MÆDICA - a Journal of Clinical Medicine

STATE-OF-THE-ART

The Contribution of Exercise Testing in the Prescription and Outcome Evaluation of Exercise Training in Pulmonary Rehabilitation

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ABSTRACT

Pulmonary rehabilitation is a comprehensive therapeutic intervention with proven efficacy in relieving symptoms and increasing exercise tolerance in patients with chronic respiratory diseases.

One of the main components of a pulmonary rehabilitation program is lower limbs exercise training. There are several ways of establishing the optimal intensity of the exercise training, using the target heart rate, symptom scores, walking tests and laboratory exercise tests with or without ventilation or gas exchange measurements. Each of these methods has advantages and disadvantages.

The gold standard in exercise capacity evaluation is cardiopulmonary exercise testing (CPET) which brings a high level of objectivity in exercise tolerance evaluation and provides information on mechanisms responsible for its decline; this allows a better training prescription and a correct evaluation of rehabilitation outcomes.

Keywords: pulmonary rehabilitation, exercise training, exercise testing

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Received on the 14th February 2012. Accepted on the 26th March 2012.

The contribution of exercise testing in the prescription and outcome evaluation of exercise training in pulmonary rehabilitation

Pulmonary rehabilitation is a complex and multidisciplinary therapy with proven efficacy in patients with symptomatic chronic respiratory diseases and limited daily activities (1,2).

Chronic obstructive pulmonary disease (COPD) is the lung disease in which this type of intervention was most studied and represents today its first indication (3-5). There are also proven benefits of pulmonary rehabilitation in other respiratory illnesses such as interstitial lung diseases, bronchiectasis, cystic fibrosis, pulmonary hypertension, neuromuscular diseases, chest deformations, asthma, etc (1,2). Pulmonary rehabilitation is also important pre and post lung transplantation, lung volume reduction surgery or surgery for lung cancer (1,2).

In association with medication, *the aims of pulmonary rehabilitation* programs are to reduce symptoms, improve the functional status, increase the level of social activity, and improve the overall quality of life for patients with chronic respiratory disease (1,2).

Patients with chronic obstructive pulmonary disease reduce their level of physical activity due to dyspnoea; this leads to progressive deconditioning and starts a vicious cycle that worsens dyspnoea, which occurs at even lower levels of activity. The loss of muscle mass due to systemic inflammation worsens this phenomenon. Respiratory muscle weakness and fatigue accelerates the shortness of breath. In this context, the *lower and upper limbs muscles exercise training associated with the training of inspiratory muscles is the main element of pulmonary rehabilitation*. Other components of a pulmonary rehabilitation program are: chest physical therapy and breathing techniques, education, nutritional and psycho-social interventions and outcome assessment (1,2).

Pulmonary rehabilitation programs are designed according to the patient's initial assessment and are based on the experience and equipment of the rehabilitation centre. The programs take place over 6 to 8 weeks and generally include 20 training sessions, each one lasting an hour and a half, including 30 to 45 minutes addressed to the endurance training of the lower limbs muscles. Exercises consist of walking, climbing stairs, cycle ergometer training and/or treadmill. Patients who cannot perform lower limbs exercises (neurologic or orthopaedic diseases) can benefit from exercise testing and training for upper limbs using special ergometers (1).

The *intensity of the exercise* is an important element of the pulmonary rehabilitation process. Although significant results can be obtained in increasing exercise tolerance and quality of life with low intensity exercises (6), better results occur in patients undergoing high intensity training (7,8). Benefits have been obtained both with constant load training and with intermittent increases of the load (=interval training, better tolerated by patients with severe COPD) (8-10).

Exercise intensity is *progressively increased* depending on patient's tolerance. Starting from a power greater than 50% of the maximal power obtained during a maximal exercise test, the training intensity can be gradually increased on a weekly basis or after five sessions (1,7,11).

The effect of physical training can be increased by adding other treatments for different groups of patients. In those with obstructive lung diseases, bronchodilators reduce dynamic hyperinflation, dyspnoea, and increase exercise tolerance in patients with limited ventilation (1,2). Oxygen supplementation during the training in hypoxaemic patients increases the oxygen delivery to the muscles, delays the occurrence of anaerobiosis, decreases ventilation and increases endurance (1,2). The association of non-invasive ventilation increases endurance in patients with chronic respiratory failure secondary to restrictive lung diseases and, maybe, to COPD (1,2).

