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Strategies of muscle training in very severe COPD patients

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ABSTRACT: There is strong evidence that exercise training, constituting the cornerstone of pulmonary rehabilitation, improves exercise tolerance, dyspnoea sensations, functional capacity and quality of life in patients with severe chronic obstructive pulmonary disease. However, intolerable sensations of breathlessness and/or peripheral muscle discomfort may prevent such patients from tolerating high-intensity exercise levels for sufficiently long periods of time to obtain true physiological training effects.

Accordingly, the major issue that arises is the selection of the appropriate training strategy, which is tailored to the cardiovascular, pulmonary and peripheral muscle limitations of the individual patient and is aimed at maximising the effect of exercise conditioning.

Within this context, the present article explores the application of strategies that optimise exercise tolerance by reducing dyspnoea sensations, namely noninvasive mechanical ventilation, oxygen and/or heliox supplementation. Administration of heliox or oxygen during exercise also increases peripheral muscle oxygen delivery, thereby delaying the onset of peripheral muscle fatigue. Particular emphasis is also given to interval exercise and resistance-muscle training as both modalities allow the application of intense loads on peripheral muscles with tolerable levels of dyspnoea sensations.

In patients with profound muscle weakness and intense breathlessness upon physical exertion, execution of short bouts of interval or local muscle strength conditioning, along with oxygen breathing, may constitute a feasible and effective approach to pulmonary rehabilitation.

KEYWORDS: Chronic obstructive pulmonary disease, dyspnoea, exercise capacity, interval exercise, peripheral muscle weakness

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Breathlessness and peripheral muscle discomfort are the most common symptoms limiting exercise tolerance in patients with severe chronic obstructive pulmonary disease (COPD). Exercise training constitutes the cornerstone of pulmonary rehabilitation as there is strong evidence that its implementation improves both exercise tolerance and health-related quality of life in these patients [1]. The intensity of exercise is a key determinant of true physiological training effects: in order to optimise this outcome, it is necessary that the intensity of exercise be as high as possible [2]. Nevertheless, in patients with severe COPD, intolerable sensations of breathlessness and/or peripheral muscle discomfort may prevent high-intensity levels being tolerated for sufficiently long periods of time to yield true physiological training effects [3]. Consequently, it is important to implement strategies to optimise exercise tolerance in severe COPD with the objective of enhancing the patient's ability to tolerate as sustained and intense a workload as possible. These strategies aim at reducing the intensity of dyspnoea sensations, either by allowing patients to sustain a higher absolute exercise-training intensity or by prolonging the cumulative time a given exercise task can ordinarily be sustained. Such strategies include noninvasive mechanical ventilation (NIV), oxygen and/or heliox supplementation and interval cycling modality. In addition, progressive resistance muscle training will be discussed within the scope of reducing leg muscle discomfort.

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NONINVASIVE MECHANICAL VENTILATION

Noninvasive positive-pressure mechanical ventilation has been shown to reduce the load on the respiratory muscles and the intensity of dyspnoea, thereby increasing exercise intensity and endurance capacity [4, 5]. In particular, in patients with severe COPD, application of proportional assist ventilation (PAV) has been shown to allow a greater intensity of exercise to be sustained for longer periods of time than sham exercise, thus potentially yielding significant training physiological effects [6]. PAV is a mode of partial ventilatory assistance with characteristics of proportionality and adaptability to the intensity and timing of spontaneous ventilatory pattern by providing inspiratory flow and pressure in proportion to the patient's effort [4]. To the extent that intrinsic mechanical loading and functional inspiratory muscle weakness in severe COPD contribute to intense dyspnoea sensations, PAV provides a symptomatic benefit by unloading and assisting such overburdened ventilatory muscles, thereby reducing the work of breathing and thus dyspnoea sensations [7].

In addition, continuous positive airway pressure (CPAP) has been reported to reduce the inspiratory threshold load on the inspiratory muscles of dynamically hyperinflated COPD patients and also to enhance neuromuscular coupling, thus improving dyspnoea sensations and exercise tolerance [8]. The commonly accepted explanation of the effects of CPAP is that it counter-balances intrinsic positive end-expiratory pressure, *i.e.* the inspiratory threshold load [8]. In two studies conducted by O'Donnell and co-workers [5, 8] in patients with severe COPD, application of CPAP of 4–5 cmH_2O during steady-state sub-maximal exercise resulted in a significant increase in exercise endurance time and a highly significant reduction in the sense of breathing effort.

