



Muscle reconditioning in COPD: main interventions and new tendencies

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ABSTRACT

Physical exercises have been a vital part in the treatment of COPD patients since some time ago. These patients frequently present intolerance to exercises of variable intensity related to the skeletal-muscle dysfunction. In this context, the physical exercise is presented as the most important branch in the pulmonary rehabilitation process. The aerobic exercise and the strength training are vital in the increment of the physical capacity and quality of life, especially for individuals who present moderate or acute forms of the COPD. Furthermore, a higher research development is currently expected in relation to the application of neuromuscular electric stimulation (NMEE) and to the judicious use of ergogenic substances such as anabolic steroids and oral creatin. Considering the negative repercussion of the muscle dysfunctions and the importance of the pulmonary rehabilitation in the treatment of COPD, this reviewing has as objective to gather information from relevant studies with regard to the main strategies for the skeletal-muscular reconditioning in patients in the last 15 years.

INTRODUCTION

The intolerance to physical exercise is frequent manifestation in patients with COPD^(1,2). This fact had once been attributed to respiratory dysfunctions that these individuals presented; however, it has been currently verified that the peripheral skeletal-muscle dysfunction is important factor for the decrease on the capacity of performing exercise among this population⁽³⁾. In this context, the persistence of this intolerance is observed even after lung transplant, situation in which the improvement of the pulmonary function occurs^(4,5).

The importance of the skeletal muscle dysfunction in the decrease on the capacity of performing exercises in patients with COPD was firstly suggested by Killian *et al.*⁽⁶⁾. These authors observed that many patients with COPD complained of lower limbs fatigue during maximal effort test without, however, reporting dyspnea as limiting factor of performance.

Considering that the ventilatory function of patients with COPD may be improved only slightly by clinical therapies, the physical conditioning plays important role with the objective of reducing the respiratory demand and the dyspnea feeling⁽⁷⁾. Dourado *et al.*⁽⁸⁾ found significant correlation between the six-minutes walking test performance and the domains "Activity" and "Impact" of the Saint George Hospital quality of life questionnaire in respiratory diseases. These findings were corroborated through linear multiple re-

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gression, suggesting the influence of tolerance on exercise and quality of life of patients with COPD. When compared to other types of treatment such as bronchodilator agents and oral teofiline, the physical exercise is associated to more significant improvements on quality of life and functional capacity⁽⁹⁾.

Currently, there are a large number of useful therapies in the rehabilitation process of individuals with COPD⁽¹⁰⁾. Among them, the following therapies can be mentioned: the oxygenotherapy, the resistive exercises, the anabolic steroids supplementation⁽¹¹⁾, the creatin supplementation and the neuromuscular electric stimulation (NMEE)⁽⁷⁾. However, there are evidences that the physical exercise is the most effective procedure in the pulmonary rehabilitation⁽¹²⁾. Associated to any other type of therapy, the physical exercise may increase significantly the physical capacity and the quality of life of patients with COPD⁽¹¹⁾.

Considering the negative repercussion of the muscle dysfunctions and the importance of the pulmonary rehabilitation in the treatment of COPD, this reviewing has as objective to gather information from relevant studies with regard to the main strategies for the skeletal-muscular reconditioning in these patients in the last 15 years. This work also aims at presenting new therapy tendencies to improve the physical capacity in patients with COPD. The bibliographic research was performed in the database *Medline and Journals@Ovid Full Text* using terms *exercise and COPD*.

AEROBIC EXERCISE

The aerobic exercise is recommended for individuals with COPD and its benefits are observed regardless the COPD stage in which patients are found⁽¹³⁾. This type of training increases the concentration of mitochondrial oxidative enzymes, the capillary action of the trained muscles, the anaerobic threshold, the $\dot{V}O_2$ max and decreases the phosphate creatin recovery time (PC) resulting in improvements of the exercise capacity⁽¹⁴⁾.

In patients with COPD, the benefits of the aerobic conditioning result in increase on the distance walked in the six-minutes walking test (TC6), improvement on the performance of quality of life questionnaires and in relief of the exercise tolerance⁽¹¹⁾. The training of the lower limbs may be performed in cycle-ergometers or treadmill walking belts or even by means of walking. Pitta⁽¹⁵⁾ compared the lower limbs training isolated in cycle-ergometer to a non-exercised control group and the results showed significant improvement of the $\dot{V}O_2$ peak, the TC6, the endurance time with constant load in cycle-ergometer, the PImax and the dyspnea feeling on the trained group, suggesting the positive effects of the lower limbs training even in the absence of other important components of the pulmonary rehabilitation process. For the upper limbs, arm ergometer, weights, sticks or elastics can be used^(10,16).

