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Review

Physical exercise – the friend or the enemy of the patient with pulmonary tuberculosis?

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Abstract

Introduction. Tuberculosis, a major cause of morbidity and mortality, is the second cause of death from an infectious disease, after HIV/AIDS. Each second, a new infection occurs around the globe. Pulmonary tuberculosis can equally affect a performance athlete as well as an aspiring athlete. Physical exercise must be individualized and customized. Pulmonary rehabilitation guides 3 recommend types of exercises for patients with obstructive pathology: stretching, cardiovascular exercise or aerobics. Exercises must be started under medical supervision and must be interrupted if: the ventricular altitude increases above the maximum estimated level for the age, oxygen saturation (SaO2). Aim. The current review aims at raising awareness on post-tuberculosis disabilities and on the fact that such a frequent pathology with major sequelae is currently being ignored, since there are very few studies on this subject. Material and Method. The purpose of this research was to summarize the current literature regarding the influence of physical activity on patients with pulmonary tuberculosis. An electronic search of Pub Med database and Web of Science was conducted until September 2018. Results and discussions: Only the studies that were published in English were included in this research. The search in the databases was performed using the following keywords: "pulmonary tuberculosis" or "physical activity in respiratory diseases". The studies from the reference list of the databases were then searched manually. Conclusions. Current pulmonary rehabilitation programs with clear evidence of clinical improvement of the chronic pulmonary pathology are being studied excessively without placing too much emphasis on tuberculosis. It is necessary to develop guidelines for these patients, with a precise onset of the rehabilitation programs, adapted and individualized exercise types, as well as other measures for assessing the outcomes.

Keywords : physical exercise, pulmonary tuberculosis, pulmonary rehabilitation

Highlights

- ✓ Although experience in this field is limited, it is necessary to think that the rehabilitation process integrates a group of actions aimed at helping patients reach an optimal mental and social functioning level.
- ✓ Current pulmonary rehabilitation programs with clear evidence of clinical improvement are being studied excessively in the field of chronic pulmonary pathology, without any target on tuberculosis.

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Introduction

Physical exercise must be individualized and customized. Pulmonary rehabilitation guidelines recommend 3 types of exercises for patients with obstructive pathology: stretching, cardiovascular exercises or aerobics (walking, jogging, jumping rope, stationary or outdoor biking, cross-country skiing, skating, canoeing), strengthening (muscle contractions for the upper part of the body). Each exercise stage has 3 components: warm up – physical exercise – cool down. The intensity of the exercise is determined by the rehabilitation physician, based on the "Rated Perceived Exercise (RPE) Scale" that evaluates personal exercise tolerance (1). Exercises are begun under medical supervision and their cessation is considered if: the ventricular altitude rises above the maximum estimated for the age, SaO2 <85% and if wheezing occurs (2).

Physical exercises are adapted to the severity of the case, sometimes being adjusted with oxygen therapy or even "nasal intermittent positive pressure ventilation" - mechanical ventilation (3-6). "Tuberculosis probably occurred at the same time with humanity." This news went around the world this past fall, following the identification of bone tuberculosis in an Egyptian mummy (7).

"Phthisis" is the old Greek term for tuberculosis. Around 460 BC, Hippocrates considered "phthisis" to be the most common disease in those times (8). The disease was associated with vampires and it was thought that if a member of a family died from it, he also drained the life of the other family members, who would gradually get ill, too (9). In March 1882, Robert Koch discovered the bacillus that causes tuberculosis, "Mycobacterium tuberculosis", for which he received the Nobel Prize. After this great discovery, things naturally progressed with the immunization against tuberculosis, the BCG vaccine being used for the first time on humans in 1921 in France (10).

Tuberculosis guidelines define tuberculosis through bacteriological or histopathological confirmation (11). From a microscopic point of view, the characteristic lesion of tuberculosis is granuloma, consisting in central necrosis and an area surrounded by a giant multinuclear cell (Langhans type) with epithelial cells and lymphocyte layer on the periphery of the granuloma (12).

As any physician wishes to reintegrate each patient to his or her prediagnostic environment, the medical rehabilitation of patients with pulmonary tuberculosis becomes an important necessity. That is why the answer to the question of whether these patients can perform sports or not, and under what conditions, should become an omnipresent certainty.

