Dyspnoea in COPD: Can inspiratory muscle training help?

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Chronic obstructive pulmonary disease (COPD) is a progressive, common and costly condition. Dyspnoea frequently limits activity and reduces health-related quality of life. In addition to impaired lung function, peripheral muscle deconditioning and respiratory muscle dysfunction also contribute to dyspnoea and reduced exercise capacity. Pulmonary rehabilitation using whole body exercise training improves peripheral muscle function and reduces dyspnoea but does not improve respiratory muscle function. Providing that adequate training intensities are utilised, specific loading of the inspiratory muscles with commercially available hand-held devices can improve inspiratory muscle strength and endurance. Several studies have investigated the effects of inspiratory muscle training on dyspnoea in COPD subjects. Results of these studies are conflicting, most likely reflecting methodological shortcomings including insufficient training load, insensitive outcome measures, and inadequate statistical power. This paper describes the origin of dyspnoea in COPD, with particular attention given to the role of inspiratory muscle dysfunction in its genesis and its possible amelioration through inspiratory muscle training. [Hill K, Jenkins SC, Hillman DR and Eastwood PR (2004): Dyspnoea in COPD — Can inspiratory muscle training help? Australian Journal of Physiotherapy 50: 169–180]

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Introduction

Chronic obstructive pulmonary disease (COPD) is the third most burdensome disease and fourth leading cause of death in Australia (Mathers et al 1999). It is associated with escalating hospital admission rates (Hurd 2000) and economic burden (Burdon and Edwards 2002) with its incidence rising rapidly in women (Burdon and Edwards 2002). Dyspnoea limiting physical activity is a common complaint in COPD patients with moderate to severe airflow obstruction (NHLBI/WHO Workshop Report 2001), and usually arises during the sixth or seventh decade of life (Celli et al 1995). The onset of dyspnoea is often insidious and may be attributed incorrectly to the effects of ageing (McKenzie et al 2003). Avoidance of activity as a strategy to limit the experience of dyspnoea leads to a sedentary lifestyle. Accompanying this lifestyle is locomotor muscle deconditioning (Maltais et al 2000) which compounds the effects of pulmonary dysfunction on dyspnoea (Sassi-Dambron et al 1995). Progression of COPD results in dyspnoea advancing from being present only during exertion to ultimately becoming an incapacitating feature during activities of daily living (McKenzie et al 2003) with reduced health-related quality of life (Shoup et al 1997).

Optimising function through a reduction in dyspnoea has been identified as a key goal in the Australia and New Zealand guidelines for the management of COPD (McKenzie et al 2003). Following appropriate pharmacological therapy, pulmonary rehabilitation is the only treatment shown convincingly to reduce dyspnoea (McKenzie et al 2003). This reduction is thought to be mediated via decreased levels of ventilation during submaximal exercise resulting from training-induced improvements in aerobic capacity of the skeletal muscles lowering blood lactate concentration and increased mechanical efficiency of these muscles (Casaburi et al 1991, O’Donnell et al 1995). It is notable that such whole body exercise training does not improve respiratory muscle strength or endurance (Belman and Kendregan 1982, Wanke et al 1994, Weiner et al 1992). Because inspiratory muscle dysfunction contributes to the origin of dyspnoea in COPD (Rochester 1991), it is possible that the addition of specific inspiratory muscle training to an existing program of whole body exercise may yield further reductions in dyspnoea.

The purpose of this review is three-fold: first, to describe the physiological origins of dyspnoea in COPD, with particular attention on inspiratory muscle dysfunction in its genesis; second, to review the results of randomised controlled trials investigating the effects of inspiratory muscle training on dyspnoea in COPD; and third, to analyse the possible mechanisms by which inspiratory muscle training may lead to a reduction in dyspnoea. In contrast, previous reviews of inspiratory muscle training in COPD have focussed on respiratory muscle function and assessment, inspiratory muscle training regimens, and the methodological limitations of inspiratory muscle training studies (Grasso 1989, Reid and Samrai 1995, Reid and Sharma 2000).

Defining and describing dyspnoea

Dyspnoea has been defined as ‘a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity. The experience derives from interactions among multiple physiological, psychological, social, and environmental factors, and may induce secondary physiological and behavioural responses’ (American Thoracic Society 1999). Put simply, dyspnoea is an unpleasant sensation of breathing arising as a consequence of complex and varied interactions. The sensation is multi-dimensional and differs in intensity (Simon et al 1990). Cerebral processes appear to alter the intensity of dyspnoea with anxiety, anger, depression, and cognitive disturbance each heightening the perception (Dales et al 1989).

Dyspnoea is a feature of many disease processes. It appears that the phraseology selected by individuals to describe their experience of dyspnoea reflects, in part, the underlying
pathophysiological origin. COPD subjects tend to choose terminology pertaining to effort associated with increased mechanical loads (Elliot et al 1991).

**Measuring dyspnoea**

Dyspnoea during exercise is usually measured using interval scales such as the Borg-Category Ratio scale (Borg 1982). This requires the patient to ascribe a value representative of the magnitude of dyspnoea, ranging from 0 to 10 anchored with simple verbal descriptions of intensity such as ‘very, very slight’ and ‘severe’ (Borg 1982). Following instruction, measurements of dyspnoea using this scale are simple to collect, reliable over short periods of time, sensitive to change, and correlate with minute ventilation and oxygen consumption during exercise in subjects with COPD (Mador et al 1995, Mahler 1992). A difference of one point has been suggested to be clinically significant (Solway et al 2002).