Moreover, pressure-support ventilation (PSV), a pressure-targeted mode in which each breath is patient triggered and supported, can effectively assist ventilation when applied noninvasively to patients with acute and chronic respiratory failure [4]. Application of PSV has been shown to yield consistent improvements in endurance capacity as assessed by walking distance [9] and by reductions in the intensity of dyspnoea during constant-load cycling [10].

Dolmage and Goldstein [11] investigated which of the two methods, PAV, CPAP or a combination of the two, was more effective in enabling very severe COPD patients to increase exercise tolerance when applied during constant-load exercise at 60–70% of maximum power. Although exercise tolerance with PAV (7.1 min) or CPAP (8.2 min) alone was not significantly prolonged compared to sham exercise (6.6 min), a combination of the methods significantly increased exercise tolerance (12.9 min). Bianchi *et al*. [12] investigated the impact of PAV, CPAP or PSV on exercise tolerance and breathlessness in severe stable chronically hypercapnic COPD patients during constant-load cycling at 80% of maximal capacity. In comparison with sham ventilation, PAV, PSV and CPAP were able to increase endurance time (from 7.2 to 12.0, 10.0 and 9.6 min, respectively) and reduce dyspnoea sensations. However, the greatest improvement was observed with PAV.

A recent study [13], which intended to provide more insight into the pathophysiological mechanisms of improvement in exercise tolerance by using NIV in COPD, implemented respiratory muscle unloading *via* PAV during high-intensity exercise (70–80% of peak) and demonstrated improved peripheral muscle oxygenation assessed by near-infrared spectroscopy despite unaltered systemic oxygen delivery in patients with advanced COPD. These findings are indicative that a fraction of the available cardiac output might be redirected from ventilatory to locomotor muscles due to respiratory muscle unloading, thereby enhancing peripheral muscle oxygen delivery and thus exercise tolerance.

OXYGEN/HELIOX SUPPLEMENTATION

Supplemental oxygen has the potential to increase the exercise tolerance of hypoxaemic COPD patients by means of an increase in arterial oxygen content and vasodilation of the pulmonary circulation [14]. These two mechanisms increase oxygen delivery to the exercising muscles and may potentially reduce carotid body stimulation at heavy levels of exercise with or without lactic acidosis [15]. Ambulatory oxygen therapy has widely been shown to increase exercise performance and to relieve exercise breathlessness in severe COPD patients [16, 17]. Studies indicate that a reduction in the rate of exercise-induced dynamic hyperinflation plays an important role in the oxygen-related relief of dyspnoea [16, 17]. In addition, improvement in exercise performance *via* oxygen supplementation was primarily related to the reduced ventilatory demand, which, in turn, led to improved operational lung volumes and delayed attainment of limiting ventilatory constraints on exercise and the onset of intolerable dyspnoea. Interestingly, supplemental oxygen generally increases exercise tolerance not only in hypoxaemic but also in non-hypoxaemic patients [16]. In fact, modest changes in sub-maximal ventilation and dynamic ventilatory mechanics have been documented to result in relatively large improvements in symptom intensity and exercise capacity [16]. Besides improving in respiratory function, oxygen supplementation has been documented to increase leg muscle oxygen delivery and oxygen uptake, thereby justifying the ability of the peripheral muscle to perform more work [18].

