Clinical Applications of Inspiratory Muscle Training

Sections

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Section 1

Many disease conditions are associated with abnormal function of the respiratory muscles. Inadequacy of respiratory muscle function can be due to a number of causes, but principally: 1) weakness and or increased fatigability of the respiratory muscles induced by structural/metabolic changes in the muscles themselves (e.g., muscular dystrophy); 2) failure of muscle activation by the nervous system (e.g., multiple sclerosis); 3) functional weakness induced by alterations in the mechanics of the respiratory system that induce an increased requirement for muscle force output (e.g., emphysema); 4) or a combination of these factors (e.g., chronic heart failure).

It is therefore not surprising that respiratory muscle training (RMT) has been applied to a wide range of clinical conditions during the past two decades. Principally, however, RMT has been applied to conditions associated with the respiratory system, especially chronic obstructive pulmonary disease (COPD). This training has taken many forms (see appendix 1), with the very early studies seeking to induce improvements in respiratory muscle endurance using systems that required subjects to hyperventilate for prolonged periods. More recently, inspiratory muscle resistance training has become the preferred method of training (inspiratory muscle training: IMT).

The first study of RMT in patients was in 1977 and demonstrated that RMT (isocapnic hyperpnoea) improved respiratory muscle endurance in patients with cystic fibrosis (Keens et al., 1977). This study was a direct response to the first published study of

RMT in healthy individuals by Leith and Bradley in 1976. Keens et al. reasoned that if respiratory muscle endurance could be improved in healthy individuals, then it may be beneficial to train these muscles in patients who's conditions made them susceptible to respiratory muscle fatigue.

The majority of research in this area has focused on adults with chronic obstructive pulmonary disease (COPD). In a meta-analysis of 17 "relevant randomised trials" of RMT in COPD patients, Smith et al. (1992) reported non-significant changes in inspiratory muscle strength in 11 studies in which it was evaluated, and in respiratory muscle endurance in nine studies in which it was evaluated. Their primary conclusion was that, "Overall, there is little evidence of clinically important benefit of respiratory muscle training in patients with chronic airflow limitation". The results of this meta-analysis are responsible for the continued reticence of many chest physicians to adopt RMT as a method of managing patients with COPD, despite a further decade of positive outcomes in clinical trials of RMT (see below). An inappropriate training stimulus (mode, frequency, intensity and/or duration) is the most likely explanation for the failure of the majority of the studies analysed by Smith et al. (1992) to generate the expected physiologic training responses. However, Smith et al. did identify a moderate treatment effect for improved functional exercise capacity in five studies in which respiratory strength or endurance did improve. In other words, in studies that had achieved an improvement in respiratory muscle performance, functional benefits were observed. Further analyses suggested that RMT might lead to marked improvements in respiratory muscle strength and/or endurance if the training stimulus is controlled such that substantial pressures are generated during inspiration. Unfortunately, many clinicians still take Smith et al.'s primary conclusions at face value and fail to consider the inadequacies of most of the studies within the meta-analysis. An updated review of the consensus on RMT in patients with COPD is given below (section 2.1).

Section 2

2.1. Chronic obstructive pulmonary disease (COPD)

This is a primarily a smoking-related condition, which includes emphysema and bronchitis. It does not tend to become symptomatic until the patient is in their middle age. There are a small proportion of patients who possess an enzyme deficiency (alpha–1 antitrypsin) that produces the signs and symptoms of COPD, without exposure to smoke, or other life-style contributors to the development of COPD; these patients are much younger.

Rationale

The rationale for RMT in patients with COPD is very strong. These patients not only have weakness of their inspiratory muscles, they also experience alterations in their chest wall mechanics that reduce the effectiveness of the diaphragm and increase the work of breathing. They also have very low lactate thresholds and a correspondingly high ventilatory demand during exercise. In other words, the balance of demand and supply is tipped heavily in the direction of demand, with the ability to supply that demand being severely diminished. Exercise tolerance is limited by extreme breathlessness, and this is the main symptom that patients report impacting negatively upon their quality of life.

In addition, recent evidence regarding the control of blood flow to the exercising limbs suggests a hitherto overlooked impact of inspiratory (especially diaphragm) muscle fatigue upon exercise tolerance in patients with COPD (and other conditions that increase the vulnerability to inspiratory muscle fatigue). This evidence points to the possibility that the fatiguing diaphragm may generate sympathetic nervous system activity that restricts blood flow to the limbs. The effect of this would be to increase fatigue in the limbs and to intensify the metabolic and sensory events associated with exercise, thus contributing to exercise intolerance. Sheel et al. (2001) have identified that the healthy fatiguing diaphragm generates strong vasoconstrictor activity in the limb muscles. Thus far, this reflex has been observed only under resting conditions. However, other research from this group supports the existence of a similar phenomenon in the limbs during strenuous exercise in healthy young men. A combination of ventilatory work due to exercise and added external inspiratory work led to a reduction in limb blood flow during exercise (Harms et al., 1997, 1998; Wetter et al., 1999). When this evidence is combined with that from Poole et al. (2001), which suggests that metabolic characteristics of the diaphragm in emphysema predispose it to premature fatigue, there is a strong circumstantial argument for training the inspiratory muscles to limit the extent of inspiratory muscle fatigue associated with ventilatory work.

