Respiratory muscles training in COPD patients

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Abstract: It is known that respiratory muscles undergo adaptation in response to overload stimuli during exercise training in stable COPD patients, thus resulting in significant increase of respiratory muscle function as well as the individual's improvements. The present article reviews the most updated evidence with regard to the use of respiratory muscle training (RMT) methods in COPD patients. Basically, three types of RMT (resistive training, pressure threshold loading, and normocapnic hyperpnea) have been reported. Frequency, duration, and intensity of exercise must be carefully considered for a training effect. In contrast with the plentitude of existing data inherent to inspiratory muscle training (IMT), literature is still lacking in showing clinical and physiological studies related to expiratory muscle training (EMT). In particular, while it seems that IMT is slightly superior to EMT in providing additional benefits other than respiratory muscle function such as a reduction in dyspnea, both the effects and the safety of EMT is still to be definitively elucidated in patients with COPD.
Keywords: respiratory muscles, pulmonary hyperinflation, dyspnea

Rationale

Systemic inflammation is now known to be an important aspect of chronic obstructive pulmonary disease (COPD) which is able to extend its effects to the skeletal muscular structure. Even if this muscular dysfunction does not similarly involve all the peripheral muscles, available evidence suggests that respiratory muscles are almost always involved (Gosselink et al 2000).

The weakness of the respiratory musculature (with reduced strength and muscular resistance) "has significant clinical consequences for COPD" (Decramer 2001) and this reason may partially explain the appearance of common symptoms like the effort dyspnea, hypercapnia, and reduced tolerance to physical exercise.

So far, a clinical study has demonstrated that respiratory muscle weakness is likely to increase health care resources and is correlated to reduced survival in COPD (Gray-Donald et al 1996).

Respiratory muscle dysfunction is attributed to multiple factors related to the presence and severity of COPD. Indeed, intrinsic (muscular and metabolism mass) as well as extrinsic factors (changes in chest wall geometry and diaphragm position, and systemic metabolic factors) may alter respiratory muscle function (Gosselink et al 2000). The mismatch between the demand for respiratory muscle work and the capacity to meet that demand is mainly caused by dynamic hyperinflation (DH) produced by the incomplete emptying of the lungs during expiration. Hence, one of the most critical factors able to impair respiratory muscle function is the pulmonary hyperinflation which induces the so-called intrinsic positive end expiratory pressure (PEEPi) generating an inspiratory threshold load which accounts for a higher ventilatory demand and a reduced tolerance during exercise. While inspiratory muscle weakness is at least

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partially attributed to hyperinflation (placing the inspiratory muscles at a mechanical disadvantage), expiratory muscle weakness is a feature of the generalized myopathy observed in patients with COPD (Decramer 2001) including very low lactate threshold (Gallagher 1994) which in turn reduces muscle oxidative enzyme activities (Whittom et al 1998).

The most common forms of respiratory muscle training (RMT) generally include both inspiratory muscle training (IMT) and expiratory muscle training (EMT) component to a various extent. IMT assumes a prominent role in this type of training and the definitive role of EMT is still under debate.

The positive influence of inspiratory muscle strengthening upon dyspnea is supported by observations on healthy young individuals (Volianitis et al 2001; Romer et al 2002) where pressure threshold IMT has also been associated with improved athletic performance. Two exhaustive meta-analyses (Smith et al 1992; Lotters et al 2002) have collected available data from randomized trials focused on the effectiveness of IMT in patients with COPD: results have shown a compelling body of evidence in favour of such training, so far included by the joint statement from the American College of Chest Physicians and American Association of Cardiovascular and Pulmonary Rehabilitation Committee (ACCP/AACVPR) among the recommended activities in the pulmonary rehabilitation programs (ACCP/AACVPR 1997). In particular, it has also been demonstrated that placing a load on the respiratory muscle during contraction is sufficient in increasing strength, thus causing a meaningful reduction of breathlessness and an increase of physical exercise ability (Lotters et al 2002). Additionally, a more recent trial that evaluated the 1-year effects of IMT (Beckerman et al 2005) provides evidence that IMT also decreases the use of healthcare services, which may translate into economic benefits as well.