Dyspnoea during activities of daily living is usually measured with either the Chronic Respiratory Disease Questionnaire (CRDQ) (Guyatt et al 1987) or the Baseline Dyspnoea Index/Transitional Dyspnoea Index (BDI/TDI) (Mahler et al 1984). The CRDQ is a disease-specific quality of life questionnaire evaluating four domains: dyspnoea, mastery, emotional function, and fatigue (Guyatt et al 1987). It is used to measure change in dyspnoea in response to an intervention or over time, with higher numbers representing less dyspnoea (Guyatt et al 1987). The CRDQ has been shown to be reproducible, valid and responsive in subjects with chronic airflow limitation (Guyatt et al 1987). A minimal clinically important difference is defined as 0.5 points per item (Jaeschke et al 1989).

The BDI/TDI quantifies dyspnoea by summation of values ascribed for three categories: functional impairment, magnitude of task, and magnitude of effort, resulting in a focal score (Mahler et al 1984). A higher focal score in the BDI is representative of less impairment at baseline, whereas a higher score for the TDI indicates a reduction in dyspnoea compared with baseline values (Mahler et al 1984). Both the BDI and TDI are reliable and valid in subjects with chronic lung disease (Mahler et al 1984, Witek and Mahler 2003). The TDI is sensitive to change in COPD subjects with a difference of one point described as clinically important (Witek and Mahler 2003).

**The origin of dyspnoea in COPD**

Complex integration of multiple afferent and efferent signals has been implicated in the perception of dyspnoea (American Thoracic Society 1999). A widely accepted view is that dyspnoea as a limiting symptom reflects disequilibrium between ventilatory capacity and ventilatory demand (Polkey 2002). Factors that increase demand on the ventilatory system are likely to result in dyspnoea when the ventilatory capacity is inadequate to meet heightened ventilatory needs.

Neuromechanical disassociation is a popular theory explaining the contribution of respiratory muscle dysfunction in the genesis of dyspnoea (American Thoracic Society 1999). This theory postulates that dyspnoea arises from
Figure 2. The relationship between force of contraction, duration of contraction, and fatigue of the diaphragm is shown. Duration of the contraction is expressed as the ratio of inspiratory time (Ti) to the total respiratory cycle (Ttot) on the ordinate. Force of the contraction is expressed as the ratio of transdiaphragmatic pressure required per breath (Pdi) to the maximum transdiaphragmatic pressure (Pdimax). The closed circle represents a normal subject breathing quietly, and the open circle represents the effects if inspiratory resistive loading (IRL). The closed triangle depicts a patient with chronic obstructive pulmonary disease breathing quietly, whereas the open triangle depicts such a patient breathing slowly and deeply, or alternatively, what might occur during acute respiratory failure (ARF). Reproduced with kind permission of Elsevier from Rochester D et al (1983): Respiratory Muscle Failure. Medical Clinics of North America. The American Physiological Society granted permission for the continued use Rochester made of data from Bellemare F and Grassino A (1982): Effect of pressure and timing of contraction on human diaphragm fatigue. Journal of Applied Physiology 53: 1190–1195.

disequilibrium between respiratory motor command (central inspiratory motor activity) and the corresponding afferent feedback from proprioceptive and other sensory receptors. Thus, when the afferent feedback relating to changes in intrathoracic pressure, respiratory muscle length, chest wall or lung movement are interpreted as insufficient for the corresponding motor command, dyspnoea arises. In COPD, measurements reflecting inspiratory muscle activity such as the percentage of maximum pressure required to generate airflow or the level of exercise ventilation have been shown to relate to the intensity of dyspnoea, adding credence to this theory (Leblanc et al 1986, O’Donnell and Webb 1993).

Factors implicated in the origin of dyspnoea

Factors contributing to the origin of dyspnoea in COPD are summarised in Figure 1 and discussed in greater detail in the following sections.

Inspiratory muscle dysfunction

In COPD, dyspnoea is greater in subjects requiring a higher proportion of their maximum inspiratory pressure to generate inspiratory airflow (Gorini et al 1996). An increase in this proportion gives rise to a sensation of inspiratory effort, postulated to result from the perception of the heightened motor command through corollary discharge within the central nervous system (El-Manshawi et al 1986, Gandevia et al 1981). In COPD subjects, inspiratory muscle weakness and inefficiency will increase the proportion of maximum inspiratory pressure required to generate inspiratory flow thereby yielding a greater sense of inspiratory effort (Gandevia et al 1981). This mechanism is likely to contribute to the origin of dyspnoea as sensations of inspiratory effort and breathlessness appear to be closely related (Killian et al 1984).

Mechanical loads on the inspiratory system

Elastic loads Elastic loads refer to those muscle loads imposed by the stiffness of the lungs and chest wall (O’Donnell 1994). These loads are increased when breathing from high lung volumes, as the associated decrease in lung and chest wall compliance requires the inspiratory muscles to generate greater negative pleural pressures during inspiration (O’Donnell and Webb 1993, Rochester 1991).