The activities performed with the upper limbs are related to intense dyspnea because some shoulder muscles are respiratory accessories as well, for example the pectoral and the latissimus dorsi muscles⁽¹⁷⁾. When involved in other activities, their function in the respiration process is decreased and, consequently the work

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of the diaphragm increases⁽¹⁸⁾. The training for the upper limbs has as objective to increment especially daily activities that are mostly performed with arms and it has already shown benefits in the muscle reconditioning of patients with COPD⁽¹¹⁾.

The aerobic exercise for the lower limbs improves the tolerance to exercise, however, presents small effect with regard to the atrophy and muscle weakness⁽⁵⁾. The lower limbs endurance training benefits have been shown proportional to the intensity in which the exercise is performed; exercises performed between 60 and 80% of the maximal work load (w) present higher endurance increment than exercises performed at low intensities⁽¹⁶⁾. Lower lactate accumulation and CO₂ production, increased quadriceps resistance and evidences of increase on the mitochondrial oxidative capacity after 12 weeks of training are clear signals of muscle adaptation to the aerobic training^(1,14).

Oliveira *et al.*⁽¹⁹⁾ associated the training of the respiratory muscles (TRM) with 40% of the P_{lmax} daily performed in pressure-dependent device to reconditioning general exercises at light intensity performed twice a week. The group submitted to both types of training improved significantly the strength in the respiratory muscles without improvement on the TC6, suggesting the ineffectiveness of the TRM with regard to the improvement of the exercise tolerance in patients with COPD.

The current recommendations for aerobic training include sessions with duration of 20 and 45 minutes and frequency of three to five times a week⁽²⁰⁾. The exercise program should be maintained for at least eight weeks⁽¹⁴⁾.

STRENGTH TRAINING

Considering that the muscle weakness contributes to the exercise intolerance in patients with pulmonary disease, the strength exercise is the rational option in the pulmonary rehabilitation process⁽¹⁶⁾. Currently, there is no sufficient number of studies and, therefore, there is no agreement with regard to the application of the strength training in patients with chronic pulmonary disease⁽⁵⁾.

The decrease on strength in patients with COPD occurs specially in the lower limbs. Gosselink *et al.*⁽²¹⁾ demonstrated that the decrease on the quadriceps strength is significantly higher than the loss of strength of pectoral muscles or of latissimus dorsi muscle and that, in the upper limbs, the strength reduction is higher in the shoulder proximal muscles⁽³⁾.

Simpson *et al.*⁽²²⁾ randomized 34 patients with severe COPD in a training group and another non-exercised control group during a eight-weeks program. The training consisted of three series of ten repetitions of three selected exercises performed three times a week. The initial intensity was of 50% of a maximal repetition (1 RM) in the first week, progressively increasing up to 85% of 1 RM in the last training weeks. The maximal voluntary strength increased between 16% and 44% for the trained group and did not change for the control group. No significant alteration on the distance traveled in the TC6 was observed in none of the groups. However, an increment on the quality of life questionnaire performance and on the muscular resistance in the trained group was verified. Troosters *et al.*⁽²³⁾ analyzed 100 patients with severe COPD and identified values significantly higher in the maximal exercise performance in TC6, in the peripheral muscular strength and in the quality of life among patients who performed six weeks of strength training in relation to those who did not train.

Treatments with muscle hypertrophy objectives do not result in increases on the endurance⁽²⁴⁾, in other words, they do not further aerobic gains, once variables such as $\dot{V}O_2$ max and anaerobic threshold do not change significantly⁽¹³⁾ and, therefore, the strength work should be associated to exercise programs that reserve part of their time to the acquisition of aerobic resistance⁽⁵⁾.

The strength training prescriptions for individuals with COPD are not yet well defined; however, the training proposed by most

researchers on this topic includes: two or three training days per week, one to three repetition series for each muscle group selected, eight to twelve repetitions, interval from two to three minutes between series; intensity of 50 to 85% of 1 RM and intensity adjustment each three or four weeks⁽⁵⁾.