Evidence

In light of the strong rationale for RMT in COPD, it is particularly ironic that there is greatest controversy about the role of RMT in managing patients with COPD. A guidelines panel organised under the joint support of the American College of Chest Physicians (ACCP) and the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) extended the work of Smith et al. (1992). This is a particularly influential grouping and many chest physicians will view their recommendations as being authoritative. Accordingly, a summary of their findings is given here.

The group (ACCP/AACVPR) considered not only physiological responses to RMT (e.g., respiratory muscle strength and lung function), but also clinical outcomes such as breathlessness and exercise capacity (ACCP/AACVPR, 1997). Of the eight randomised and controlled studies of RMT, three studies measured breathlessness ratings and five studies included measures of functional or exercise capacity (e.g., 6 or 12 min walking distance). Harver et al. (1989) and Lisboa et al. (1994) reported a significant reduction in the severity of breathlessness, as measured by the ‘Baseline and Transition Dyspnoea Indexes’ (scales to measure changes in breathlessness), in response to RMT. Importantly, both studies reported significant correlation coefficients between the changes in inspiratory muscle strength (MIP) and changes in breathlessness ratings with RMT, suggesting a causal relationship between these parameters. In contrast, Larson et al. (1988) observed no change in “shortness of breath” as measured on a five-point scale. However, these authors failed to provide evidence that this scale was appropriate (valid, reliable and sensitive) for measuring breathlessness and their results must be viewed in this light.

The studies reviewed by the ACCP/AACVPR reported variable changes in exercise tolerance following RMT. The distance walked during a timed test was increased in two studies (Pardy et al., 1981; Larson et al., 1988), whereas two studies showed no change after to RMT (Guyatt et al., 1992; Preusser et al., 1994). Interestingly, a significant increase in inspiratory muscle strength (MIP) with RMT was observed in those groups who improved exercise capacity. In contrast, MIP did not change following RMT in the two studies that reported no difference in the 6 or 12 min walking distance. Collectively, these four studies suggest that exercise capacity increases when the stimulus or load placed on the respiratory muscles with RMT is sufficient to augment inspiratory muscle strength.

Four other studies examined specific RMT concurrent with general whole body exercise training in COPD patients (Berry et al., 1996; Dekhuijzen et al., 1991; Goldstein et al., 1989; Wanke et al., 1994; Weiner et al., 1992). In three studies, the groups who performed RMT and whole body exercise exhibited significant increases in inspiratory muscle strength (MIP) and had significantly greater increases in exercise tolerance compared with the groups who did exercise only (Dekhuijzen et al., 1991; Wanke et al., 1994; Weiner et al., 1992). In one study (Berry et al., 1996) patients who performed RMT did not improve MIP; therefore, the respiratory muscle training stimulus was inadequate, and their data must be viewed accordingly.

The general consensus communicated by the ACCP/AACVPR guidelines was that RMT should be considered in “selected patients [those with inspiratory muscle weakness] who remain symptomatic despite optimal therapy” (ACCP/AACVPR, 1997). However, it can be argued that because RMT reduces breathlessness and improves exercise tolerance and performance in *healthy* individuals, it is reasonable to suppose that all patients with COPD can benefit from RMT.

Based on the scientific evidence contained within the reviews articles of the ACCP/AACVPR (1997) and Smith et al. (1992), it is clear that many of the studies reviewed failed to achieve the expected increase in respiratory muscle function, and unsurprisingly, also failed to document any improvements in functional parameters such as breathlessness and exercise tolerance. When selected randomised controlled studies that included adequate training loads and measured clinical outcomes are considered, improvements in breathlessness and/or exercise tolerance are observed with RMT.

Since the ACCP/AACVPR review was published in 1997, a number of further studies of RMT have been published and are summarised below:

Lisboa et al. (1997) observed significant improvement in inspiratory muscle strength after IMT (pressure threshold). This was accompanied by improvement in exercise tolerance and breathlessness. The authors conclude that, "inspiratory muscle training using a threshold device…relieves dyspnoea, improves performance of daily life activities, and reduces the metabolic cost of exercise in patients with chronic airflow limitation".

Similar results were obtained by de Lucas Ramos (1998) who undertook a controlled trial of IMT (pressure threshold) in 35 stable COPD patients. The IMT group (n=20) exhibited a significant improvement in inspiratory muscle strength, a reduction in breathlessness during exercise, and an increased exercise tolerance. However, the patients did not display any improvement in lung function; this is in contrast to Lisboa et al. (1997) and others. The authors concluded that, "specific training of inspiratory muscles does not appear to improve lung function in patients with COPD, it is accompanied by a decrease in sense of dyspnea during exercise and greater tolerance".

