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Rehabilitation therapies in stable chronic obstructive pulmonary disease

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Abstract
Introduction. Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease. The pulmonary rehabilitation (PR) is a mutidisciplinary and comprehensive intervention in symptomatic patients with COPD. **Objective.** This review aims to synthesize evidence from available studies on the relative efficacies of different methods of rehabilitation therapies in patients with stable COPD. **Material and Methods.** A search was performed on the databases Pubmed, Embase, ResearchGate. Of the 410 articles retrieved from databases, only 20 met the inclusion criteria. Two reviewers independently reviewed selected eligible studies. **Results.** Rehabilitation is a multidisciplinary intervention in symptomatic patients with COPD, including speleotherapy, halotherapy, muscular training, soft tissue manual therapy and neuromuscular electrostimulation. All of the case-control studies using speleotherapy reported improved respiratory function to varying degrees and there were improvements in lung functional tests including forced vital capacity (FVC), forced expiratory volume in 1 second (FEV 1), oxygen saturation, partial pressure of oxygen in arterial blood, and partial pressure of carbon dioxide in arterial blood. In addition, halotherapy has been associated with relief of respiratory conditions such as COPD, asthma and cystic fibrosis by its bactericidal effect, improvement of immunity and rheological properties of secretions. Respiratory muscle training is a part of rehabilitation for COPD subjects. In patients who can not perform physical activity, neuromuscular electrostimulation (NMES) increased 6 minute walking distance and time to symptom limitation exercising at a submaximal intensity and reduced the severity of leg fatigue on completion of exercise testing. **Conclusion.** The management of COPD should include a multidisciplinary therapy, including rehabilitation therapies as an adjuvant to the medical treatment, especially because due to the high prevalence, mortality, and morbidity, COPD will be one of the biggest public health challenges in the next century.
Key words: *Rehabilitation therapy, COPD, Halotherapy, Speleotherapy, Muscular Training,*

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease caused by alveolar and/or airway abnormalities and characterized by persistent respiratory symptoms and airflow limitation, usually due to significant exposure to noxious particles or gases (1). COPD has become a problem of public health that occurs in >10% of adults over 40 years old and accounts for >5% of physician office visits and 13% of all hospitalizations, with the majority of patients remaining undiagnosed and untreated (2,3,4). Obstructive sleep apnea (OSA), diabetes, osteoporosis, depression/anxiety, musculoskeletal impairment and cardiovascular diseases are frequent and important comorbidities in COPD, often under-diagnosed, and associated with poor health status and prognosis. Due to the high prevalence, mortality, and morbidity, COPD will be one of the biggest public health challenges in the next century.

To minimize the burden of COPD for the health care system, three cornerstones can be defined: smoking cessation, reduction of acute exacerbations and comorbidity management (5). Mutidisciplinary approach combines these aspects in an integrative intervention including other therapies such as speleotherapy, halotherapy, muscle training, soft tissue manual therapy intervention, neuromuscular electrostimulation. Because respiratory and limb muscle dysfunction have been recognized as indicators for disease progression independent of lung function (6), physical exercise has become an indispensable measure to invert skeletal muscle dysfunction (7), improve exercise capacity and health-related quality of life (HRQoL) and reduce exacerbations.

According to ATS/ERS pulmonary rehabilitation is a mutidisciplinary and comprehensive intervention in symptomatic patients with COPD. It becomes a part of an individual patient's plan of treatment and is initiated in order to optimize functional status, enhanced participation in physical and social activities, improve the quality of life and reduce healthcare cost by stabilizing or reversing the systemic manifestations of the disease (8). In the last five years some research has focused on the roles of rehabilitation therapy in chronic obstructive pulmonary disease and its comorbidities.

Objective. This approach aims to synthesize evidence from available studies on the relative effectiveness of different methods of pulmonary rehabilitation in patients with stable COPD.

Materials and methods

This search was performed on the databases Pubmed, Embase, ResearchGate. The following key words were used: Halotherapy, Speleotherapy, Muscular Training, Manual Therapy, Neuromuscular Electrostimulation (NMES). They were applied on following disease conditions: chronic obstructive pulmonary disease (COPD). Inclusion criteria were: studies evaluating short and long term effects of speleotherapy, halotherapy, inspiratory or expiratory muscle training, neuromuscular electrostimulation, manual therapy (soft tissue manual intervention), in stable COPD patients. Studies had to include one of these outcomes: dyspnea, quality of life, exercise capacity, 6 minute walking test. Exclusion Criteria: We excluded studies that did not meet the above criteria.