The **preliminary evaluation before the inclusion into a pulmonary rehabilitation** program begins with a discussion between the doctor and the patient regarding the rehabilitation process and the outcomes. The evaluation includes (1,2):

- medical history
- physical examination
- investigations: chest radiography, spirometry, arterial oxygen saturation, electrocardiogram, hematology tests, complex pulmonary function tests, echocardiography, ± Holter monitoring, etc.
- exercise tests: walk tests and laboratory test with an ergometer
- evaluation of symptom scores during exercise (dyspnoea, muscular fatigue, pain)

- evaluation of daily activities and of psycho-social impact of the disease
- nutritional status assessment.

Initial evaluation of exercise capacity can be done using simple field tests or complex tests which require special equipment and experienced technicians.

Among the standardized field tests, the most simple to perform and the most popular is the *six-minute walk test (6MWT)*. This test requires minimal equipment which includes a corridor of 30 to 50 m, a timer and a pulse-oximeter (12). The patient has to walk as much as he/she can in six minutes. Before and after the test heart rate, arterial oxygen saturation (SaO_2) and symptoms scores are measured (12). Total distance walked (six-minute walk distance, 6MWD) and significant desaturation (at least 4 points from the pre-test value) are important prognostic parameters (13-15).

Another field test is the *shuttle test,* during which the subject walks between two landmarks in the rhythm suggested by an audio recording. There is no time limit and the test ends when the patient cannot sustain the pace any longer. The total distance walked during the incremental shuttle test (ISWT) correlates with the peak oxygen consumption (VO_2 peak), a parameter which is provided by the cardio-respiratory exercise test (16,17).

The *complex tests use ergometer devices* (treadmill or bicycle). Tests could be incremental, with gradual increase of the exercise intensity, or constant, when the endurance is tested (resistance to a certain level of exercise).

Exercise tests without ventilation monitoring allow exercise tolerance assessment only by measuring the maximum exercise power obtained (Wmax). Arterial oxygen saturation, heart rate, blood pressure, symptoms score, and (ideally) real time electrocardiogram are monitored during the test.

Cardio-pulmonary exercise testing (CPET) is the gold standard in evaluating exercise intolerance. It adds the measurement of oxygen consumption (VO_2), carbon dioxide production (VCO_2) and ventilation parameters (total ventilation V_E, inspiratory capacity, etc.), values which allow the calculation of many important indices used for interpretation. Acid-base balance parameters, lactate and other muscle enzymes concentration during exercise can be measured by serial arterial blood sampling.

Incremental testing is performed using individualized protocols based on the expected level of exercise for each patient. The main measured parameters are peak oxygen consumption (VO_2 peak) and aerobic exercise capacity with the determination of the anaerobic threshold (AT, or lactate threshold LT). Different mechanism involved in exercise intolerance can be identified using CPET: respiratory, cardio-vascular, muscular, psychological.

The carbon dioxide production and oxygen consumption ratio (VCO_2/VO_2 or respiratory exchange ratio RER) is an indicator of the subject's effort. A value ≥1.15 at the end of the test is the proof that a maximal test was performed. A value below 1 and the absence of hemodynamic and electrocardiographic abnormalities at the peek effort reflects a submaximal effort, but it can also be observed in subjects with respiratory limitation of exercise capacity (18).

The calculation of predicted values for peak oxygen consumption (VO2 peak), maximum power (Wmax) and other parameters is done using validated formulas (19,20). Values depend on subject's characteristics (age, weight, height) and can be adjusted with the level of physical activity and resting functional parameters.

The concept of anaerobic threshold refers to the moment when a high increase in blood lactate is observed during incremental exercise, with secondary increase of both blood carbon dioxide levels and ventilation. Normally, this phenomenon occurs at a level of exercise over 40% of the maximum intensity achieved by the subject during the incremental cardio-pulmonary test. Anaerobic threshold is an excellent predictive parameter of the highest power that can be supported for long periods of time (18,21). Oxygen consumption and ventilation stabilize (steady-state) during exercise at the anaerobic threshold or below it.

The upper limit of power at which both oxygen consumption and anaerobic threshold can be maintained at a high but constant level is named *critical power* of the subject (CP) (18, 22). This parameter separates the intensity of sustainable effort from the non-sustainable effort. In young healthy subjects critical power is generally observed at an oxygen consumption level of approximately 50% of the difference between anaerobic threshold and the VO_2 peak, and at a blood lactate level of 4-5 mmol/L. In COPD patients critical power is closer to the maximum power than in healthy subjects (23,24).

Endurance tests assess the kinetic of oxygen consumption in transition from rest to low exercise level or from a level of exercise to another; this correlates with the patient's level of training (18).

Methods of prescribing the intensity of endurance training for lower limbs muscles in pulmonary rehabilitation

1. *Establishing the target heart rate*

Published long time ago, the Karvonen formula recommends the increase in exercise intensity until a certain heart rate value (HR) is reached (25,26).