Threshold loads A consequence of pulmonary hyperinflation (see below) is a positive intra-alveolar pressure at end expiration, as expiration is incomplete and inward recoil of the lungs and chest wall persists (Marchand and Decramer 2000, O’Donnell 2002). This has been termed intrinsic positive end expiratory pressure (Marchand and Decramer 2000) and represents a threshold load which must be overcome during the succeeding inspiratory effort before flow can commence (O’Donnell 2002).

Resistive loads Narrowing of peripheral airways imposes a resistive load on both the inspiratory and expiratory muscles (Rochester 1991). In COPD, this narrowing occurs as a result of the loss of elastic support of airways (in the case of emphysema) and inflammation. Most commonly this inflammatory reaction is induced by inhalation of noxious particles or gases (such as those present in cigarette smoke). The inflammatory reaction causes narrowing of the lumen and fibrosis of the airway wall, culminating in fixed obstruction to airflow (NHLBI/WHO Workshop Report 2001).

Conditions reducing inspiratory muscle strength and efficiency

Pulmonary hyperinflation Peripheral airway narrowing and loss of elastic recoil leads to gas trapping during expiration, resulting in a progressive increase in functional residual capacity, termed pulmonary hyperinflation (NHLBI/WHO Workshop Report 2001, Rochester 1991). These changes limit the ability of the ventilatory system to accommodate the rise in alveolar ventilation during exercise by increasing tidal volumes (Marin et al 2001) resulting in abnormally high increases in respiratory rate (Moss and Make 1993). The consequent reduction in expiratory time in the presence of expiratory airflow limitation leads to an incomplete expiration further tending to increase end expiratory lung volume and reduce inspiratory reserve capacity (Moss and Make 1993, O’Donnell and Webb 1993). This dynamic pulmonary hyperinflation is associated with dyspnoea during both walking (Marin et al 2001) and cycle ergometry exercise (O’Donnell and Webb 1993).

Besides imposing elastic and threshold loads on the inspiratory muscles, pulmonary hyperinflation results in a suboptimal length-tension relationship of the diaphragm (Rochester et al 1979). The flattening and shortened resting length of the diaphragm decreases its pressure-generating capacity through mechanical disadvantage (Lahrmann et al...
Therefore relief of dyspnoea following a reduction in pulmonary hyperinflation with treatment is likely to be the consequence both of decreased threshold and elastic loading and of improved diaphragmatic mechanics (Lahrmann et al 1999).

Respiratory muscle fatigue

Inspiratory muscle fatigue reduces inspiratory muscle strength (Supinski et al 1987) and is therefore likely to increase the sense of respiratory effort. The pattern of breathing adopted, specifically the components of inspiratory pressure and inspiratory time, influence the development of respiratory muscle fatigue (Bellemare and Grassino 1982) and the perceived magnitude of a respiratory load (Killian et al 1982). The mean inspiratory pressure (expressed as a proportion of maximum) multiplied by the duty cycle (inspiratory time expressed as a proportion of total respiratory cycle time) is defined as the tension-time index which is a primary determinant of diaphragmatic fatigue (Bellemare and Grassino 1982). If the tension-time index is maintained above 0.15 for a prolonged period of time, fatigue may develop (Bellemare and Grassino 1982). This relationship between pattern of breathing and the development of inspiratory muscle fatigue is shown in Figure 2 (Rochester and Arora 1983).

Respiratory muscle oxygen consumption

In COPD the percentage of total oxygen consumption required by the respiratory muscles is estimated to be 8 to 12 times higher than that required by healthy individuals during exercise and quiet breathing respectively (Rochester 1991). The higher respiratory muscle oxygen consumption reflects the increased load on, and reduced efficiency of, the respiratory muscles (Cherniack 1959, Field et al 1982) and may contribute to dyspnoea and exercise limitation (Aliverti and Macklem 2001). Reduced oxygen supply to the diaphragm increases lactate concentration and the rate of inspiratory muscle fatigue (Jardim et al 1981), thereby potentially decreasing the maximum force-generating capacity of the inspiratory muscles (see respiratory muscle fatigue), giving rise to dyspnoea through heightened neuro-mechanical disassociation.

Weight loss

Compared with those of normal weight, underweight COPD patients have weaker inspiratory muscles and report higher levels of dyspnoea (Sahebjami and Sathianpitayakul 2000). The reduced diaphragmatic mass (Thurlbeck 1978) and disproportionate atrophy of type II muscle fibres (Marchand and Decramer 2000) reported in underweight COPD subjects are both likely to contribute to the impairment of inspiratory muscle strength and consequent heightened sensation of dyspnoea.