COMBINED TRAINING

Bernard *et al.*⁽²⁵⁾ compared the classic aerobic training in cycle-ergometer to this modality associated to weightlifting strength training and concluded that the association resulted in no significant differences in relation to the $\dot{V}O_2$ max, TC6 and to the quality of life indicatives when compared to the aerobic training alone. However, they observed that the strength training resulted in less intense dyspnea if compared to the cycle exercise and, consequently more tolerated by patients. When the aerobic training is compared to the strength training alone, the effects are similar in both modalities, except with regard to the $\dot{V}O_2$ max that respond better to the aerobic training⁽²⁶⁾.

Dourado *et al.*⁽²⁷⁾ randomized 15 patients with COPD from light to severe in a 36-sessions program of strength training alone with three series of 8-12 RM in bodybuilding machines with intensity ranging from 50 to 80% of 1 RM (n = 8) or combined (two series of 8-12 repetitions with 50-80% of 1 RM) with light aerobic exercise involving free walking and reconditioning general exercises with dumbbell (n = 7). The groups were submitted to evaluation of pulmonary function, strength and muscular resistance, exercise maximal capacity ($\dot{V}O_2$ max), aerobic resistance with constant load in treadmill, TC6, quality of life and dyspnea feeling. A significant improvement on the muscular resistance and TC6 was observed in both groups with no statistical difference between them. However, the quadriceps muscle resistance, the aerobic resistance with constant load in treadmill and the quality of life score improved significantly only for the strength training group alone. These findings suggest the improvement on the muscle strength and capacity of performing exercises in both training regimen. However, the strength training alone showed higher association with the improvement on the quadriceps muscle resistance, aerobic resistance in test with constant load in treadmill and quality of life in these patients with COPD when compared to the combined training with light aerobic exercise.

When the total aerobic training protocol is divided into treadmill, cycle-ergometer and arm ergometer and compared to strength training alone, the effects are similar with relation to the functional capacity and to the quality of life in both modalities⁽²⁶⁾.

NEW TENDENCIES

Androgen administration

The muscle growth depends on the adequate hormonal supply and the reduction on the amount of anabolic hormones causes muscular deficiency⁽⁴⁾. The effects of the anabolic hormones supplementation on the musculature of patients with COPD have only recently been evaluated⁽¹¹⁾.

In men, the aspects of higher concernment with regard to the androgen administration are hyperplasia and prostate cancer, reduced levels of HDL cholesterol and eventual toxicity⁽⁴⁾. Although hyperplasia and prostate cancer are uncommon in individuals with reduced hormonal levels, the testosterone therapy seems not to induce the development of these diseases⁽²⁸⁾. Besides, the testosterone administration in aged individuals with hormonal deficiency does not affect significantly the HDL cholesterol levels⁽²⁹⁾.

Among the main risk deriving from the androgen administration in women, virilization, skin reactions, side effects in plasmatic lipids and changes of behavior must be mentioned⁽⁴⁾. The androgen-prolonged therapy may increase risks of cardiovascular events due

to the decrease on the HDL cholesterol. With regard to the correlation of the androgen supplement and breast cancer, the literature present data not much consistent⁽⁴⁾.

Schols *et al.*⁽³⁰⁾ were the first authors to evaluate the effects of the anabolizant steroid therapy in patients with COPD in a large dimension randomized study, controlled and placebo group involving 203 patients. The patients were divided into two groups as follows: The first group was composed of patients with weight loss (< 90% of the ideal weight) and loss of lean body mass (< 67% of the ideal weight for men and < 63% for women) and the second group without alterations of these parameters. Later, the patients were randomized into three groups: the first group (P) of patients who received placebo and supplementary nutrition (N = 420 Kcal); the second group (N) of patients who received only supplementary nutrition and the third group (N + A) of patients who received supplementary nutrition + intramuscular nandrolone every two weeks (1 ml for men and 0.5 ml for women). When submitted to an 8-weeks general physical exercise program the three groups increased significantly P_{lmax} at the first four weeks, however, from the fourth to the eighth weeks, only group N + A remained presenting significant increase in relation to the control group. With regard to the 12-minutes walking test, all groups improved significantly with no statistical difference between them at the end of the 8 weeks.

In this study⁽³⁰⁾, the group of patients with nutritional deficit and the group without nutritional deficit both gained weight; however, the weight gain was higher in undernourished patients. However, the individuals who received anabolizant therapy obtained weight gain due to the increase of the mass free of fat with no adiposity alteration while patients who received complementary nutrition alone presented no alteration on the mass free of fat, being adiposity the responsible for the weight gain. Therefore, in this study, the nandrolone therapy was able to improve the nutritional status of patients with COPD, being important perspective in this matter.