Larson et al.'s study (1999) compared the effects of IMT (threshold loading), cycle ergometer training and the combined effect of and cycle ergometer training in COPD patients. They noted no benefits of IMT alone, and no additional benefit of combining IMT and cycle ergometer training. However, their IMT protocol generated relatively modest improvements in inspiratory muscle strength (IMT alone = 10% and exercise+IMT = 20%) compared to other studies (Lisboa et al., 1997 = 34%; Weiner et al, 2000 = 25%; Sachez Riera et al., 2001 = 50%). Thus, the absence of a benefit of IMT to exercise tolerance may be due to the inadequacy of the IMT training stimulus.

Nield (1999) reported the results of a pilot study of IMT (pressure threshold) in four patients with COPD. This was an uncontrolled trial on a very small number of subjects, but the author does report improvements in a number of indices of breathlessness.

Weiner et al. (2000) examined the influence of a sequential combination of interventions designed to improve breathlessness in patients with COPD, viz., bronchodilator therapy, exercise and IMT (threshold loading). They noted that the most significant effect upon breathlessness was following IMT, with the other two interventions providing only small improvements. Exercise provided the greatest improvement in exercise performance, with the addition of IMT providing a further small increase in performance. The authors report that, “the most significant improvement [in breathlessness] was associated with IMT and not with the long-acting bronchodilator and exercise training”.

In the study by Scherer et al. (2000), the effect of RMT (isocapnic hyperpnoea) was assessed in 15 patients with COPD, and compared to that of 15 control patients who undertook breathing exercises with an incentive spirometer. They observed significant improvements in respiratory muscle endurance and exercise tolerance in the training group, concluding that, “respiratory muscle endurance training…improves respiratory muscle and exercise performance, health-related quality of life, and dyspnoea”. Similar findings were obtained by Sanchez Riera et al. (2001) used a target-flow incentive spirometry system to train the inspiratory muscles of 10 patients with COPD (control group n=10). The IMT group exhibited significant improvements in inspiratory muscle function, breathlessness, walking capacity, and health-related quality of life. The benefits of RMT to respiratory breathlessness, exercise tolerance and quality of life were confirmed in the most recent published study of RMT in COPD patients by Covey et al. (2001). They examined the effect of IMT (threshold loading) in a group of severely impaired COPD patients in a controlled trial. They identified improvements in inspiratory muscle strength and endurance, as well as a reduction in the sense of respiratory effort experienced during a loaded breathing task. Most importantly, the IMT group experienced a significant improvement in the respiratory symptoms associated with activities of daily living.

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, there remain some researchers who ascribe these improvements to mechanisms other than an adaptation to a muscle training stimulus. Prof. John Moxham and Dr Michael Polkey remain adamant that IMT does nothing more then enhance the patients' ability to utilise the muscle that they already have, and that there is no genuine training response. However, recent evidence presented at the European Respiratory Society meeting in 2000, and in press with the American Journal of Respiratory & Critical Care Medicine (one of the flagship journals of respiratory medicine), provides evidence to the contrary. Ramirez-Sarmiento et al. (in press) took biopsy samples from the external intercostals muscles (inspiratory muscles of the rib cage) of patients with COPD following five weeks of pressure threshold IMT. They observed a significant increase in the size of type 2 muscle fibres following IMT. This is very strong evidence that IMT induces genuine remodelling of inspiratory muscles.

In conclusion, a recent review published in a Belgian academic journal by Prof. Marc Decramer (2001) noted that there is now evidence that both inspiratory and peripheral muscle dysfunction “have significant consequences for patients with COPD”. He further observed that there is evidence that both factors are negatively related to exercise tolerance and reduced quality of life. In addition, he noted that inspiratory muscle weakness is a determinant of survival and utilisation of healthcare resources in these patients. Decramer observed that treatment of inspiratory muscle weakness is possible and that it has “been shown to produce beneficial effects”. Prof. Decamer is an influential figure within the European Respiratory Society and this review may herald the start of a new era in the role of IMT in the management of patients with COPD.

2.2. Asthma

Despite some obvious similarities between the symptoms of patients with COPD and asthma (breathlessness and exercise intolerance), there have been surprisingly few studies of RMT in patients with asthma.

Rationale

Asthma is a condition associated with reversible airways obstruction. Breathlessness is strongly related to the sense of respiratory muscle effort, which is increased in asthma due to airway narrowing, and hyperinflation (also seen in COPD). Hyperinflation results from the inability to breathe out fully to the respiratory system's relaxation volume due to airway collapse and closure. The consequence of this is the requirement to breathe at higher ranges of the lung volume where the elastic load to breathing is greater. The increased respiratory effort associated with this is exacerbated by the fact that the inspiratory muscles are also weaker at higher lung volumes.

There is evidence that patients with asthma have weaker inspiratory muscles than normal subjects; this is probably due to their avoidance of physical activities that induce breathlessness.

Evidence

In the first study of IMT in patients with asthma, Weiner et al. (1992) observed improvements in a range of outcomes following a six month period of pressure threshold IMT. Improvements included: inspiratory muscle strength (27%); lung function; asthma symptoms; hospitalisations for asthma; absence from school or work. The most impressive finding was an 81% reduction in the consumption of broncholdilator medication, and one third of patients in the IMT group also ceased using corticosteriod medication.