Morphological and biochemical factors

A shift in the proportion of muscle fibres from type II (fast twitch, glycolytic) to type I (slow twitch, oxidative) has been demonstrated in the diaphragm of patients with severe COPD (Levine et al 1997). These changes, postulated to develop in response to chronic loading (Levine et al 1997), may improve the ability of the diaphragm to withstand fatigue, potentially at the expense of its maximal force-generating capacity (Gosker et al 2000, Marchand and Decramer 2000). Other factors which may reduce inspiratory muscle strength include corticosteroid-induced myopathy, chronic gas exchange abnormalities, chronic inflammation and hormone or electrolyte disturbances (Casaburi 2000, Maltais et al 2000).
Other causes of dyspnoea in COPD

Locomotor muscle dysfunction The quadriceps muscles of patients with COPD have been shown to have abnormal morphology and biochemistry including a reduction in type I fibres, an increase in the percentage of type IIb fibres (Whittom et al 1998), and a reduction in the concentration of oxidative enzymes (Maltais et al 2000). Impairment in skeletal muscle oxidative capacity has been postulated to explain the early dependence on anaerobic energy systems seen during exercise in COPD, characterised by an unusually early and steep rise in arterial lactate concentrations (Maltais et al 1996). Lactic acidosis stimulates chemoreceptor drive and ventilation, increasing inspiratory motor command, thereby promoting dyspnoea (Casaburi et al 1991, O’Donnell and Webb 1993).

Gas exchange abnormalities Decreased single-breath diffusing capacity for carbon monoxide and exercise-induced desaturation characterise COPD patients with severe dyspnoea (O’Donnell and Webb 1992). Abnormal gas exchange arising as a consequence of ventilation/perfusion mismatch can contribute to the genesis of dyspnoea (American Thoracic Society 1999, NHLBI/WHO Workshop Report 2001). Hypoxia may result in increased reliance on anaerobic energy systems with subsequent lactate production stimulating ventilation, contributing to dyspnoea. Supporting this hypothesis is the finding that administration of supplementary oxygen to COPD subjects during exercise reduces lactate concentration and ventilation (O’Donnell et al 1997). Such a reduction in ventilation would also reduce pulmonary hyperinflation and, in turn, dyspnoea resulting from this mechanism (Marin et al 2001, O’Donnell and Webb 1993).

In patients with lung disease, acute hypercapnia elicits a chemoreceptor-driven increase in inspiratory motor command, which gives rise to dyspnoea (American Thoracic Society 1999, Manning and Schwartzstein 1995). Chronic carbon dioxide retention has also been associated with greater dyspnoea during activities of daily living (Gorini et al 1996). However this relationship is unlikely to be due to carbon dioxide-induced increases in chemoreceptor activity, as gradual renal compensatory activity acts to buffer pH changes and minimise medullary chemoreceptor stimulation (American Thoracic Society 1999). A more likely cause of this relationship is the gradual deterioration in lung mechanical properties and inspiratory muscle function referred to earlier, which results in a relatively high force required for each breath and the subsequent development of a rapid, shallow breathing pattern (Begin and Grassino 1991, Gorini et al 1996). Such a breathing pattern minimises inspiratory muscle fatigue, inspiratory muscle effort and dyspnoea, but at the expense of alveolar ventilation (Begin and Grassino 1991, Gorini et al 1996). Thus greater dyspnoea reported by COPD patients with chronic carbon dioxide retention is more likely to arise from neuromechanical disassociation due to an imbalance between load and the capacity of the inspiratory muscles to cope (Gorini et al 1996).

Inspiratory muscle training

Despite the reductions in dyspnoea demonstrated following whole body exercise training in COPD (Lacasse et al 2002) measures of inspiratory muscle strength and endurance remain unchanged (Wanke et al 1994, Weiner et al 1992). This is probably because the increased ventilation accompanying whole body exercise is of insufficient intensity to induce a training effect in the inspiratory muscles (Kraemer et al 1996). However, it is possible to improve inspiratory muscle function using techniques which selectively load the inspiratory muscles at a level greater than that experienced during whole body exercise, prompting investigation of the role of inspiratory muscle training. While several studies have been undertaken, it remains unresolved whether improvements in inspiratory muscle function can reduce dyspnoea during the activities of the daily living in these patients.

Loading the respiratory muscles

Low pressure–high flow loads Normoacapnic hyperpnoea was first described as a method for training the respiratory muscles of healthy subjects in 1976 (Leith and Bradley 1976) and COPD subjects in 1980 (Belman and Mittman 1980). It involves training the respiratory muscles by voluntarily ventilating at high levels for a prolonged period (usually 15 minutes) (Belman and Mittman 1980). The load imposed requires the generation of low pressures but high flows (Reid and Sharma 2000), and is therefore analogous to the high ventilatory demands placed on the respiratory muscles during exercise (Belman 1993). Widespread use of the technique has not eventuated because of the need to use complex breathing circuits to ensure stable levels of carbon dioxide (Belman and Mittman 1980) and the difficulty in accurately determining the inspiratory muscle load due to the inter- and intra-individual variability in airflow obstruction (Clanton et al 2002). This modality is therefore usually reserved for laboratory-based trials with few studies reporting its use in the clinical setting (Ries and Moser 1986, Scherer et al 2000).

High pressure–low flow loads The inspiratory muscle training loads most commonly described in the literature are high pressure–low flow in nature, imposed by external mechanical loading devices. Such loads can be achieved by either resistive or threshold devices.