Recommended HR = (HRmax - HRrest) × recommended intensity + HRrest

- HRmax is the maximum predicted heart rate, ex. HRmax = 220 – age (years)
- HRrest is the lowest value of the heart rate measured at rest in the morning of the evaluation day
- Recommended intensity of exercise is the percentage of the maximum predicted exercise intensity at which the training is performed. Both minimum and maximum targets of exercise intensity can be calculated
- The formula can use the results of a maximal exercise test instead of predicted values for HRmax and maximum exercise intensity.

For example: a 60 years old subject with HRrest 80/minute starts the training program at an intensity of 50% of the maximum predicted. We might recommend physical exercise to achieve and maintain, for a given time, a minimum heart rate calculated with the above formula: HR recommended = (220 - 60 - 80) × 0.5 + 80 = 120 / minute.

If the same subject have a maximal exercise test in which a maximum HR of 140 was reached and we want to start a training program at 50% of the peak intensity achieved during this test, then the recommended minimum HR is (140 - 80) × 0.5 + 80 = 110 / minute.

If we want to establish an upper limit of exercise intensity (e.g. 80% of maximum predicted/ achieved), the HR will be calculated for this level and the subject will modulate his/her efforts to maintain heart rate within the established range.

The method has many limitations, apart from the lack of a complete evaluation of patient's exercise capacity. In many patients the heart rate at rest varies considerably from day to day (11). In patients treated with beta-blockers heart rate will not increase significantly during exercise. Patients with severe respiratory diseases with low respiratory reserve and/or desaturation during exercise reach lower values than predicted for heart rate and peak oxygen consumption. Most COPD patients with severe obstruction are unable to exercise over a „critical intensity" (24,27), whose level cannot be established only by the heart rate.

2. *Using the symptoms score*

It is considered that a reasonable level of exercise is reached when the level of dyspnoea is 4 to 6 on the Borg scale (28,29). If the patient becomes familiar with the symptom score, it is believed that he/she could continue training until the target score is achieved.

This method might be recommended for home-based training, together with the heart rate monitoring described above. The authors do not recommend these methods alone, in the absence of a rigorous evaluation made by laboratory exercise testing.

3. *Using the results of field tests*

Depending on the walk tests results we can be prescribe a *training using walking,* by choosing a speed of 80% of the average speed during the 6 minute walk test (6MWT) or 75% of the speed of the incremental shuttle test (ISWT) (11).

More interesting is the calculation of the power of the *cycle ergometer training* starting from the walk tests parameters. This is useful to those centres that are equipped with training bicycles, but do not have access to a laboratory for standardized exercise testing. Luxton (30) and Hill (31) proposed regression equations estimating the peak power (Wmax) obtained by a patient on a cycle ergometer, starting from the distance walked on the 6MWT or ISWT:

(Luxton 1) Wmax = 103.217 + (30.500 × gender) + (-1.613 × age) + (0.002 × 6MWD × weight) (30)

(Luxton 2) Wmax = 84.094 + (27.003 × gender) + (-1.003 × age) + (0.002 × ISWTD × weight) (30)

(Hill 1) Wmax = (0.122 × 6MWD) + (72.683 × height) - 117.109 (31)

(Hill 2, modified after reference 31) Wmax = 17.393 + (1.442 × 6MWD × weight) / 1,000

- gender: use 0 for a female patient and 1 for a male; weight in kilograms; height in meters; age in years
- 6MWD: the distance walked during the 6MWT; ISWTD: the distance walked during the ISWT
- the original formulas use the walking tests *work* (= *distance × weight*)

For example, if our 60 years old patient with a height of 165 cm and a weight of 70 kg walks 400 meters during 6MWT, the maximum power that he could achieve on a cycle-ergometer can be calculated as follows: (Luxton 1) Wmax ≈ 93 W, (Hill 1) Wmax ≈ 52 W, (Hill 2) Wmax ≈ 58 W.

The method has been criticized because the values of the maximum calculated power differ significantly between one another when calculated by different types of equations (32), as it can be seen from the above examples. Also, the calculated maximum power values differ from the maximal power obtained in other incremental studies (33). Using the fat-free mass instead of weight, combined with the 6MWD, was proposed in a formula that might better estimate the maximal work rate in COPD patients (34).

4. Using maximal exercise testing without ventilation measurements

The maximum tolerated exercise intensity obtained (Wmax) will be used for the prescription of the muscular training. Other measured parameters during exercise are important for safety reasons: decrease in SaO_2, electrocardiographic abnormalities, alarm symptoms, etc.