In a pilot study, McConnell et al. (1998) assessed the efficacy of just three weeks of IMT (POWERbreathe®) upon breathlessness and exercise tolerance in 18 patients with mild/moderate asthma. The data were consistent with those of Weiner et al. (1992), with subjects in the IMT group (n=9) displaying improvements in lung function, as well as a 12.4% reduction in breathlessness during exercise. The patients also reported an increased inclination to take part in physical activity. No changes were reported in the control group.

In the only other published study of IMT in patients with asthma, Weiner et al. (2000) examined the influence of IMT (pressure threshold) upon consumption of medication and breathlessness in a group of patients with mild asthma who were "high consumers" of bronchodilator medication (more than one puff per day). After 3 months of IMT, the IMT group displayed an increase in inspiratory muscle strength of 17%, a reduction in breathlessness during a loaded breathing task, and a 38% reduction in their use of broncholdilator medication.

Despite the limited number of studies in asthma, all three have shown significant improvements in functional outcome measures following IMT, with no adverse side effects. Perhaps the most persuasive finding from the point of view of patient management is the reduction in the consumption of inhaled medication; this has significant cost implications for the health service.

2.3. Cystic Fibrosis (CF)

Rationale

Patients with CF experience many of the alterations in respiratory mechanics that afflict patients with COPD and asthma, e.g., hyperinflation, airway obstruction, increased work of breathing. In contrast, inspiratory muscle weakness does not appear to be present. However, it is reasonable to suppose that IMT will alleviate the symptoms of CF in the same way that it does in COPD.

Evidence

The first clinical trial of IMT was in patients with CF (Keens et al, 1977). The study showed that RMT (isocapnic hyperpnoea) could improve inspiratory muscle endurance in patients with CF. Understandably, for the first study of its type, it did not seek to examine the potential benefits of RMT to exercise tolerance. The first study to assess this was in 1982, when Asher et al (1982) examined the effect of four weeks of IMT (flow resistive). The training produced modest changes in inspiratory muscle strength (10%) and endurance, and no change in exercise performance in 11 patients with CF. This finding was replicated in the most recent study of RMT in patients with CF by de Jong et al., 2001. The authors also failed to demonstrate significant improvements in lung function, exercise tolerance or breathlessness after six weeks of IMT (pressure threshold). The authors ascribe this to the low training intensity used (20-min at 40% of inspiratory muscle strength) and the consequently modest improvements in inspiratory muscle strength (17%) and endurance.

In contrast, Sawyer and Clanton (1993) found that 10 weeks of IMT (pressure threshold) generated significant improvements in inspiratory muscle strength (13%), lung function and exercise tolerance in children with CF. Although the increase in strength was modest in this study, the training protocol required the subjects to breathe against the training load for 30-min daily (at 50-60% of inspiratory muscle strength); this training stimulus is likely to generate improvements in endurance, rather than strength. The greater training intensity and longer duration of the intervention may explain the discrepancy between this study and that of Asher et al. (1982) and de Jong et al. (2001).

Withnall et al. Campbell et al. and Heward et al. (2000) each presented data at the European Respiratory Society meeting in 2000. The three abstracts report data from the same group of subjects. Collectively, they reported significant improvements in inspiratory muscle function, diaphragm thickness, lung function and exercise performance after eight weeks of IMT (TIRE system) in patients with CF and healthy subjects. They also reported a reduction in resting energy expenditure in the CF patients, which they ascribe to a reduced work of breathing after IMT. The discrepancies between studies suggest that there may be protocol-specific differences in outcome, that are dependent upon the magnitude of the training stimulus and the adaptations elicited in the inspiratory muscles.

2.4. Chronic/congestive heart disease (CHF)

Rationale

Both the peripheral and respiratory muscles of patients with CHF display abnormalities (histochemical, metabolic, vascular). Furthermore, inspiratory muscle strength has been identified as an independent predictor of prognosis; in other words, patients with the weakest inspiratory muscles showed the greatest risk of mortality and *vice versa* (Meyer et al., 2001). There is also evidence that the inspiratory muscles of CHF patients are placed under considerable load during exercise and that they exhibit fatigue (Hughes et al., 2001). This weakness and fatigue has been suggested to contribute to the breathlessness and exercise limitation seen in these patients (Hughes et al., 2001; Chua et al., 1995). The impaired cardiac output of patients with CHF may be exacerbated still further by the influence of diaphragm fatigue upon limb blood flow described in section 2.1, making them even more vulnerable to exercise intolerance.

Evidence

The first study to examine RMT in patients with CHF was conducted in 1995 (Mancini et al., 1995). Fourteen patients were studied before and after three months of supervised IMT (combination of isocapnic hyperpnoea, maximum static inspiratory efforts & pressure threshold loading). Training produced improvements in strength (37%) and endurance of the respiratory muscles (57%) in the training group (n=8). The training group also experienced a reduction in breathlessness during activities of daily living, as well as performance during sub-maximal and maximal exercise tests. The authors suggest that RMY may provide “a simple and useful adjunct to medical therapy” for patients with CHF.