Results

Database search resulted in 410 titles and abstracts that were relevant for the present topic; after selecting articles published in the last five years, 106 articles remained for further selection. After exclusion of all the irrelevant studies for our purpose were regarding the aim, 20 articles were finally included in this research.

Key words	Study results	Study selected
Speleotherapy	9	3
Halotherapy	8	3
Muscular Training	28	5
Manual therapy	29	3
Neuromuscular electrostimulation	32	6

Key words „-Speleotherapy" OR „-Halotherapy" OR „-Muscular training" OR „-Manual Therapy" OR „-Neuromuscular electrostimulation"
n=410

Articles resulted after the application of inclusion and exclusion criteria
n=106

Articles included in the final review
n=20

Speleotherapy and halotherapy

Chronic airflow obstruction, often belonging to panting and reduced walking distance distinguish COPD (9,10) and chronic character of symptoms directly influences patient's quality of life. Respiratory physiotherapy, bronchodilators, smoking cessation, rehabilitation, inhaled drug treatments and antibiotics are available treatment methods. Severe medication side-effects and allergic responses made physicians prefer to use natural salt as an adjuvant treatment in stable COPD.

Speleotherapy in the treatment of COPD imply applying normal salt in a reserved atmosphere as a therapy for disease treatment (11). It is recommended by the broader community and is often described as a reviewed treatment method for people with chronic and allergic respiratory diseases, using the specific and unique feature of the environment, especially particles contained in the air of underground spaces, mostly karst caves. In Eastern Europe, natural salt caves were used for the relief of respiratory symptoms. The unique properties of the microclimate in caves are the constant air temperature of moderate to high humidity, the presence of fine aerosol elements (sodium, potassium, magnesium and calcium), as well as the lack of airborne pollutants and pollen in the air. Nowadays, salt caves are used for treatment at health centers in Austria, Poland, Slovakia, Romania, Azerbaijan, Kyrgyzstan, Russia and Ukraine (12).

All of the case-control studies reported improved respiratory function to varying degrees and improvements in lung functional tests including forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), oxygen saturation, partial pressure of oxygen in arterial blood and partial pressure of carbon dioxide in arterial blood (13). On the other hand, the results are contradictory because another study showed no significant difference of FEV1/FVC in patients using speleotherapy (11). Also, there was statistically significant improvement in recorded 6-minute walk distant parameter in subjects with speleotherapy (P=0.02), while in control group there was no significant improvement (P=0.23). These findings were similar to a previous study reporting that patients in the case group had a statistically significantly improved six minutes walking test (6MWT) by 90 meters ($p<0.01$) (14) and another study reported an improvement by with 75 meters ($p<0.01$) (15). Moreover, patients receiving speleotherapy improved their clinical condition which was scored each day by the participants and physician jointly in the basis of symptoms and complaints. It was suggested that the improved clinical state for stable COPD patients improved their life quality by decreasing exacerbations, reducing hospitalization, improving physical tolerance and reduces fatigue (13).

Speleotherapy has beneficial impact on the immunological status which has improved by 97.8% in the treatment group, more exactly the reduction of inflammatory process during exacerbations and the normalization of the subpopulation of CD4+ and CD8+ lymphocytes with the increasing in the neutrophil phagocytosis activity (16). In addition, taking into account the importance of mental status, other studies showed that rehabilitation programs which included speleotherapy improved depression and anxiety in patients with stable COPD (17,18).

On the other hand, **halotherapy** is used as an alternative for speleotherapy in regions that do not have karst caves. Halotherapy is a treatment consisting of inhalation of small salt particles in a controlled environment of a halochamber. This room is designed to replicate the natural microclimate of a salt cave. Halotherapy treatment has been associated with relief of respiratory conditions such as COPD, asthma, cystic fibrosis, as well as relieving in tegumentary conditions such as eczema and dermatitis (13).

Although the claimed effects of halotherapy are plenty, such as bactericidal effect, improvement of immunity, improved rheological properties of secretions, a single study has looked at immunological changes during halotherapy and suggested changes in T-Lymphocyte activity (16). Halotherapy has been shown to relieve symptoms in smokers and in patients with respiratory symptoms in general. Another study which compared saline inhalation (inhalation of saline solution through specialized equipment without halochamber) with halotherapy in the treatment of patients with COPD reported an improvement in FEV 1% in both groups. Moreover, halotherapy has a beneficial statistically significant effect on 6 minute walking test and on the patient's quality of life, as measured by Saint George's Respiratory Questionnaire (SGRQ) (19). In addition, no patients experienced side effects, which indicates that the treatment is safe and well tolerated; halotherapy seems to be better tolerated than saline inhalation (20).