In this study, we aimed to analyze the indication of permission or restriction for the patient diagnosed with pulmonary tuberculosis to practice sports and under what conditions he can do so.

The purpose of this research was to summarize the current literature regarding the influence of physical activity on patients with pulmonary tuberculosis. An electronic search on Pub Med database and Web of Science was conducted until September 2018.

Only the studies that were published in English were included in this research. In the databases, the search was performed using the following keywords: "pulmonary tuberculosis" or "physical activity in respiratory diseases". The studies from the reference list of the databases were then searched manually.

The inclusion criteria concerned only the articles written in English, the studies published in the last 10 years and all the studies performed in vitro, ex vivo and in vivo.

The exclusion criteria were reviews of literature and studies about tuberculosis that were correlated with other respiratory diseases.

Discussions

Since the vast majority of tuberculous infectious cases are pulmonary tuberculosis types and they are an important source of contagious diseases, the focus of studies and research is based on this aspect. The current problem is the post-tuberculosis sequela healing, which involves an increased addressability of patients to medical systems, with a decrease in the quality of life of these patients (considered healed from an infectious point of view).

With all the standard treatment regimens that seek complete healing, the lung has a spectacular regenerative capacity that can sometimes be chaotic even before the disease is diagnosed. By trying to stop intense local inflammatory processes, fibroblast activation occurs, which will initiate regenerative processes through fibrosis and compromise pulmonary elasticity (13).

Unfortunately, pulmonary tuberculosis is not the disease of the past, but a disease of the present. It still is a major cause of morbidity and mortality worldwide (14). Tuberculosis is the second cause of mortality due to the fact that it is an infectious disease (the main cause being HIV/AIDS) (15). According to the World Health Organization's (WHO) reports in 2016, around 10.6 million people worldwide suffer from tuberculosis and 1.8

million die from this disease (16). "M. tuberculosis" is found in about one third of the world's population, it affects mostly the lungs, but it can also affect other organs and parts of the body. More than two-thirds (79.1%) of these cases presented pulmonary TB, 14.6% had only extrapulmonary TB, while 6.3% were diagnosed with both pulmonary and extrapulmonary TB (17). Each second, there is a new infection occurring around the globe.

The changes, the etiology, the appearance of chronic diseases sanatoriums significantly reduced the incidence of tuberculosis, even before Streptomycin and other antibiotics began to be used in standard regimens. However, tuberculosis remained a serious threat to public health. The UK Medical Research Council, founded in 1913, calls for tuberculosis research (18), proof that it still poses a threat to public health.

Unfortunately, Romania is the country with the highest number of cases of tuberculosis in the European Union, with a global incidence of about 70% per 1,000 inhabitants. We are also the country with the highest number of multidrug-resistant (MDR) tuberculosis cases in Europe (19).

According to the national registry data, extra-pulmonary tuberculosis cases range between 8% and 10%. The diagnosis of extra-respiratory TB is made by the "organ" specialist along with the pulmonologist, the treatment being prescribed by the respiratory physician, just like the rehabilitation programs for the extra-respiratory forms (12).

In Romania, there are general legal regulations regarding the monitoring, prevention and control of tuberculous infections (19), but there are no regulations regarding the minimization of sequela healing.

In addition to the increased incidence of new cases, which have specifically established follow-up management, post-tuberculosis sequela healing, with increased patient addressability to medical systems and decreased life quality of these patients (considered healed), remains without a standardized evaluation and follow-up protocol.

The World Health Organization calls for medical involvement to put an end to tuberculosis and for the complete healing of patients without sequelae. Several attempts to establish protocols to track the sequela healing tendency have been made and also to implement them at the 2-month active treatment evaluation when the patient is reassessed radiologically and bacteriologically, according to the current tuberculosis guidelines (20).

At present, there is no follow-up management for patients after the termination of the antituberculosis therapy (21) and, for young people who develop secondary fibrosis, this lack of follow-up can lead, in time, to a "disability" for life with reduced tolerance to effort (22).

Probably because of the high risk of contamination, not too much attention has been paid to the effects of pulmonary tuberculosis in terms of physical disability during therapy and post-therapy. However, a bacteriologically negative patient is no longer a contagious patient, so that pulmonary evaluation can be complete and safe.