Cahalin et al. (1997) examined the influence of eight weeks of the IMT (pressure threshold) upon breathlessness at rest and during exercise. Inspiratory muscle strength increased by 24% in the 14 patients studied. Breathlessness was lower at rest and during exercise after two weeks of training (29%) and remained at this lower level for the remainder of the study period.

Johnson et al. (1998) used pressure threshold IMT and trained their subjects for eight weeks. Inspiratory muscle strength improved by 25% in the training group (and 12% in the control group). Whilst the study failed to demonstrate any statistically significant difference in the response of the two groups, there was a consistent reduction in breathlessness, and improvement in exercise performance in the IMT group (with little change in the sham training control group). The subject numbers are small and the lack of significance may reflect the poor reliability of their tests, combined with small subject numbers.

In an abstract published in 1998, Darnley et al. report the effect of a four-week programme of IMT (flow resistive) in nine patients with chronic coronary artery disease. Inspiratory muscle function was improved after training (velocity of diaphragm shortening) and this was accompanied by a 6.4% improvement in exercise capacity, which was statistically significant. Fewer patients were limited by breathlessness during the exercise test after the IMT, than before. The authors conclude that IMT "can improve exercise capacity, diaphragm function and symptoms in patients with chronic coronary heart disease".

Weiner et al. (1999) examined the influence of three months of IMT (pressure threshold) upon 20 patients with CHF. The training group (n=10) increased inspiratory muscle strength by 37% and endurance by 42% (no changes in the control group). There was also a small improvement in lung function, as well as exercise tolerance (23%) and breathlessness. The authors conclude that IMT may "prove to be a complimentary therapy in patients with CHF".

Most recently, Martinez et al (2001) have reported the effects of a six-week programme of IMT (pressure threshold) in 20 patients with CHF. The group was divided into two groups, each with a differing training intensity. Inspiratory muscle strength and endurance improved in both groups, but to a greater extent in the higher intensity-training group. There was also an 8% improvement in exercise tolerance in the high intensity-training group. Unfortunately, this paper is in

Spanish, and the detail available in the English abstract is limited. It is clear that the study deign is not very strong and that some of the changes are not statistically significant. Nonetheless, the data are consistent with the findings of previous investigators.

Finally, Weiner et al. (1998) have examined the benefits of prophylactic IMT in patients about to undergo coronary artery bypass graft surgery. Their rationale was that post-operative pulmonary complications are the main causes of morbidity and mortality and that inspiratory muscle weakness may contribute to this. They studied 84 patients, half of whom received between two and four weeks of IMT (pressure threshold) prior to surgery, and half of which undertook sham training. There was a significant deterioration in inspiratory muscle strength, lung function and blood gases in the sham-training group, whereas these parameters were maintained at their pre-operative values in the training group. Furthermore, only two of the training group required post-operative mechanical ventilation longer than 24 hours, whereas this was required by 11 of the sham-training group. The reduction in post-operative complications is consistent with the findings of Nomori et al. (1994). Weiner et al. suggest that it is reasonable to conclude that pre-operative IMT may prevent “most of the perioperative pulmonary complications, may shorten the time of mechanical ventilation and hospitalization, and may decrease mortality”.

2.5. Neuromuscular disease

Neuromuscular disorders include Duchenne muscular dystrophy (DMD), and neurodegenerative diseases such as multiple sclerosis (MS).

Rationale
Respiratory complications are a common cause morbidity and mortality in patients with neuromuscular disease. The underlying mechanism is the respiratory muscle weakness that accompanies these conditions. However, despite the clear rationale for increasing inspiratory muscle strength in these patients, the ability of diseased muscle to respond to a training stimulus remains controversial. Generally, the more severe the patients’ disease, the less likely they are to respond to training.

Similarly, the more rapid the progress of their disease, the less likely they are to show a training effect. However, the reverse is also true. A study by Winkler et al. (2000) supported the efficacy of RMT in patients with neuromuscular disease. They identified a dose-dependent relationship between the number of training sessions and improvements in inspiratory muscle function, provided that the progress of the disease was not too rapid (<10% fall in vital capacity in the year prior to enrolment in the study).

Evidence

There is a great deal of contradiction within the early literature in this area, largely for the reasons given above. The most recently published study on patients with neuromuscular disease (primarily DMD) is that by Koessler et al. (2001), who reports the results of a two year study of IMT in three group of patients. The three groups differed in the severity of their lung function impairment (~40%, ~60%, ~80% predicted vital capacity). The training protocol consisted of targeted resistive breathing exercises and maximum static inspiratory manoeuvres. They noted improvements in inspiratory muscle strength and lung function (vital capacity) in all three groups. The authors conclude that IMT is effective in improving and stabilising vital capacity in patients with neuromuscular disease for a period of up to two years.