Resistive loads Resistive inspiratory muscle training devices provide a range of different sized apertures to impose varying resistive loads (Harver et al 1989). The primary disadvantage of this method is the interdependence of flow and inspiratory pressure (Figure 3a) (Belman et al 1986). In practical terms this means if inspiratory flow rates are not controlled, patients can lower the training load imposed by the device by manipulating their breathing pattern (Reid and Sharma 2000). Training programs utilising resistive loading have usually prescribed repeated submaximal inspiratory efforts, with sessions between 15 and 30 minutes in duration, once to four times a day, seven days a week and for between six and eight weeks (Belman and Shadmehr 1988, Belman et al 1986, Harver et al 1989, Pardy et al 1981, Patessio et al 1989, Sonne and Davis 1982) at a training intensity ranging from approximately 30–70% of maximum inspiratory pressure (Dekhuijzen et al 1991, Harver et al 1989).

Threshold loads Threshold inspiratory muscle training devices impose a threshold or critical opening pressure that must be overcome prior to inspiratory flow commencing (Flynn et al 1989). During the task, inspiratory muscles initially perform an isometric contraction until the threshold valve opens to allow inspiratory flow, after which the contraction becomes isotonic in nature. In contrast to resistive loading, threshold loading has the advantage of inspiratory
pressure being largely independent of flow rate (Nickerson and Keens 1982) such that manipulations in breathing pattern to change inspiratory flow rates will not alter the inspiratory load imposed by the device (Figure 3b) (Eastwood and Hillman 1995). For this reason threshold loading devices have become a popular choice with which to train the inspiratory muscles. Generally, training programs using threshold devices have applied similar strategies to those described using resistive devices (Berry et al 1996, Larsen et al 1988, Villafranca et al 1998).

Specificity of training related improvements

As with whole body exercise performance, improvements in measures of inspiratory muscle function follow the principle of task specificity, reflecting the prescribed method of training (Romer and McConnell 2003, Tzelepis et al 1994). High pressure–no flow contractions yield strength gains, whereas high flow–low pressure contractions improve maximum inspiratory flow rates (Romer and McConnell 2003, Tzelepis et al 1994) and measures of inspiratory muscle endurance (Scherer et al 2000). Training protocols employing a combination of pressure and flow loads yield gains in strength, maximal inspiratory flow rates (Romer and McConnell 2003, Tzelepis et al 1994), and inspiratory muscle endurance (Belman and Shadmehr 1988). Transfer of improvement from pressure-based training to flow-based measures of endurance appears possible when the training load is maximised (Belman and Shadmehr 1988). While most studies employing continuous (without rest) training protocols prescribe loads between 30% and 50% of the baseline maximum inspiratory pressure (Harver et al 1989, Lisboa et al 1997, Ramirez-Sarmiento et al 2002, Riera et al 2001, Villafranca et al 1998), some report using training loads as high as 70% or even 80% of baseline inspiratory muscle pressure (Berry et al 1996, Dekhuijzen et al 1991). However, a recent study using an interval-based training program allowed considerably higher training loads to be achieved (up to 95% of the baseline maximum inspiratory pressure) thus potentially maximising gains in inspiratory muscle function (Sturdy et al 2003).

Effects of inspiratory muscle training on inspiratory muscle strength and endurance

Several recent randomised controlled trials of inspiratory muscle training employing protocols of repeated submaximal efforts imposed by external loading devices, report gains in inspiratory muscle strength or endurance in the experimental group compared with baseline measurements (Lisboa et al 1997, Ramirez-Sarmiento et al 2002, Villafranca et al 1998, Weiner et al 2000) or gains greater than those reported in the control group (Larsen et al 1999, Riera et al 2001). Prescribing training loads as low as 22% of the previously determined maximum inspiratory pressure appears capable of improving inspiratory muscle endurance, but not strength (Preusser et al 1994). It appears that training loads of at least 30% of the maximum inspiratory pressure are required before improvements in strength are achieved (Larsen et al 1988). This observation is in keeping with the conclusions of a recent meta-analysis of inspiratory muscle training that described improvements in both inspiratory muscle strength and endurance when the analysis was restricted to studies employing loads of at least 30% of maximum inspiratory pressure (Lotters et al 2002).

Studies comparing differing intensities of inspiratory muscle training in COPD demonstrate more pronounced gains in strength and endurance in those subjects training at the higher intensity, suggesting a dose-dependent response in training adaptations (Belman and Shadmehr 1988, Larsen et al 1988, Lisboa et al 1997, Preusser et al 1994, Villafranca et al 1998). In addition to the improvements in inspiratory muscle strength and endurance, structural changes in muscle morphology indicative of adaptation have recently been reported following inspiratory muscle training in COPD (Ramirez-Sarmiento et al 2002). These changes included an increase in the proportion of type I fibres and an increase in the size of the type II fibres in the external intercostal muscle (Ramirez-Sarmiento et al 2002).