In patients with severe COPD, supplementation with normoxic heliox decreases turbulence within medium to large airways, increases expiratory flow rate and reduces the work of breathing, as well as the degree of exercise-induced dynamic hyperinflation and the intensity of dyspnoea, thereby enhancing exercise tolerance. However, there is emerging evidence [19] indicating that enhanced exercise tolerance with heliox is also due to an increase in locomotor muscle oxygen delivery during constant-work rate sub-maximal exercise. Enhanced oxygen delivery to peripheral muscles following administration of heliox during exercise in severe COPD may occur *via* a number of mechanisms, namely: 1) improved cardiac output secondary to reduced intra-thoracic pressures and/or pleural pressure swings; 2) improved arterial oxygen content; and 3) blood flow redistribution from respiratory to peripheral muscles secondary to reduction in the mechanical load of the respiratory muscles [19]. A recent study in patients with severe COPD [20] confirmed that heliox administration during constant-load exercise (at 75% of peak capacity) reduces total respiratory muscle power by unloading both inspiratory and expiratory muscles, as well as improving central haemodynamic responses (increase in stroke volume) and arterial oxygen content. These findings [20] confirmed those of a previous study showing faster cardio-dynamic responses following heliox administration [19] but disputed suggestions that the increase in locomotor muscle oxygen delivery, as inferred by deoxyhaemoglobin kinetics determined by near-infrared spectroscopy (an index of tissue oxygen extraction), was indicative of blood flow redistribution from the respiratory to locomotor muscles as heliox administration during exercise improved blood flow and oxygen delivery to both respiratory and locomotor muscles. In addition, reductions in the degree of exercise-induced dynamic hyperinflation with heliox administration have been shown to be associated with improvements in several indices of cardio-circulatory function [21].

INTERVAL EXERCISE

Intensity and duration of exercise are important determinants of the physiological adaptations that occur in response to training. In patients with COPD, there are indications that greater physiological benefits can be obtained through high-intensity compared with moderate-intensity exercise training [2]. However, high-intensity exercise training may not be appropriate for those COPD patients who are unable to sustain such intensities for long periods of time due to symptom limitation. In fact, patients with severe COPD are so limited by dyspnoea and/or locomotor muscle weakness that their ability to exercise is restricted to very low-intensity levels [3].

In addition, premature occurrence of lactic acidosis consequent to reduced peripheral muscle oxygen delivery and muscle fibre dysfunction puts particular stress on the ventilatory system in COPD. Thus, the small increase in arterial lactate concentration observed during interval exercise compared with continuous exercise [22–24] appears to be beneficial to COPD patients by reducing some of the acid stimulus to breathe [2], thereby allowing ventilation and dyspnoea sensations to be tolerated for a prolonged period of time. VOGIATZIS *et al.* [23] have shown that using interval exercise, patients with severe COPD can almost triple the total exercise duration with significantly lower and more stable metabolic and ventilatory responses compared with continuous exercise. Although patients exercised for longer time (~30 min) at a higher intensity (100% of peak exercise capacity) with the interval mode, they had lower metabolic demands and less ventilatory restrictions at the end of symptom-limited exercise (fig. 1) [23].

Conversely, when exercising continuously without any rest periods, severe COPD patients can tolerate high work rates (50–80% of their maximum exercise capacity) for only 5–12 min, at the end of which they are completely exhausted [24]. At intensities of 65–85% of peak exercise capacity, COPD patients can sustain only 4–5 min of exercise [24] and only up to 13 min for lower intensities (50–60% of peak exercise capacity) [24]. As such, implementing continuous exercise training for patients with severe COPD will be ineffective as they will have to interrupt exercise in order to rest for several minutes before they start exercising again. In contrast, interval training can enable patients to complete short periods of high-intensity exercise that would not be possible with a continuous exercise mode. When patients exercise for short periods of time (*e.g.* 30 s) alternated with short rest intervals of 30 s, they complete the total work with moderate exertion and relatively stable metabolic and ventilatory response (fig. 1) [22, 23]. Indeed, patients with severe COPD can endure high-intensity interval training in a rehabilitation setting for long periods of time with