2.6. Spinal cord injury (SCI)

Rationale

Spinal cord injury is associated with respiratory compromise. Depending upon the level of the spinal cord injury, this can be severe, with almost complete loss of function to all but the diaphragm, sternocleidomastoids, scalenes and trapezoids. Thus, SCI is associated with inadequate ventilation and extreme breathlessness. Even lower cord injuries result in impaired inspiratory function, because the normal mechanics of the thorax and abdomen are disrupted. Maintaining and improving the function of the remaining muscle is important for the maintenance of adequate ventilation, the avoidance of inspiratory muscle fatigue, and minimising the risk of respiratory infections due to impaired cough efficacy.

Evidence

Two early studies of IMT in patients with tetraplegia confirmed the ability to train the inspiratory muscles of patients with SCI (Gross et al., 1980; Hultgren et al., 1980). IMT (flow resistive) improved strength, endurance and resistance to inspiratory fatigue. A more recent study by Zupan et al. (1997) demonstrated that improvements in inspiratory muscle strength following IMT (incentive spirometry) were accompanied by improvements in lung function. Similar results were obtained by Liaw et al. (2000) and Ehrilich et al. (1999). The latter study also demonstrated reductions in the incidence of respiratory infections, and physiotherapy treatment time declined progressively throughout the period of the 12-month training intervention. Uijl et al. (1999) used inspiratory endurance training (target flow resistive) and observed no improvement in inspiratory muscle strength or lung function, but did note improvements in the endurance of the inspiratory muscles, as well as maximal aerobic capacity. This suggests that it may be necessary to induce improvements in strength in order to improve lung function, but that exercise tolerance can be improved by both inspiratory muscle endurance and strength training.

2.7. Miscellaneous disease

Rationale

In most of the conditions listed below, the rationale for inspiratory muscle relates to imbalance of ‘supply and demand’; in other words, conditions in which inspiratory muscle function is diminished, and/or inspiratory muscle work is increased as a result of disease.

Evidence

Bronchiectasis (BE): this is a respiratory disease with many features in common with COPD, except that it occurs in younger individuals and is often precipitated by respiratory illness (e.g., pneumonia) in childhood. Newall et al. (2000) reported the results of a study in 19 patients with BE at the European Respiratory Society meeting in 2000. After eight weeks of IMT (POWERbreathe®) inspiratory muscle strength improved significantly in the training group (n=10), but not the sham training control group. There were also significant improvements in lung function, exercise tolerance and quality of life in the IMT group that were not observed in the control group.

Postpolio syndrome: this condition is often associated with in inspiratory muscle dysfunction. In a study of five patients by Weinberg et al. (1999), exercise was limited by ventilatory insufficiency, as indicated by abnormal blood gas values during exercise. A subsequent study of IMT in ten postpolio patients by Klefbeck et al. (2000) revealed that ten weeks of IMT improved inspiratory muscle endurance capacity and activities of daily living, but did not improve whole-body endurance capacity. The authors concluded that IMT "can increase respiratory muscle endurance and improve well-being in patients with prior polio". Similar results were reported in an abstract at the 2001 European Respiratory Society meeting by Gross et al. (2001).

Myasthenia Gravis (MG): this is an autoimmune disease associated with generalised weakness and fatigue, which includes weakness of the inspiratory muscles inducing breathlessness at rest and during exercise (Weiner et al., 1998). In a study of RMT in two groups of patients with MG (one with moderate disease, the other with severe), Weiner et al. observed significant improvements in the strength and endurance of the inspiratory muscles of both groups following IMT (pressure threshold). These improvements were accompanied by improved lung function and reduced breathlessness. The authors conclude that RMT, "may prove useful as a complimentary therapy with the aim of reducing dyspnea (breathlessness) symptoms, delay the breathing crisis and the need for mechanical ventilation in patients with MG".

Chronic renal failure: this condition is associated with generalised muscle weakness. Weiner et al. (1996) assessed the influence of three months of IMT (pressure threshold) upon twenty patients who were receiving chronic haemodialysis. The training group (n=10) displayed improvements in inspiratory muscle function and functional capacity that were not seen in the sham training control group.

Patients undergoing lung resection: lung volume resection (removal of a lung, or lobes) is a common treatment for lung cancer patients, as well as those with severe COPD. Most patients experience a reduction in respiratory muscle function post-operatively, as well as a decline in lung function. Weiner et al. (1997) tested the hypothesis that pre-operative IMT might enhance inspiratory muscle strength, and lung function, both pre- and post-operatively. Their study of 32 patients who underwent either pneumonectomy or lobectomy confirmed this hypothesis.

Patients taking oral corticsteriods: High doses of corticosteriods are myopathic, inducing generalised muscle wasting and loss of function, including the inspiratory muscles (Weiner et al., 1993). Weiner et al. (1995) hypothesised that the inspiratory muscle weakness induced by the corticosteriods might impair lung function. Since high doses of steroids are frequently given to patients with lung disease to control lung inflammation, it is possible that this treatment may have unwanted side-effects. Accordingly, Weiner et al. (1995) assessed the influence of acute administration of oral corticosteriods upon the inspiratory muscle and lung function of 12 patients (without respiratory disease). They compared the spontaneous responses to corticosteriods (n=6), with those observed when the corticosteroids were administered by an accompanying programme of IMT (pressure threshold). They observed significant reductions in inspiratory muscle strength (~30%), endurance (~50%) and lung function (forced vital capacity down by almost 15%) during the eight-week course of medication in the group that did not receive IMT. In contrast, inspiratory muscle and lung function remained stable in the IMT group in response to the course of medication. The authors concluded that in order to prevent the detrimental influence of corticosteriods, particularly in respiratory patients in whom inspiratory muscle weakness is already present, IMT might be implemented “to prevent the adverse effect of the drug”.