Effects of inspiratory muscle training on dyspnoea and exercise capacity

To date, only six randomised controlled trials have reported the effects of inspiratory muscle training, when performed in isolation, on dyspnoea measured with the CRDQ, the BDI/TDI, or Borg scores at the end of exercise testing (Table 1a). Of these, four trials utilised training loads that appeared likely to yield gains in inspiratory muscle strength above baseline measures and also reported significant reductions in dyspnoea during activities of daily living (Harver et al 1989, Lisboa et al 1997, Riera et al 2001, Scherer et al 2000). These findings are summarised in Figure 4, which plots the relationship between the improvement in inspiratory muscle strength and the reduction in dyspnoea for those studies using the TDI. The association between these variables is strong \(r = 0.94\) although not statistically significant \(p = 0.06\), possibly because of the limited number of studies available for this analysis. The trend towards a significant association suggests that inspiratory muscle training protocols which induce greater improvements in inspiratory muscle strength

![Figure 4. Relationship between change in PImax and TDI in the experimental groups following IMT for studies summarised in Table 1a, using TDI as the outcome measure for dyspnoea. PImax and TDI are expressed as the change in experimental groups above the change in control groups.](image-url)
may also result in larger reductions in dyspnoea. Whether the magnitude of the reduction in dyspnoea during activities of daily living is actually dependent upon the magnitude of gain in inspiratory muscle strength will require studies designed to specifically address this question. Notably, three of these studies demonstrated post-inspiratory muscle training improvements in walking tests of functional exercise capacity with either similar or reduced end-exercise Borg scores, suggesting a faster pace was achieved with equal or less dyspnoea (Hsiao et al 2003, Lisboa et al 1997, Riera et al 2001). A reduction in dyspnoea during activities of daily living is seen in COPD patients following whole body exercise training (Lacasse et al 2002) and also following inspiratory muscle training, prescribed at an adequate training intensity. Hence, an important question is whether combining inspiratory muscle training with whole body exercise training confers additional reductions in dyspnoea beyond those seen following whole body exercise training alone. To date, only three randomised controlled trials measuring dyspnoea with the Borg or CRDQ have addressed this question (Table 1b) (Berry et al 1996, Larsen et al 1999, Wanke et al 1994).

Two of the three studies demonstrated improvements in inspiratory muscle strength above gains reported in the control groups following the addition of inspiratory muscle training to a standard program of whole body exercise (Larsen et al 1999, Wanke et al 1994). In the study by Wanke et al (1994), greater gains in whole body exercise capacity were described in the subjects receiving both inspiratory muscle training and cycle ergometry training compared with the improvements described in the subjects receiving cycle ergometry training in isolation. The addition of inspiratory muscle training yielded a 38% increase in inspiratory muscle strength from baseline measurements. The Borg scores at end-exercise were similar between the groups, suggesting that the group receiving inspiratory muscle training combined with cycle ergometry training were able to achieve higher work rates before dyspnoea limited performance (Wanke et al 1994). In the study by Larsen et al (1999), the improvement in inspiratory muscle strength following the addition of inspiratory muscle training to a program of cycle ergometry training was only 20% above baseline measures and did not translate into further gains in whole body exercise capacity or reductions in dyspnoea relative to the gains made by those subjects receiving cycle ergometry training alone.

As with dyspnoea, perhaps improvements in measures of whole body exercise capacity following inspiratory muscle training are likely to be related to the magnitude of the gains in inspiratory muscle strength. From the results of all studies presented in Table 1a and 1b, it appears that a minimum of 30% improvement in inspiratory muscle strength from baseline measures is necessary before improvements in exercise capacity are conferred (Hsiao et al 2003, Lisboa et al 1997, Riera et al 2001, Scherer et al 2000, Wanke et al 1994). Mechanisms by which inspiratory muscle training may reduce dyspnoea

As dyspnoea appears to arise, at least in part, from the neuromechanical disassociation of inspiratory motor command and afferent feedback from pulmonary and chest wall mechanoreceptors (American Thoracic Society 1999), therapies capable of reducing this disequilibrium may ameliorate dyspnoea. Training-induced gains in inspiratory muscle strength result from both hypertrophy of muscle fibres (Ramirez-Sarmiento et al 2002) and adaptation of neural pathways (Huang et al 2002). In healthy individuals, strength gains following inspiratory muscle training correlate with a reduction in inspiratory motor command, possibly reflecting a decrease in the percentage of motor units required for a ventilatory task (Huang et al 2002). If inspiratory muscle training in patients with COPD results in a similar lower utilisation of motor units for specific ventilatory tasks, this should decrease the perception of inspiratory effort and dyspnoea.

In COPD patients, inspiratory muscle training using threshold devices has been demonstrated to increase the velocity of shortening and reduce inspiratory time during loaded breathing tasks (Flynn et al 1989, Villafranca et al 1998). Providing the total respiratory cycle time remains unchanged, adopting a reduced inspiratory time during exercise would increase expiratory time for any given level of ventilation (Belman and Shadmehr 1988). Such an increase in expiratory time could reduce dyspnoea by decreasing dynamic pulmonary hyperinflation (Marin et al 2001, O’Donnell and Webb 1993) as well as increasing relaxation time and oxygen delivery to the diaphragm (Buchler et al 1985), thereby reducing inspiratory muscle fatigue (Bellemare and Grassino 1982). However, to date is remains unclear whether such changes in breathing pattern occur during exercise following inspiratory muscle training.

As is the case with peripheral muscles following whole body exercise training (Maltais et al 1996), it is possible that inspiratory muscle training induces changes in muscle metabolism which reduce dyspnoea. Improved efficiency of the respiratory pump muscles with a decrease in inspiratory muscle oxygen requirement has been postulated to account for the lower levels of ventilation and coexistent reduction in oxygen consumption during exercise following inspiratory muscle training (Lisboa et al 1997). In severe COPD it is possible respiratory muscle work contributes to the high blood lactate levels during exercise (Engelen et al 1995). Changes reflecting improved oxidative capacity of the respiratory muscles reported following inspiratory muscle training in COPD (Ramirez-Sarmiento et al 2002) may serve to lower lactate production (Bouttellier and Piwko 1992) or facilitate increased lactate metabolism (Spengler et al 1999) thereby contributing to the reduction in exercise ventilation (Lisboa et al 1997).