There is still debate in regards to which is the mechanism responsible for the enhanced inspiratory muscle force output (strength) following IMT. Some authors argue that inspiratory muscles of COPD patients are already well adapted to chronic loading and do not express any adaptation in response to training. Nonetheless, a substantial increase in the proportion of type I fibers (by 38%) and in the size of type II fibers (by 21%) of the external intercostal muscles have been found after IMT (Ramirez-Sarmiento et al 2002). These structural changes presumably represent adaptive effects with the genuine remodeling of inspiratory muscle structure during IMT.

In contrast with the plentitude of existing data inherent to IMT, the literature is still lacking in showing clinical and physiological studies related to EMT. The first and complete study that explored the efficacy of EMT has shown that the change in expiratory muscle strength and endurance and the six-minute walk distance were significantly greater after EMT compared with controls; however, this advantage did not translate into any significant change in the sensation of dyspnea during daily activities (Weiner et al 2003a). In another study EMT has been compared with both IMT and combined IMT+EMT, showing that there is no additional benefit in including EMT to the training of the respiratory muscles (Weiner et al 2003b).

Overall, the inclusion of a specific RMT in a typical program focused on rehabilitation of symptomatic COPD is recommended.

Patient selection

So far, the general guideline consensus (ACCP/AACVPR 1997) indicated that RMT should be considered in "selected patients with inspiratory muscle weakness or with ventilatory limitation during physical activity, who remain symptomatic despite optimal therapy".

It appears obvious that providing IMT in a patient with maximal inspiratory pressure (MIP) below 60 cmH_2O, can allow optimal benefits for that patient. However, adding IMT might also benefit those patients with preserved and higher inspiratory muscular abilities. Similarly, highly trained athletes with MIP values above 120 cmH_2O have also shown improvements in dyspnea and exercise performance (Volianitis et al 2001; Romer et al 2002). These data support the notion that since there are no known side-effects of IMT, this modality of training attenuates respiratory effort sensation irrespectively of the functional status of the inspiratory muscle.

Thus it is likely that all the patients with symptomatic COPD (well-motivated patients with low response to other treatments) can benefit from RMT. To confirm this assumption, the most recent consensus on pulmonary rehabilitation considers IMT as an "adjunctive therapy in pulmonary rehabilitation, primarily in patients with suspected or proven respiratory muscle weakness" (ATS/ERS 2006).

Although, RMT is associated with intra-thoracic decompression, there are almost no side-effects associated with the training itself (Pardy et al 1988). Furthermore, patients with heart failure experience no deterioration of their cardiac

output during training. Hence, with the exception of patients with unstable asthma and low perception of dyspnea, a history of spontaneous pneumothorax or emphysema bubbles near pleura, there are no contraindications for IMT.

RMT can be delivered as an in-patient, out-patient, or domiciliary program setting, and it is typically administered and supervised by suitably trained physiotherapists. It may be implemented as a stand-alone intervention or as part of a comprehensive program of pulmonary rehabilitation. The domiciliary setting is generally the most convenient for the patient and it usually follows a period during which patients' RMT is closely supervised in an in-patient or out-patient clinic. Involvement of family members may also be beneficial as they can provide encouragement and sustain patient's motivation.

Techniques

The three most common used modalities of RMT in patients with COPD are based on breathing against resistive loading (RL), breathing against pressure threshold loading (PTL) and voluntary normocapnic hyperpnea (NH).

Resistive loading

This method requires individuals to inspire or expire via a variable-diameter orifice, whereby, for a given airflow, the smaller the orifice the greater the load achieved. Although RL may improve respiratory muscle function (Aldrich and Karpel 1985; Clanton et al 1985) conclusions from these studies should be interpreted with caution. A reasonable limitation of inspiratory RL is that inspiratory pressure, and consequently the training load, varies with flow rate according to a power function and not just to the orifice size (Pardy et al 1988). Therefore, it is crucial that the individual's breathing pattern is monitored during training, thus allowing for the provision of a quantifiable training stimulus.

In their meta-analysis on IMT delivered on patients with COPD, Smith and coworkers (1992) concluded that the use of inspiratory RL without controlling the inspiratory flow rate fails to elicit significant improvement in inspiratory muscle function. On the other hand, several studies which provided feedback control of flow rate during RL resulted in effective benefits, with particular regard to strength, dyspnea and physical exercise tolerance (Harver et al 1989; Belman and Mittman 1991; Sanchez Riera et al 2001). Nonetheless, such modifications require additional hardware, because of the increasing cost and complexity of this type of IMT.