Snoring: Furrer et al. 1999 have reported benefits to those suffering from snoring following RMT (isocapnic hyperpnea) in an abstract to the American Thoracic Society.

Section 3

The following conditions are associated with respiratory muscle dysfunction and/or increased work of breathing and may benefit from RMT. To my knowledge, there have been no published studies of RMT in these groups.

3.1 Parkinson's disease

Parkinson's is often associated with inspiratory muscle dysfunction and patients have a higher perception of breathlessness than normal people (Weiner et al. (2002).

3.2 Obesity

Obesity changes the mechanics of the chest wall (Ferretti et al., 2001) and the operation of the diaphragm, increasing respiratory effort sensations and breathlessness. In addition, obesity increases the energy (and respiratory) demand of exercise. Ferretti et al. (2001) observed an increase in breathlessness in the supine position in very obese individuals, ascribing it, in part, to dynamic hyperinflation and the associated increase in inspiratory muscle work load.

3.2 Sarcoidosis

This condition is of unknown origin, but is associated with muscle abnormality in 50-80% of patients. Baydur et al. (2001) have examined the respiratory muscle performance, lung function and breathlessness in these patients. They noted significantly impaired lung function and respiratory muscle strength (~40%) in the patients. Breathlessness was more strongly correlated with respiratory muscle strength than with lung function.

3.3 Kyphosis and/or scoliosis

In kyphoscoliosis (KS), lung volumes are reduced, respiratory elastance and resistance are increased, and breathing pattern is rapid and shallow. In an abstract presented to the Physiological Society in 1996, Caine & McConnell reported the relationship between the kyphosis associated with old age, and lung function. They observed a negative relationship between lung function and the severity of kyphosis, which was eliminated in the sub-group of subjects who had the strongest inspiratory muscles. In other words, strong inspiratory muscles appeared to overcome the detrimental influence of kyphosis upon lung function.

3.4 Surgery of the thorax or upper abdomen

Siafakas et al. (1999) reviewed the detrimental influence of various types of surgery upon respiratory muscle function. Whilst the review concludes that respiratory muscle function is an important pre-operative assessment, it stops short of recommending the pre-operative enhancement of their function (by training) in order to avoid post-operative pulmonary complications. However, evidence from Weiner et al. (1997, 1998) and Nomori et al. (1994) suggests that IMT is beneficial for those undergoing thoracic surgery.

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Appendix 1

In general, RMT studies have utilised at least one of the following modes of training: 1) voluntary isocapnic hyperpnoea; 2) resistive loading; 3) pressure threshold loading; 4) elastic loading; and 5) incremental threshold loading. These training modes are described below.

Voluntary Isocapnic Hyperpnoea

Voluntary isocapnic hyperpnoea (VIH) training requires individuals to maintain high target levels of ventilation for up to 30 min. In order to prevent lowering of $PaCO_2$, subjects may simply re-breathe through a dead space. However, most studies have employed more elaborate apparatus that supply supplemental O_2 to avoid hypoxaemia, while at the same time keeping $PaCO_2$ constant (Leith and Bradley, 1976). Training sessions are typically conducted 3 to 5 times per week at ~70-90% MVV and the training effect is evaluated by monitoring the change in the time to volitional exhaustion during either sustained or incremental isocapnic ventilation. Both healthy subjects (Leith and Bradley, 1976) and patients with airway disease (Belman et al., 1986) appear to show improvement in respiratory muscle function with this type of training.

Unfortunately, VIH is a relatively time consuming and physically demanding mode of RMT. Thus, well-trained athletes may fail to improve or even inhibit exercise performance if VIH is conducted at the expense of whole-body endurance training. It usually requires regulation of gas exchange, making VIH difficult to implement outside of the laboratory. Furthermore, it bestows little benefit in terms of the maximal pressure generating capacity of the respiratory muscles.

Resistive Loading

Inspiratory resistive loading requires individuals to inspire via a variable diameter orifice whereby, for a given flow rate, the smaller the orifice the greater the resistive load. Anderson (1979) used a 7.5 $cmH_2O{\cdot}L^{-1}{\cdot}s^{-1}$ resistive load at the expiratory outlet of a one-way valve whilst inspiratory loading was provided by endotracheal tube connections. A simplified version of this device, incorporating nine resistive orifices, a one-way valve, and a mouthpiece was later introduced (Vitapep, Medic-Aid Ltd., Chichester, UK). A similar device, utilising a variable orifice to provide a resistance to flow, has also been used to train the respiratory muscles (Pflex, Healthscan Ltd., Upper Montclair, New Jersey). Kim (1981) described a comparable principle of loading that could be used during normal exercise training whereby the mid-section opening of a mouthpiece, constructed from dental impressions of the upper and lower jaw, was used to regulate airflow. Interchangeable rings of differing opening diameter allowed flow rate to be adjusted.