Ferreira *et al.*⁽³¹⁾ evaluated the influence of the steroid oral administration on BMI, anthropometric measures, respiratory muscular strength and exercise capacity in 23 undernourished patients with COPD and with P_{lmax} < 60% of the predicted value. For the group studied, 250 mg of intramuscular testosterone and 12 mg of oral stanozolol were administrated every day during 27 weeks. For the control group, only placebo was administrated. Both groups participated in the inspiratory muscular training from week 1 to week 27 and cycle-ergometer exercises during weeks 18 to 27. The group that received anabolic steroids increased body weight while control group lost weight. The BMI, the percentile of fat-free mass and the arm circumference presented results significantly better in the group of study if compared to the control group. However, no significant difference in P_{lmax}, TC6 and in the exercise maximal capacity was observed. Furthermore, no adverse effect caused by the oral administration of anabolic steroids was observed.

The short-duration therapy with anabolic steroids may be an additional intervention for the improvement of the body composition and the exercise tolerance in diseases that present chronic loss of lean body mass as the case of COPD, especially due to the antagonistic effects in relation to the muscle and bone losses typical of the glucocorticoid therapy. Although, the short-duration well-controlled anabolizant therapy presented no adverse effect in patients with COPD so far⁽³²⁾.

Neuromuscular electric stimulation

The neuromuscular electric stimulation (NMEE) is already usually used in the rehabilitation of patients with neuromuscular and orthopedic diseases and, more recently, it has been used in the skeletal-muscle dysfunction as in the case of the chronic cardiac insufficiency⁽⁷⁾.

Neder *et al.*⁽³³⁾ randomized 15 patients with severe COPD as follows: 9 patients in the 6-weeks of domiciliary NMEE group and

6 patients in the control group. The quadriceps strength and resistance, the physical capacity and the quality of life were evaluated. Significant improvements of the muscular function, exercise tolerance and the dyspnea component of the quality of life questionnaire (CRQ) were verified in the group studied.

Therefore, The NMEE was useful especially in patients who presented severe COPD and relevant muscle-skeletal dysfunction. The benefits of this type of therapy may be particularly evident in patients with relevant dyspnea, unable to be submitted even to extremely light physical activities. In this type of patient, the NMEE may soften the effects of the muscular dysfunction, making the participation in pulmonary rehabilitation programs involving physical conditioning possible⁽⁷⁾.

Creatin supplementation

The simplest and rapid method to obtain energy involves the ATP-CP: CP + ADP \Rightarrow ^{kinase creatin} ATP + C system⁽¹⁴⁾. However, the muscle cells are able to store only small amounts of CP and, therefore, the amount of energy produced by the ATP-CP system is limited. This system supplies energy for muscular contraction at the beginning of a given exercise and in high-intensity exercises and of duration shorter than 5 seconds⁽¹⁴⁾.

The CP depletion may limit the performance of high-intensity short duration exercises. With regard to patients with COPD, due to the CP depletion be even higher than in control individuals⁽³⁴⁾, these activities represent, for example, the ascending of one step in a stair or walking in higher velocity than the usual⁽⁷⁾.

The creatin supplementation may increase the lean body mass, the time required for the muscular fatigue, improve the performance in sprint activities and increase muscular strength⁽³⁵⁾.

In aged individuals, Gotshalk *et al.*⁽³⁶⁾ found results that indicate positive effects in the muscular performance in men between 59 and 73 years of age submitted to creatin administration. The benefits of the creatin supplementation are expressed as the higher ability in developing daily activities. In short, the creatin administration during a short period (7 days) results in increase on muscular strength and power in aged individuals with no adverse effect.

There are no published researches in the evaluation of the creatin supplementation effects as part of the pulmonary rehabilitation so far. The use of creatin in patients with COPD is not indicated until enlightening results are published in literature⁽⁷⁾.

FINAL CONSIDERATIONS

Undoubtedly, the most effective components of the pulmonary rehabilitation are those related to physical activity as the aerobic exercises, peripheral and respiratory resistive exercises, besides the association of both modalities. Currently, the scientific community is interested in developing coadjuvant therapies with the objective of maximizing the effects of physical conditioning programs. In this context, the anabolic steroids therapy starts being evaluated and the NMEE and the creatin therapy, so far incipient, open new perspectives with regard to strategies for the skeletal-muscle reconditioning in patients with COPD.

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