5. Using cardio-pulmonary exercise testing (CPET)

Patients with chronic respiratory diseases, especially those with COPD are often elderly and may have significant co-morbidities. Cardio-pulmonary exercise testing (CPET) provides the greatest amount of information on factors that decrease exercise tolerance: ventilatory limitation, desaturation, myocardial ischemia, decreased cardiac output, deconditioning, poor effort), but also indicates potential risks of the exercise, by monitoring the electro-cardiogram, blood pressure, etc. An important element is to establish the onset of lactic acidosis.

Physiological changes associated with increased exercise tolerance are the decrease of lactic acidosis, ventilation, and heart rate at a certain level of exercise, and the increase of mitochondrial enzyme activity and capillary density in the trained muscle groups (11, 18). To obtain these results, the exercise intensity should be prescribed at *the highest value tolerated by the patient without cardiovascular side effects* (8,11).

It was proved that COPD patients are able to tolerate high levels of their maximal physical capacity for a long period of time, which is probably explained by the fact that a slight decrease of ventilation below the limiting level is well tolerated. Casaburi and colleagues have shown that high intensity training programs (80% of Wmax in the incremental test) are more effective than less intense (50% of Wmax) (7). In these subjects, in the absence of cardiovascular limitation, the training program may begin at the intensity of the anaerobic threshold or above it, with progressive increase in the limits of tolerance (7,8,11). In patients who cannot reach the anaerobic threshold during incremental test, training can begin at a level closer to the maximum intensity obtained (11, 35). Using the anaerobic threshold as a landmark when it is reached or knowing that it has not been reached during standardized test, will allow selecting higher intensities targets, proved to be more efficient in COPD patients.

Training prescription for patients with chronic respiratory diseases other than COPD follows similar rules:

- uses the same parameters - heart rate, dyspnoea score, peak power, peak oxygen consumption, anaerobic threshold
- is modulated by the same precautions - avoiding cardiovascular adverse effects, severe desaturation, excessive muscle fatigue
- may include strategies for energy conservation (in pulmonary fibrosis), shorter sessions (in neuromuscular disorders), smaller targets for the training intensity (in pulmonary hypertension) (1,2,11).

Assessing the effects of rehabilitation and the overall effectiveness of a pulmonary rehabilitation program

Immediate benefits on an individual basis refer to:

- increase in exercise tolerance
- decrease of symptoms
- improvement of the quality of life
- better understanding of the disease, the available therapeutic options, the medical system.

Long-term benefits are:

- decrease in the number of exacerbations that require emergency assistance
- decrease in health-care system costs (1, 2,11).

The reason for increased exercise tolerance could be the increase of the training level or of the motivation, improvement of the ventilatory parameters and/or improvement of the ventilation-perfusion mismatches.

The increase in exercise tolerance is quantified by the same tests applied before entering the program. Arguments for increased tolerance are the decrease of the heart rate or of the dyspnoea / muscle fatigue scores and the increase of the distance walked during field tests (36-38).

Incremental CPET shows an increase of the peak oxygen consumption (VO_2 peak) and of the maximum power achieved (Wmax), an increase of the anaerobic threshold, decrease of symptom scores and of the ventilation level and decrease of the heart rate and blood lactate concentration. The increase in peak oxygen consumption in patients with COPD is, on average, of 18% compared to the initial (baseline) value and of 11% compared to control subjects (24,36,39).

Constant cardio-pulmonary tests show improvement of the VO_2 kinetics and of the endurance, explained by optimizing the physiological response to effort (the decrease of ventilation, carbon dioxide production, and blood lactate). Endurance is increased more than 80% (on average) from baseline. Increased endurance during moderately to high exercise (75-80% of peak VO_2 or initial Wmax) is the most sensitive variable in detecting positive effects of the therapeutic interventions (24,39).

In conclusion, lower limbs muscles training is a key element of a pulmonary rehabilitation program. There are several methods of prescribing the training intensity. The simple ones (target heart rate, symptom scores) can be easily used, but lack the rigorous exercise capacity measurements and raise safety concerns. The field tests and exercise tests without ventilation measurements add information and safety precautions. The gold standard in exercise capacity evaluation is cardiopulmonary exercise testing (CPET) which brings a high level of objectivity in exercise tolerance evaluation and provides information on mechanisms responsible for its decline; this allows a better training prescription and a correct evaluation of rehabilitation outcomes.

Our purpose is to emphasize in another article the results of an evaluation of different training prescriptions for our patients included in the pulmonary rehabilitation program.

LETTER OF INTENTION / CONFLICT OF INTEREST NOTIFICATION

I undersigned, certify that I do not have any financial or personal relationships that might bias the content of this work.

The paper was not sponsored by a company.

All the authors agreed upon the data analysis and the conclusions of the manuscript.

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