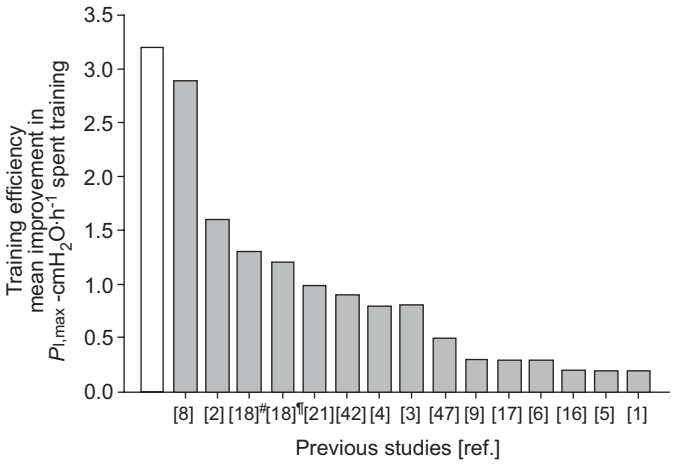

FIGURE 4. A comparison of the training efficiencies for randomised controlled trials of inspiratory muscle training in chronic obstructive pulmonary disease reporting a significant improvement in inspiratory muscle strength from baseline measures. Training efficiency is expressed as the mean improvement in maximum inspiratory pressure ($P_{I,max}$) per hour of time spent training (*i.e.* loaded breathing). Studies are numbered as they appear in the reference list. □: present study. #: training efficiencies of the inspiratory muscle training (IMT) programmes performed with a threshold device; ¶: training efficiencies of the IMT programmes performed with a targeted resistive device. The high-intensity IMT programme described in the present study resulted in a mean improvement of 3.2 cmH_2O·h^{-1} of training.

IMT in COPD, which have reported significant improvements in inspiratory muscle strength above baseline measures [1–6, 8, 9, 16–18, 21, 42, 47]. The protocol prescribed in the present study resulted in a mean gain of 3.2 cmH_2O in $P_{I,max}$ for every hour spent training (*i.e.* time spent loaded breathing). The two studies with the closest training efficiencies also employed interval-based training protocols [2, 8].

Improvements in QoL, dyspnoea, fatigue and exercise capacity

Overall QoL increased in both groups, largely due to improvements in dyspnoea during ADL. The increases of 1.4 points per item (95% confidence interval (CI) 1.9–1.0) in dyspnoea during ADL and 0.9 points per item (95% CI 1.2–0.6) in fatigue following H-IMT exceed the threshold for a clinically meaningful improvement (0.5 points per item) [48]. The improvement in dyspnoea during ADL is comparable with gains reported by others after 4 [6] and 6 months of IMT [17]. While of smaller magnitude than the H-IMT group, significant improvements in overall QoL and dyspnoea during ADL were also seen following 8 weeks of S-IMT. Although it is possible that these gains are related to the modest increase in inspiratory muscle strength following S-IMT, the absence of change in any other physiological measure of inspiratory muscle function or exercise capacity suggests that the improvement in questionnaire-based assessments is probably due to acquiescence bias [49], ''Hawthorne'' or ''Rosenthal'' effects [50]. This finding highlights the importance of a control group when employing questionnaire-based outcome measures.

Relative to the changes seen in the S-IMT group, both dyspnoea during ADL and fatigue improved a further 0.6 points per item following H-IMT, a difference that exceeds the threshold for a clinically meaningful improvement [48]. It is likely that the improvement in dyspnoea during ADL following H-IMT is related to greater inspiratory muscle strength, with less dyspnoea resulting from a reduction in respiratory motor output and perception of inspiratory effort [51, 52]. Such a mechanism may also play a part in the improvements demonstrated in the CRDQ domain of fatigue.

H-IMT had little effect on whole-body exercise capacity. When compared with S-IMT, no change in any measure collected at maximum or sub-maximum work rates during cycle ergometry testing was demonstrated following H-IMT. Furthermore, the increase in 6MWD following H-IMT was modest (27 m), and although statistically significant may not be clinically meaningful [53]. These findings are consistent with the results of previous randomised controlled trials of IMT in COPD, which, despite reporting gains in inspiratory muscle function [1–3, 15, 17, 18, 43, 54] and changes in external intercostal muscle morphology [8], have generally failed to demonstrate substantial improvements in exercise capacity measured *via* incremental cycle ergometry tests [3, 8, 17, 54], time to exhaustion exercising at a constant sub-maximal workload [43, 54], or field walking tests [1, 2, 8, 15, 18, 54]. Furthermore, the observation that subjects undergoing H-IMT achieved maximum ventilation during the cycle ergometry test equal to $97.5 \pm 14.8\%$ of their estimated maximum voluntary ventilation does not support the contention that COPD subjects with a ventilatory limitation to exercise are more likely to demonstrate large improvements in exercise capacity following IMT [7].

Conclusions, clinical implications and future directions

The present authors have demonstrated that interval-based, progressively increased, fully supervised H-IMT allows subjects with moderate-to-severe COPD to achieve very high training loads, yielding large improvements in inspiratory muscle strength and endurance over a relatively brief total training period. Despite the significant improvement in inspiratory muscle function, it appears unlikely that IMT alone, even when optimised and applied to subjects with a ventilatory limitation during exercise, is capable of yielding meaningful improvements in exercise capacity in COPD.

However, high-intensity inspiratory muscle training does result in significant and clinically meaningful improvements in dyspnoea during activities of daily living and fatigue. Therefore, it may be of particular benefit to chronic obstructive pulmonary disease patients who report dyspnoea during activities of daily living and/or fatigue, but are unable to effectively participate in whole-body exercise training because of comorbid conditions, such as musculo-skeletal impairments. Further study is required to investigate the effects of combining high-intensity inspiratory muscle training and whole-body exercise training on dyspnoea during activities of daily living and fatigue.

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