Pressure threshold loading

This technique requires individuals to produce a negative pressure sufficient to overcome the load of the device and thereby initiate inspiration. Threshold loading allows variable loading at a detectable intensity by providing near flow independent resistance to inspiration. It has been achieved in several ways, by way of a weighted plunger (Nickerson and Keens 1982), a solenoid valve (Bardsley et al 1993), a constant negative pressure system (Chen et al 1998), or a spring-loaded poppet valve (Larson et al 1988; Gosselink et al 1996; Caine and McConnell 2000). The spring characteristics are linear such that a given change in spring length results in the same change in valve opening pressure at each spring length. The valve only opens when the inspiratory pressure generated by the patient exceeds the spring tension. Expiration is unimpeded and occurs via the expiratory flap valve.

Threshold loading has been shown to induce improvements in strength (Larson et al 1988; Lotters et al 2002), maximum rate of muscle shortening (Romer et al 2002; Villafranca et al 1998; Romer and McConnell 2003), maximum power output (Lisboa et al 1994; Villafranca et al 1998; Romer and McConnell 2003), and muscle endurance (Lisboa et al 1994; Weiner et al 2004). Due to its flow independence, PTL training can be undertaken without monitoring the individual's breathing pattern. In addition, PTL using a device with a mechanical poppet valve is both portable and easy to use, with evidence of efficacy when implemented in a domiciliary setting, as well as in long-term use (see also Figure 1). To cut short, although it appears to be as effective as RL, PTL (probably due to its simplicity, reliability and "user-friendliness") has been implemented most widely, especially using the poppet valve method.

Voluntary normocapnic hyperpnea

To the best of our knowledge, the NH technique has been applied in very few studies (Belman and Mittman 1980; Levine et al 1986). This method requires individuals to maintain high target levels of ventilation up to 30 minutes. To prevent hypocapnia, subjects simply rebreathe through a dead space. Training sessions are typically conducted 3 to 5 times per week at about 70%–90% of maximal sustainable voluntary ventilation and the training effect is evaluated by monitoring the change in the time to exhaustion during either sustained or incremental isocapnic ventilation. Because the complicated equipment needed to prevent hypocapnia this technique has usually been carried on in hospital facilities

Figure 1 A threshold loading device practically adopted for inspiratory muscle training.

or research laboratory, and it has not been available for domiciliary purposes.

Outcomes

Interpretation of the data relating to RMT in patients with COPD has been hampered by some studies with inadequate experimental designs; flaws have often included a failure to apply basic training theories. The negative outcomes of most studies contributed to early scepticism about the value of RMT. However, in the overall assessment of the respiratory muscle training it is also important to consider both physiological (eg, respiratory muscle strength and lung function) and clinical responses (eg, individual's dyspnea, exercise tolerance, and even quality of life).

From the individual's functional ability, the efficacy of RMT needs to be assessed in terms of inspiratory and expiratory muscle function. The most straight-forward non-invasive assessment of respiratory muscle function are MIP and maximal expiratory pressure (MEP). These measures are indicative for weakness of the respiratory muscles and are indirectly assessed through the maximal and voluntary pressure generated during inspiration or expiration. To confirm the importance of the appraisal of the respiratory muscle function measurements there are updated documents

in recent literature clarifying these aspects (ATS/ERS 2002; Troosters et al 2005). An argument favoring the use of MIP is that this functional improvement is linked to changes in dyspnea; additionally, it has been clearly defined that changes in dyspnea only occur when training results in improved muscle strength. This has been so far recognized in clinical trials (Harver et al 1989; Lisboa et al 1994). Regular monitoring of MIP also provides both reassurance that patients are adhering to the prescribed training regimen, and the basis for resetting training loads: ideally, monitoring should be undertaken once per week.