Patients with COPD and comorbidities such as OSA (Overlap syndrome, prevalence 0,5-1%) (21) have more exacerbations of the respiratory symptomatology, a situation in which the halotherapy and the CPAP therapy have many benefits, but the therapeutic success is primarily ensured by the patients' compliance (22). The presence of various microbiological and inorganic structures on the inner surface of CPAP masks and tubes emphasizes the risk of microbial and inorganic elements inhalation into the upper and lower airways, so the microclimate and the hygiene of CPAP device, including masks and tubing is very important (23,24,25).

Muscular Training program

In COPD, changes in the anatomy of the airways and lung parenchyma occur as the result of bronchial hypersecretion and bronchoalveolar instability. These changes cause expiratory flow limitation and air trapping, known clinically as dynamic hyperinflation. This phenomenon leads to increases in expiratory reserve volume, residual volume (RV) and end expiratory lung volume (EEV). The increase in EEV limits Tidal volume and inspiratory reserve volumes resulting in a negative impact on the inspiratory capacity (IC). The changes alter the position of the ribs causing a state similar to sustained inspiration over time, often referred to as "inspiratory block"(26).

COPD can cause systemic alterations such as systemic inflammation, skeletal muscle dysfunction, peripheral muscle weakness and inspiratory and expiratory muscle weakness by changes in the composition of muscle fibers and muscle atrophy (27,28). Thus, the treatment of this disease should be multidisciplinary and respiratory physiotherapy may act by improving the functional capacity of these subjects (29).

Because of the COPD comorbidities, like cardiovascular diseases and Obstructive Sleep Apnea (OSA), the importance of screening programs for these pathologies is evident in COPD patients. Some studies showed that only overweight itself produces early changes in cardiovascular status of the patient by decreasing the left ventricular ejection fraction, thickening the interventricular septum, increasing left ventricular mass and implementing early diastolic dysfunction (30).

Respiratory muscle training is a part of rehabilitation for stable COPD subjects, as it promotes benefits such as improved pulmonary function and respiratory muscle strength, reduction of dyspnea severity, improved exercise tolerance and enhanced functionality and quality of life. Studies that prove the efficacy of inspiratory muscle training (IMT) in subjects with stable COPD show that this training leads to a reduction of dyspnea and improve the pulmonary function, respiratory muscle strength, and functional capacity (27). IMT improves inspiratory muscle strength, quality of life (SGRQ), exercise capacity (quantified by 6MWT) and decreases dyspnea. Dyspnea during constant load tests was significantly decreased with IMT alone and IMT improved the walked distance during 6MWT with 43 meters-, with a statistical significance (31).

Studies have shown that respiratory muscle weakness is associated with increased mortality in subjects with COPD (32). In obese COPD patients the clinicians have to introduce a weight reduction programme in order to minimize the effect of excessive adipose tissue on the disease evolution. McDonald et al. demonstrated that the association between diet and resistance exercise training in obese COPD patients determined an improvement of clinical outcomes including health status, symptoms and functional capacity. Importantly, when calorie restriction is coupled with resistance exercise training and protein intake is maintained, it does not result in reduced skeletal muscle mass (33). In addition, expiratory muscle weakness is a risk factor for readmission to hospital due to exacerbations (34), and a recent study showed that the degree of airflow obstruction and hyperinflation is related to expiratory muscle strength (35). A recent systematic review showed that in normal subjects, the combination of IMT plus expiratory muscle training (EMT) is more effective in increasing the performance exercise compared with IMT or the control group (36).

In addition, some important comorbidities of COPD are obesity, OSA and metabolic syndrome including type 2 diabetes, which can complicate the evolution of stable COPD (37). Between these pathologies there is a synergic relation, because due to anatomical and physiological factors and treatment with corticosteroids increases fat deposition in the neck region, central obesity becoming a risk factor for OSA in the general population (38,39). One of the most important interventions in the treatment of OSA is the nutrition program along with a training program in order to reduce OSA severity, improve sleep quality and increase respiratory muscle endurance in patients with COPD (40,41). The purpose is to obtain weight loss, to reduce the apnea-hypopnea index and the severity of OSA but, in selected cases with associated craniofacial deformities, early orthodontic treatment could be beneficial (42,43,44).

Soft tissue manual therapy intervention

Manual therapy (MT) has been described as a therapeutic intervention that uses the hands to provide treatment to the musculoskeletal and/or visceral systems. MT includes techniques such as massage, myofascial release, muscle energy technique, ligament balance, joint mobilization and joint manipulation. The suggestion that MT can deliver ongoing benefits for people with COPD is a new approach (45).