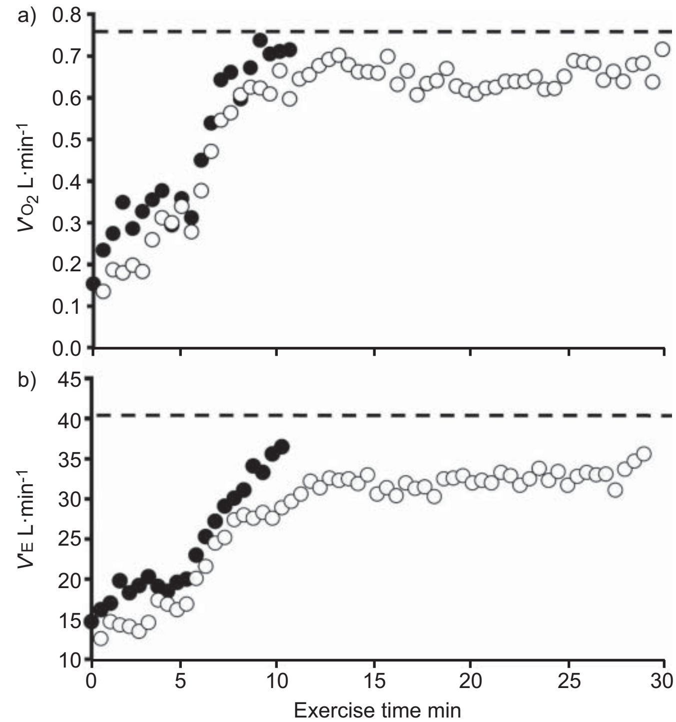

FIGURE 1. a) Oxygen uptake (V'_{O_2}) and minute ventilation (V'_E) in a patient with severe chronic obstructive pulmonary disease (forced expiratory volume in 1 s 0.85 L) during interval (○) and constant-load (●) exercise protocols. Interval exercise was sustained for 30 s at 100% of peak baseline capacity alternated with 30 s rest, whereas constant-load exercise was sustained at 75% of peak baseline capacity. – – – – – represents a) peak V'_{O_2} or b) maximal voluntary ventlation. Modified from [23].

lower symptoms of dyspnoea and leg discomfort compared with the conventionally implemented continuous training [25–27]. A recent study demonstrated that interval exercise training allows severe COPD patients (Global Initiative of Chronic Obstructive Lung Disease stage IV) to exercise at a sufficiently high intensity to obtain true physiological training effects manifested by improvements in muscle fibre size, typology and capillarisation [28].

PROGRESSIVE RESISTANCE MUSCLE TRAINING

Patients with severe COPD are often exposed to the risk of profound peripheral muscle de-conditioning as a result of disease severity and progression. Intense leg discomfort sensations often deter COPD patients from participating in daily activities that require body mobility and strength. Since skeletal muscle weakness has a negative impact on exercise tolerance in the majority of patients with severe COPD, an intervention of resistance exercise during pulmonary rehabilitation is deemed essential [1]. Accordingly, rehabilitation experts often prescribe resistance muscle training programmes, as clinical outcomes are definitely promising for the severe COPD patient [29].

In a recent systematic review of 18 controlled trials, mainly including patients with severe COPD, significant effects for increases in muscle strength after short-term progressive resistance exercise were demonstrated [30]. The key features of progressive resistance exercise protocols used in these trials included an average of 12 weeks of training, with training sessions taking place two to three times per week. A median of five resistance exercises for the muscles of the arm, leg and trunk were performed during each exercise session. The majority of the training sessions comprised two to four sets of eight to 12 repetitions for each exercising muscle group, at intensities progressing from ~30% to ~90% of one-repetition maximum.

In a study evaluating the effectiveness of progressive resistance exercise in nine trials [30], the adaptations made after concluding the training programme were important for increasing arm and leg muscle strength in severe COPD patients. More specifically, a meta-analysis was conducted and showed an increase of 25% in maximum knee extensor muscle strength after progressive exercise training compared to no intervention or aerobic training that showed an increase of only 10% in the knee extensor muscle strength. However, progressive resistance exercise did not show significant improvements in maximal exercise capacity or respiratory function [30]. Body composition was examined in two trials and showed an increase in total lean mass and a reduction in total fat percentage after 12 weeks of progressive resistance exercise [31, 32].

Accordingly, short-term progressive resistance muscle training can be beneficial for severe COPD patients in terms of enhancing muscle strength and increasing the performance of some daily activities. Progressive resistance exercise can increase arm and leg muscle strength and improve the performance of tasks, such as stair climbing and rising from sitting [30]. However, the effects of progressive resistance exercise on measures of body composition, psychological function and societal participation still remain inconclusive.

CONCLUSION

Exercise training should be tailored to address the individual patient's limiting factors (central cardiorespiratory and/or peripheral muscle) to exercise. In patients with intense dyspnoea symptoms, interval exercise is more appropriate than continuous exercise. Resistance exercise should be complementary to interval exercise so as to improve the strength of both the upper and the lower body muscles. In patients with profound muscle weakness, interval and resistance exercise should constitute a training priority. Future research is required and it should scrutinise the longer term outcomes and optimal methods for maintaining rehabilitation-induced physiological adaptations in patients with severe COPD.

STATEMENT OF INTEREST

None declared.

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