It is notable that a significant positive relationship exists between the percentage increase in MIP and the relative magnitude of the IMT load (Pardy and Rochester 1992), thus suggesting that the higher the load relative to the subject's inspiratory muscle strength, the greater is the increase in strength achieved. The existing data suggest that to achieve a 20% increase in MIP, a load of ≥30% MIP is then required (Lotters et al 2002). The lack of effectiveness of training at a load <30% of MIP is supported by previous observation (Presseur et al 1994) showing that MIP failed to improve significantly after 12 weeks of IMT at a load equal to 22% of MIP. Reid has recommended the following parameters for IMT in COPD: an initial training interval as short as 3–5 min, progressing to two 15 min or one 30 min session per day, 4–6 days per week at a training intensity of 40%–70% MIP indefinitely (Reid et al 2004). Finally, more recent studies (Sturdy et al 2003; Hill et al 2006) have examined the feasibility of using high-intensity, interval-based threshold loading IMT (a total of about 20 minutes alternating cycles of 2-minutes of breathing at the maximum load tolerable, followed by 1 minute of rest).

The results regarding duration of MIP's improvements have been studied in only one randomized trial of IMT (Weiner et al 2004): in this study the largest improvement of MIP has been recorded during the first 3 months of their study (32%), then followed by a smaller increase (~6%) in the four subsequent 3-month blocks of IMT. The early plateau effect of IMT has been observed so far in pathology (Larson et al 1988; Lisboa et al 1997) as well as in healthy individuals. The development of a plateau cannot be ascribed to a lack of load progression (increasing the training load to accommodate increases in MIP), since it occurs regardless of this measure. Instead, it is a reflection of a basic property of muscle adaptation to strength training stimuli, which necessitates periodic changes in the training stimulus in order to maintain the adaptation process. Despite the now overwhelming evidence that RMT, and particularly IMT using threshold loading, produces improvements in inspiratory muscle function, which in turn result in functional benefits to COPD patients, some researchers still ascribe these improvements to mechanisms other than an adaptation to a training stimulus. Ramirez-Sarmiento and coworkers (2002) observed a significant increase in the size of type 2 muscle fibres taking biopsies from the external intercostals muscles following 5-week IMT; this is very strong evidence that IMT induces genuine remodeling of inspiratory muscles.

Assessments of individual's functional capacity (in terms of 6-minute or 12-minute walked distance) and dyspnea (BDI, TDI) are measures often associated with respiratory muscle strength recording. The effect of RMT by isocapnic hyperpnea in COPD patients has been translated into benefits of both respiratory muscle endurance and exercise tolerance, concluding that "respiratory muscle endurance training … improves health-related quality of life" (Scherer et al 2000). Similar findings have been obtained using a target-flow incentive spirometry system to train the inspiratory muscles, thus showing a significant increase of the distance walked at 6 months with respect to controls (Sanchez Riera et al 2001).

Significant improvements are also evident in dyspnea and health-related quality of life. The benefits of RMT to respiratory breathlessness, exercise tolerance and quality of life were confirmed in a recent published study of RMT by threshold loading method in severely impaired COPD patients (Covey et al 2001). The improvements in inspiratory muscle strength and endurance, paralleled the reduction in the sense of respiratory effort experienced during a loaded breathing task and in the respiratory symptoms associated with activities of daily living. These respiratory muscle function benefits have also been recently confirmed in terms of 6-minute walked distance and quality of life by using a high-intensity, interval-based threshold loading IMT (Hill et al 2006).

Conclusions and clinical implications

Like other skeletal muscles, respiratory muscles undergo adaptation in response to stimuli overload during exercise training in stable COPD patients, thus resulting in significant increases of strength and endurance and in a clinically significant change of dyspnea sensation at rest and during exercise. Three types of RMT have been reported, (resistive training, pressure threshold loading, and normocapnic hyperpnea) with no data, at present, to support one method over the other.

For a training effect, the frequency, duration, and intensity of exercise must be considered. A number of factors are associated with successful outcomes after RMT; a training frequency of 1–2 times per day for a total amount of 30 minutes, with a frequency of 3–5 days per week for a duration of 6 weeks has been suggested and may induce desired changes. With concern to the inspiratory load, the evidence supports the use of training loads that exceed 30% of MIP with a repetition duration dependent upon the load, as higher loads cannot be sustained as long as lower loads.

While it seems that IMT is slightly superior to EMT in providing additional benefit other than respiratory muscle function such as a reduction in dyspnea, the effects and the safety of EMT in patients with COPD is yet to be elucidated.

Therefore, actual evidence for RMT, in addition to regular exercise training in stable COPD patients with or without respiratory muscle weakness, needs to be further implemented.

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