Cruz-Montecinos showed that management strategies which include manual therapy designed to address the soft tissues of the chest wall has the potential to produce immediate improvements in lung function in patients with severe and very severe COPD (26). Another study reported similar results, but included a combination of soft tissue therapy and thoracic mobilization (46). Moreover, reduced tonicity in the muscles, fascia and ligaments of the neck and chest would facilitate an improvement in the passive components of expiration by reducing the extent of any inspiratory block. In support of this concept are the results of a recent study, which reported a correlation between pulmonary function and postural alignment and mobility of the chest in patients with COPD (47). Improvements in mechanical efficiency may also explain the increase in oxygen saturation and decrease in respiratory rate, which if sustainable, could alter input to the central and peripheral chemoreceptors. The decrease in heart rate may be the result of the decreased residual volume, where lower pressure within the lungs leads to a reduction in pulmonary hypertension. Therefore, a single application of an MT protocol consisting of several soft tissue techniques has the potential to deliver immediate improvements in lung function for people with severe and very severe COPD. The doctors should be trained in order to recommend the proper technique, because the MT techniques that use compression/decompression maneuvers can increase airway obstruction by accelerating airflow to the extent that airways collapse (26).

Neuromuscular electrostimulation

For a long time, COPD was considered to be a respiratory disease, but, additionally, COPD produces inactivity, which promotes further loss of exercise capacity (deconditioning) through the loss of muscle mass, creating a "vicious" circle. Weakness, atrophy, structural and metabolic changes have been observed in limb muscles, which in turn, can have a negative impact on exercise tolerance. Peripheral muscle dysfunction in people with COPD is characterized by: reduced percentage of the oxidative fibres (type I) in relation to glycolytic fibres (type IIa and IIb), decreased activity of most oxidative enzymes while glycolytic enzyme expression is increased, reduced capillary density or capillary-to-fibre ratio and mitochondrial dysfunction. Taken together, these changes contribute to an overall reduction in the oxidative capacity of the muscles of patients with stable COPD and overlap syndrome. Exercise protocols have traditionally focused on aerobic training, however, more recently, increased emphasis has been placed on resistive training because of the importance of maintaining or improving muscle bulk and strength in this group of patients. Unfortunately, some debilitated patients with COPD are unable to sustain an adequate training intensity and duration, leading to reduced activity or even to the patient being confined to their home or bed and accentuating the deterioration of the overall health status of this individual. Moreover, several investigations have reported the benefits of pulmonary rehabilitation beside using neuromuscular electrostimulation (NMES) to reverse some of the negative changes occurring in the peripheral muscles of patients with stable COPD. NMES has been extensively used as a technique to improve muscle function and structure in different areas of rehabilitation and sports training programs [48], required in patients with overlap syndrome that associate excessive daytime sleepiness, limited physical activity and a lower quality of life in order to improve sleep quality and to reduce OSA severity (49,50,51).

Kucio C et al. suggested that physical exercise results in decreased symptoms of skeletal muscles function disorders, which constitute the most common extrapulmonary symptoms of COPD. Physical training prevents further muscle damage which leads to decreased strength and endurance, while at the same time increasing exercise tolerance. The results of this study indicate that due to the application of traditional pulmonary rehabilitation in combination with NMES of 35 Hz frequency, a substantial increase of distance in the 6 minute walking distance in relation to the distance covered before the study was observed. The increase in exercise tolerance does not correlate with improvements in spirometric values (FVC, FEV1, FEV1%FVC), nor with gasometric parameters (partial oxygen pressure - pO2 and partial pressure of carbon dioxide - pCO2). However, the observed improvement of exercise tolerance results from increased strength and endurance of skeletal muscles of lower limbs subjected to NMES therapy (52). Another study showed that NMES, when applied in isolation, increased quadriceps force and endurance, 6MWD and time to symptom limitation exercising at a submaximal intensity, and reduced the severity of leg fatigue on completion of exercise testing (53).

Conclusion

COPD is an ever-growing global problem with systemic implication and multiple comorbidities. Although pharmaceuticals have been extensively studied and utilized, their disease-modifying effects are limited and dependent on patient adherence.

The management of COPD should include a multidisciplinary therapy; individualized pulmonary rehabilitation as an adjuvant to the medical treatment, by effective methods, such as speleotherapy, halotherapy, muscular training, manual therapy (soft tissue manual therapy) and neuromuscular electrostimulation.

Declaration of conflict of interests

The author does not have any financial interest involving the companies and/or materials mentioned in this article.

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