**Why is inspiratory muscle training not part of the standard management?**

Despite the theoretical benefits, the role of inspiratory muscle training in COPD remains unclear and it is currently not included as a standard component of a pulmonary rehabilitation program in the evidence-based guidelines (American Thoracic Society 1999, Morgan et al 2001, Ries et al 1997). The inconclusive evidence for inspiratory muscle training offered by randomised controlled trials may be due, at least in part, to methodological inadequacies including insufficient training intensities, insensitive outcome measures and inadequate statistical power. The recent meta-analysis of inspiratory muscle training studies reported improvement in inspiratory muscle function and a reduction in dyspnoea following inspiratory muscle training (Lotters et al 2002). This finding pertains to groups of COPD patients and it is important for clinicians to consider that the response of individuals to inspiratory muscle training may be more variable. As inspiratory muscle weakness is not the only
The effects of inspiratory muscle training (IMT) and whole body exercise (WBE) on dyspnoea in COPD were assessed in randomised controlled trials (RCTs).

**Table 1a.** Randomised controlled trials investigating the effect of inspiratory muscle training in isolation on dyspnoea in COPD

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Mean FEV₁ % pred</th>
<th>Compliance monitoring for IMT</th>
<th>Control group training</th>
<th>Training protocol</th>
<th>Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harver et al 1989</td>
<td>Trained = 10 Control = 9</td>
<td>Trained = 43 Control = 33</td>
<td>Home training: diaries, phone calls, lab visits</td>
<td>Sham trainer</td>
<td>Reseitive flow feedback</td>
<td>Up to 32% of current PImax at FRC</td>
</tr>
<tr>
<td>Guyatt et al 1992</td>
<td>Trained = 43 Control = 39</td>
<td>Trained and control &lt; 70</td>
<td>Home training: visits from nurse</td>
<td>Sham trainer, breathing exercises</td>
<td>Reseitive, no feedback</td>
<td>Up to the maximum tolerable for 10 mins</td>
</tr>
<tr>
<td>Lisboa et al 1997</td>
<td>Trained = 10 Control = 10</td>
<td>Trained = 40 Control = 37</td>
<td>Home training: lab visits 1/7</td>
<td>10% PImax at FRC</td>
<td>Threshold</td>
<td>30% of current PImax at FRC</td>
</tr>
<tr>
<td>Scherer et al 2000</td>
<td>Trained = 15 Control = 15</td>
<td>Trained = 50 Control = 52</td>
<td>Home training: diary, lab visits 1/7</td>
<td>Incentive spirometry</td>
<td>Normocapnic hyperpneoa</td>
<td>60% of initial MVV, progressed</td>
</tr>
<tr>
<td>Riera et al 2001</td>
<td>Trained = 10 Control = 10</td>
<td>Trained = 38 Control = 41</td>
<td>Home training: lab visits 6/52</td>
<td>Sham trainer, relaxation exercises</td>
<td>Reseitive flow feedback</td>
<td>30% of current FRC</td>
</tr>
<tr>
<td>Hsiao et al 2003</td>
<td>Trained (threshold) = 10 Trained (resitive) = 10 Control = 10</td>
<td>Trained (threshold) = 50 Trained (resitive) = 50 Control = 54</td>
<td>Home training: diaries, phone calls, lab visits 2/52</td>
<td>No training</td>
<td>Threshold or resistive with flow feedback</td>
<td>50% of current PImax at RV</td>
</tr>
</tbody>
</table>

**Table 1b.** Randomised controlled trials investigating the cumulative effects of inspiratory muscle training with whole body exercise on dyspnoea in COPD

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Mean FEV₁ % pred</th>
<th>Compliance monitoring for IMT</th>
<th>Control group training</th>
<th>Training protocol</th>
<th>Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wanke et al 1994</td>
<td>IMT + EX = 21 EX alone = 21</td>
<td>IMT + EX = 44 EX alone = 48</td>
<td>Supervised sessions</td>
<td>EX alone</td>
<td>Threshold</td>
<td>12 max sniffs, progressed from 10 mins at 60-70% baseline Pdi at FRC</td>
</tr>
<tr>
<td>Berry et al 1996</td>
<td>IMT + EX = 8 SIMT + EX = 9</td>
<td>IMT + EX = 47 SIMT + EX = 48</td>
<td>Home training 4/7, diary, supervised 3/7</td>
<td>SIMT + EX or SIMT + stretches +br EX</td>
<td>Threshold</td>
<td>Up to 80% baseline PImax at RV</td>
</tr>
<tr>
<td>Larsen et al 1999</td>
<td>IMT alone = 14 control = 12</td>
<td>IMT alone = 46 control = 55</td>
<td>Home training, MD, diaries, visits by nurse</td>
<td>EX alone, IMT alone or education</td>
<td>Threshold</td>
<td>Up to 60% of current PImax at RV</td>
</tr>
</tbody>
</table>