Since 1964, Chapman and Hollander have written that, based on their experience with 454 patients with active tuberculosis "placed on a program of intensive physical exercise, combined with chemotherapy", the tuberculosis syndrome was minimized.

In 2016, ATS included tuberculosis among the diseases that can be part of rehabilitation programs (5).

However, specific protocols for evaluating the patient with tuberculosis and the ideal time to do physical effort have not been developed yet, each physician adapting to established respiratory disease protocols.

The assessment of the pulmonary function is the starting point in the subsequent conduct of patients, as all research in the field points out (5).

The quality of life assessment is done through the same questionnaires as for patients with COPD: St. George's Respiratory Questionnaire (SGRQ) and Chronic Respiratory Disease Questionnaire (CRQ) (23), as well as the mMRC scale and the 6-minute walk test, are the strongest predictors of the quality of life of a patient with secondary or idiopathic pulmonary fibrosis (24).

Dyspnea assessment, physical exercise tolerance assessment and a 6-minute walk test could be associated with the complete assessment of a patient with pulmonary tuberculosis (after bacteriological negativity is determined) in order to assess the risk of sequela healing.

The 6-minute test is a useful method for indirect exercise effort assessment in patients with moderate to severe lung disease. The test is widely used for pre- and post- programs of respiratory and cardiac recovery and pre- and post-cardiopulmonary surgery (25).

Only by thoroughly evaluating a patient with pulmonary tuberculosis can we understand if he/she will become a patient with sequelae, a patient with post-tuberculous syndromes (traction bronchiectasis, secondary pulmonary fibrosis, etc.) and whether the life quality of this patient will be significantly impaired.

Respiratory medical rehabilitation is considered to be the "third medicine" after preventive medicine and pharmacology. A comprehensive rehabilitation program should include a multidisciplinary team: the physician, the pulmonologist, the physical therapist, the recovery assistant, the dietician, the psychologist, the social worker and the general practitioner (2).

Currently, rehabilitation programs are accepted for all patients with obstructive pulmonary pathology and clinical manifestations of dyspnea. Dyspnea is objectively assessed by an MMRC ≥3. There are exclusion criteria that make it impossible for patients to participate in rehabilitation programs: uncontrolled cardiovascular conditions, orthopedic or neurological disorders that reduce mobility or lack of cooperation (2).

The following are types of rehabilitation programs:

1. `Inpatient` - patients hospitalized due to disability or in convalescence after an exacerbation. The average length of hospitalization is reduced to 20 days.
2. `Outpatient` - patients regularly attend rehabilitation sessions and are encouraged to continue their physical training at home.
3. `Home patient` - home rehabilitation through the home-care system; the duration ranges between 6 weeks to 18 months (26).

A pulmonary rehabilitation program includes several components: simple respiratory muscular recovery exercises, neuromuscular stimulation, psychosocial counselling, nutritional assessment and medical education (27).

Lower limb exercises are the foundation pillars of the entire training. Walking is necessary for most daily activities, many rehabilitation programs using it (sometimes on the treadmill) as a preferable way of training. Some people prefer to practice on a stationary bicycle. Choosing an exercise that is comfortable and satisfying for an individual increases the desire to participate in it on the long term (28).

Frequently, the training of the lower muscles is the starting point of a rehabilitation program (26). The exercise of upper limbs is also beneficial to people with chronic lung disease, who have difficulty breathing or show other symptoms during their normal daily life activities, such as hair washing or laughter (28). Such training is necessary because chronic pulmonary disease can cause loss of respiratory muscle function. Also, the use of breathing devices to strengthen the muscles is usually used in conjunction with traditional aerobic exercise and it helps reduce breathing and increase effort capacity (26, 28).