Although inspiratory resistive loading may improve respiratory muscle function (Aldrich and Karpel, 1985; Clanton et al., 1985b), the findings should be interpreted with caution. An inherent limitation of inspiratory resistive loading is that inspiratory pressure, and thus training load, varies with flow rate and not just orifice size (Pardy et al., 1988). Therefore, it is vitally important that breathing pattern is monitored during this mode of training if a quantifiable training stimulus is to be provided. With the exception of the work of Clanton et al. (1985), studies of inspiratory resistance have controlled neither lung volume nor the breathing strategy during pre- and post-training evaluation of respiratory muscle function. Although a modified resistive loading device can be used to control for flow (Belman and Shadmehr, 1991; Belman and Shadmehr, 1988), such modifications require complex and expensive hardware making this form of RMT impractical for routine use.

Pressure Threshold Loading

Inspiratory pressure threshold loading requires individuals to produce a negative pressure sufficient to overcome a threshold load and thereby initiate inspiration. Threshold loading permits variable loading at a quantifiable intensity by providing near flow independent resistance to inspiration. This has been achieved with a weighted plunger (Clanton et al., 1985b; Eastwood et al., 1994; Eastwood and Hillman, 1995; Flynn et al., 1989; Nickerson and Keens, 1982), a spring-loaded poppet valve (Caine, 1998; Caine and McConnell, 2000; Copestake, 1995; Gosselink et al., 1996; Johnson, Cowley et al., 1996; Larson et al., 1988), a solenoid valve (Bardsley et al., 1993), and a constant negative pressure system (Chen et al., 1998). Threshold training can be utilised effectively without regulating breathing pattern or gas exchange. In addition, threshold loading has the potential to be both portable and easy to use.

Elastic Loading

Training of the respiratory muscles has occasionally utilised a procedure requiring strapping of the rib cage or abdomen. This procedure is more often used as a tool for modelling respiratory mechanics than it is for conditioning the respiratory muscles (Bradley and Anthonisen, 1980; Hussain and Pardy, 1985). Elastic loading typically reduces tidal volume (V_T) and inspiratory time (T_I) such that breathing frequency (f_R) increases with increasing inspired minute ventilation ($\dot{V}_E$) often being maintained (Daubenspeck, 1995). Furthermore, the pressure required of the muscles is dependent upon lung volume (i.e., the higher the V_T, the higher the pressure required). Nevertheless, some investigators have had success using this method of loading as a mode of IMT (Baranov et al., 1998; Delhez et al., 1966; Furian et al., 1998).

Whilst elastic loading appears attractive due to its simplicity of use, it is generally difficult to standardise and quantify the additional work imposed on breathing and thus falls out of favour with those wishing to standardise training loads. Furthermore, elastic loading is a relatively time consuming and physically demanding mode of IMT. However, a loading device has recently been described and tested which appears to bypass several of the aforementioned criticisms (Cline et al., 1999; Gonzalez et al., 1999). In contrast to previous models using external chest wall restriction, loading was quantifiable and reproducible, did not vary with chest volume, and allowed for subject mobility such that exercise could be performed. In addition, the authors were able to maintain V_T constant while increasing $\dot{V}_E$, thus closely mimicking the breathing strategies of whole body exercise. To date, the loading device has not been used to specifically train the inspiratory muscles, although further studies are underway to determine the functional benefits of the device in the context of exercise performance (J.R. Coast, personal communication).

Incremental Threshold Loading

Chatham et al. (1996a) described a novel approach to IMT based on the Test of Incremental Respiratory Endurance (TIRE) technique described by the same group previously (Chatham et al., 1995). The TIRE system utilises an electronic manometer attached via a serial interface to a computer and dedicated software. Initially, the subject performs several sustained maximal inspiratory efforts to provide a baseline pressure-time profile. The subject is then presented with a pressure-time profile typically set at 80% of the maximal effort. The maximum manoeuvre is then repeated six times with 60 s recovery between efforts before the resting time is reduced to 45 s. The subject is required to complete another six efforts, whereby the recovery time is reduced to 30 s and the user repeats the exercise. There are six different levels in all with diminishing recovery times down to 5 s between breaths. The exercise is terminated when the subject either completes the full range of breathing exercises or falls beneath the reference pressure-time profile.

The authors claim that the training technique can be applied to a range of subject populations because the respiratory work during loaded breathing is fixed in direct relation to individual capacity. However, the functional relevance of this form of IMT is questionable since sustained maximal inspiratory efforts bear no relation to the dynamic function of inspiratory muscles during whole body endurance exercise. Training sessions are physically demanding and time consuming (a complete training session typically takes 30 min). Furthermore, the dedicated hardware and software are expensive to purchase making this mode of training inaccessible to most individuals.