Key for Tables 1a and 1b:
N = number of subjects; FEV₁ %pred = forced expiratory volume in 1 second expressed as a percentage of the predicted value; IMT = inspiratory muscle training; SIMT = sham inspiratory muscle training; PImax = maximum inspiratory mouth pressure; FRC = functional residual capacity; RV = residual volume; BDI = baseline dyspnoea index; TDI = transitional dyspnoea index; CRDQd = dyspnoea domain of the Chronic Respiratory Disease Questionnaire; 6MWD = distance achieved in the six-minute walk test; lab = laboratory; MD = monitoring device; MVV = maximum voluntary ventilation; min(s) = minute(s); ISWT = incremental shuttle walk test; EX = whole body exercise; br ex = breathing exercises; Pdi = transdiaphragmatic pressure; * = significant difference from baseline measures; † = significant difference in post training measures between treatment and control groups; ‡ = significant difference in post training measures in those groups receiving inspiratory muscle training compared with those groups that did not. Difference between groups receiving inspiratory muscle training is not significant.
### Dyspnoea in COPD

<table>
<thead>
<tr>
<th>Training duration</th>
<th>IMT frequency</th>
<th>Inspiratory muscle strength % change from baseline</th>
<th>Inspiratory muscle endurance in trained group</th>
<th>Outcomes</th>
<th>Changes in dyspnoea in trained group</th>
<th>Changes in dyspnoea in control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/52 7/7 15 min sessions 2 x daily</td>
<td>7/7</td>
<td>Trained = 32* Control = 12</td>
<td>Not assessed</td>
<td>BDI/TDI</td>
<td>TDI = 3.5**</td>
<td>TDI = 0.3</td>
</tr>
<tr>
<td>6/12 7/7 10 min sessions 5 x daily</td>
<td>6/7</td>
<td>Trained = 0.2 Control = 1.6</td>
<td>No difference between groups</td>
<td>CRDQd, Borg end exercise</td>
<td>No difference between groups</td>
<td>Borg not reported</td>
</tr>
<tr>
<td>10/52 6/7 30 min sessions once daily</td>
<td>5/7</td>
<td>Trained = 34* Control = 19</td>
<td>Not assessed</td>
<td>BDI/TDI, Borg end exercise</td>
<td>No difference between groups</td>
<td>TDI = 3.8**, lower Borg at end 6MWD**</td>
</tr>
<tr>
<td>8/52 5/7 15 min sessions 2 x daily</td>
<td>6/6</td>
<td>Trained = 30 Control = 17</td>
<td>Improvement**</td>
<td>BDI/TDI</td>
<td>TDI = 4.7</td>
<td>TDI = 2.9</td>
</tr>
<tr>
<td>6/12 6/7 15 min sessions 2 x daily</td>
<td>5/5</td>
<td>Trained = 48** Control = -4</td>
<td>Improvement**</td>
<td>BDI/TDI, CRDQd, Borg end exercise</td>
<td>TDI = 4.7**, CRDQd 1.6**, improved ISWT same end exercise Borg **</td>
<td>TDI = 0.2, CRDQd &lt; 0.2, no change in ISWT or end exercise Borg</td>
</tr>
<tr>
<td>8/52 5/7 15 min sessions 2 x daily</td>
<td>4/4</td>
<td>Threshold trained = 39* Resistive trained = 43* Control = 18*</td>
<td>Improvement**</td>
<td>Borg end exercise</td>
<td>Improved 6 MWD same end exercise Borg</td>
<td>No change in 6 MWD or end exercise Borg</td>
</tr>
</tbody>
</table>

**Note:** The table above summarizes the outcomes of inspiratory muscle training (IMT) on dyspnoea in COPD. The training protocols varied in duration, frequency, and additional exercises (EX). The outcomes were assessed using various methods such as Borg scale, CRDQd, and TDI. Significant improvements in Borg scores and CRDQd suggest that IMT can help reduce dyspnoea in COPD patients.
contributor to dyspnoea in COPD (see Figure 1), inspiratory muscle training yielding improvements in inspiratory muscle function may not benefit all COPD patients. Furthermore, the meta-analysis did not report additional benefits in those studies combining inspiratory muscle training with whole body exercise training on dyspnoea and functional exercise capacity. Subgroup analysis of these studies revealed greater improvements in inspiratory muscle strength in those subjects with weaker inspiratory muscles and therefore inspiratory muscle training offered in conjunction with whole body exercise training is more likely to benefit those subjects with marked inspiratory muscle weakness (Lotters et al 2002).

In conclusion, inspiratory muscle weakness in COPD is known to contribute to dyspnoea (Hamilton et al 1995) and exercise limitation (Gosselink et al 1996). It appears that specific loading of the inspiratory muscles with commercially available hand-held devices, using training intensities of at least 30% of the previously determined maximum inspiratory pressure can improve inspiratory muscle strength and endurance (Lotters et al 2002). Results of randomised controlled trials investigating the role of inspiratory muscle training in reducing dyspnoea in COPD are promising but not conclusive and further research is warranted to identify possible predictors of improvement. Closer attention to training intensity, outcome measures and statistical power will help optimise training regimens and provide better guidance regarding the role of inspiratory muscle training in pulmonary rehabilitation programs.

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References


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