There are some adjustments to rehabilitation programs for extended fibrosis. Oxygen therapy is frequently administered during training to patients with significant desaturation, despite limited evidence for this practice. The American Thoracic Society (ATS)/ the European Respiratory Society (ERS) for rehabilitation programs recommend oxygen supplementation during exercise training for interstitial pathology. Additional oxygen would normally be given to these patients during exercise to prevent significant desaturation. There is insufficient evidence to show that this practice has better rehabilitation results, such as greater improvements in exercise capacity (3). However, there was a greater increase in exercise tolerance, especially in patients with restrictive ventilatory dysfunction, in which physical exercise (cycling) was supplemented with oxygen therapy. There has been a reduction in lactic acid in the blood, which is responsible for muscle fatigue (4).

Also, antitussive therapy associated with the rehabilitation programs, remains an alternative for patients with persistent cough (29) and does not involve the reactivation of the bacillary pathology. Coughing should be carefully evaluated and, if due to interstitial pathology, non-specific cortisone or antitussive therapy may be used (29). Cortisone therapy should be given for a short time, since long-term care may favor myotonia and decrease responsiveness to the rehabilitation program (30).

Following the literature on comparative rehabilitation groups (COPD post-TB seps), 9-12 months of pulmonary rehabilitation bring the same benefits: improvement of dyspnea and physical performance, the latter being quantified by the Borg scale and the 6-minute walk test. A 50-54 m increase of the walk test is considered clinically significant in many studies (31), but some authors consider that a 30-meter increase in physical performance in the walk test is satisfactory (27). One must also take into account the particular aspect that tuberculosis is an independent risk factor for COPD, even in non-smokers (5). Studies show that there is a genetic predisposition for this association (32).

Despite having completed the treatment, many patients with pulmonary tuberculosis remain disabled. It is necessary to establish specific post-treatment rehabilitation programs for individualized and effective regimens included in standard treatment regimens (33).

If all the other components of a rehabilitation program are added to all physical resources, it will definitely be a success. Supportive and nutritional measures are absolutely important. It is known that tuberculosis is a

consumptive disease and the ascending weight curve is a favorable evolution marker (34).

The nutritionist and sometimes the endocrinologist must be part of a complex rehabilitation program. Hormones and hypothalamic neuropeptides (acting as neurotransmiters and neuromodulators in the central nervous system) play an important role in breathing regulation and bronchopulmonary morphology (35), perhaps also in the regeneration processes, this field being still under study.

Psychological support is extremely important because depression and anxiety are often associated with tuberculosis. Cases of depression and severe anxiety are statistically significant (32.20% for moderate depression, 32.20% for severe and 40.68% for moderate anxiety) according to studies in our country (36).

Quitting smoking is mandatory when initiating rehabilitation therapies, this being another reason for psychological support, which is difficult to achieve in many cases. Active smoking during a rehabilitation program may cause its failure. The sole clinical evaluation of smokers is not enough. The biomarkers of tobacco exposure are the most useful tools for this purpose. The concentration of carbon monoxide in the exhaled air is a reliable proof of recent smoking (37-39).

The main idea of rehabilitation programs is that significant results are obtained if the therapy begins with the early and mild phases of interstitial pathologies (40) and if it is combined with all other resources (nutritional, behavioural, psychological support) (41).

We know that the selection in sports is done early, in an individualized manner, depending on the sporting sector concerned, after a thorough examination according various selection criteria, including the functional one (42).

Therefore, the aim is to improve the pulmonary function and to avoid disability from the early stages.

Pulmonary rehabilitation (PR) is the most effective therapeutic intervention for reducing dyspnea and improving the physical performance and the quality of life, according to the GOLD report from 2017 (43, 44). The indication of pulmonary rehabilitation should be present in any patient diagnosed with interstitial and symptomatic pulmonary syndrome (dyspnea, fatigue, decreased physical tolerance) (45, 46).

After a complete rehabilitation program of 6 months, the benefits are maintained for approximately 1 year (47), as evidenced by many clinical trials, which is why these patients should always be reinstated in rehabilitation programs.

Conclusions

Current pulmonary rehabilitation programs with clear evidence of clinical improvement are being studied excessively in the field of chronic pulmonary pathology, without any target on tuberculosis.

It is necessary to develop guidelines for these patients, with a precise onset of the rehabilitation program, adapted and individualized physical exercises, as well as other measures for evaluating the outcomes.

Although experience in this field is limited, it is necessary to think that the rehabilitation process integrates a group of actions aimed at helping patients reach an optimal mental and social functioning level.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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