

The Benefits of Pulmonary Rehabilitation Program on Post-Tuberculosis Bronchiectasis

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Abstract

Pulmonary rehabilitation has emerged as a recommended standard of care for patients with chronic lung disease. As in chronic obstructive pulmonary disease (COPD), persons with other forms of chronic respiratory disease commonly experience deconditioning and decreased quality of life. The aim of this prospective study is to determine the effect of a 4-week pulmonary rehabilitation program (PRP) on patients diagnosed with post-pulmonary tuberculosis bronchiectasis in the Philippines. The participants were above 18 years of age, diagnosed to have stable Post-Pulmonary tuberculosis bronchiectasis with chest computerized tomography (CT) scan or chest radiograph showing bronchiectatic changes, consented to attend the PRP sessions and be included in the study. The subjects underwent PRP for 4 weeks with a total of 8 sessions and determination of Forced expiratory volume at 1 second (FEV1), forced vital capacity (FVC), quality of life determination using the Saint George Respiratory Disease Questionnaire (SGRQ), and exercise endurance using the 6-minute walking test (6 MWT), before and after the PRP. A total of fourteen patients, six males and eight females, aged from 28 - 72 years old, completed the 4-week pulmonary rehabilitation program. There were four ex-smokers and ten non-smokers with concomitant asthma and COPD in some patients. There was significant improvement in the 6-minute walk test and quality of life after 4 weeks of rehabilitation program among the subjects with p value for 6 MWT at $p = 0.0001$ and $p = 0.008$ for SGRQ. Conclusion: Pulmonary rehabilitation program led to a significant improvement in exercise capacity and health related quality of life among patients with post-pulmonary tuberculosis bronchiectasis.

Keywords

Pulmonary Rehabilitation, Post-Tuberculosis Bronchiectasis, Post-Tuberculous Lung Disease

1. Introduction

Bronchiectasis is a heterogeneous and chronic disorder of the major bronchi and bronchioles characterized by permanent abnormal dilatation and destruction of bronchial walls [1]. The induction of bronchiectasis is based on the vicious cycle concept wherein repeated infectious insults on the airways cause persistent inflammation, impairment of drainage of secretions, airway obstruction, and eventual destruction of these airways [2]. The classic clinical manifestations of bronchiectasis are cough and the daily production of mucopurulent and tenacious sputum lasting months to years [3]. Less specific complaints include dyspnea, hemoptysis, wheezing, and pleuritic chest pain [2].

Infectious etiologies for bronchiectasis are varied and a significant cause is tuberculosis (TB) [2]. Endobronchial tuberculosis commonly leads to bronchiectasis, either from bronchial stenosis or secondary traction from fibrosis [3]. The Philippines ranked fourth among all countries with the highest tuberculosis incidence in 2020 with 1 million Filipinos still having active tuberculosis [4]. Tuberculosis also ranks as the 12th leading cause of death in the country in 2020 and there is no data on the number of Filipinos suffering from post-TB sequelae [4]. Worldwide, The Union estimates a total of 155 million TB survivors alive in 2020 with, as much as 50% of these individuals, still complaining of residual cough, dyspnea, weakness and impairment in their physical capacity [5]. The Union, together with a global consensus of TB experts, labelled this constellation post-TB sequelae as Post-TB Lung Disease (PTLD) when there is “evidence of chronic respiratory abnormality, with or without symptoms attributable at least in part to previous pulmonary tuberculosis.” [5].

Pulmonary rehabilitation has emerged as a recommended standard of care for patients with chronic lung disease based on a growing body of scientific evidence [6]. The primary goal is to restore the patient to the highest possible level of independent function. Pulmonary rehabilitation is an evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decreased daily life activities [7].

Rehabilitation programs for patients with chronic lung diseases are well-established as a means of enhancing standard therapy in order to control and alleviate symptoms and optimize functional capacity [6] [7] [8]. It has also been applied successfully to patients with other chronic lung conditions such as interstitial diseases, cystic fibrosis, bronchiectasis, and thoracic cage abnormalities [6]. Recent guidelines on the management of bronchiectasis likewise strongly recommend pulmonary rehabilitation intervention and regular exercise for adult patients with bronchiectasis and exercise capacity limitation with the goals of improving the patients’ symptoms and physical capacity [2] [3].

On the other hand, studies on tuberculosis leading to bronchiectasis and the subsequent role of pulmonary rehabilitation in post-tuberculosis bronchiectasis are scanty and more data are needed, particularly from countries with high burden of pulmonary tuberculosis [9] [10] [11] [12] [13]. This scarcity of specific

evidence on PTLD and the benefits of pulmonary rehabilitation are acknowledged by The Union so that the First International Symposium on Post-TB disease was held to establish the “Clinical standards for the assessment, management and rehabilitation of post-TB lung disease” with 75 global TB experts comprising the consensus panel [14]. The aim of the implementation of these standards was to gather evidence while management and rehabilitation of PTLD may be performed in a rational, cost-effective and standardized manner [14].

This study aims to add to the needed data on PTLD and pulmonary rehabilitation intervention in PTLD by determining the effect of a 4-week pulmonary rehabilitation program on patients diagnosed with Post-Pulmonary tuberculosis Bronchiectasis based on Chest X-ray and/or CT scan as to spirometry, quality of life, and functional capacity, before and after the program.

2. Methods

2.1. Subjects

Fourteen patients, male and female, were enrolled in this prospective study and underwent the out-patient pulmonary rehabilitation program of the Philippine General Hospital in 2015. The subjects underwent an out-patient pulmonary rehabilitation program for 4 weeks, given 2 times a week with a total of 8 sessions. The subjects included were all above 18 years of age, diagnosed to have Post-pulmonary tuberculosis bronchiectasis, which have completed tuberculosis treatment, with chest CT Scan or chest radiograph showing bronchiectatic changes, consented to attend PRP sessions and join the study. Exclusion criteria were uncontrolled co-morbid illnesses limiting performance of measured parameters & significantly affecting quality of life such as: severe cardio-vascular disease, uncontrolled diabetes mellitus with or without end-organ damage, debilitating or uncontrolled malignancies, psychological or intellectual defects limiting comprehension, and physical defects limiting mobility or ambulation. None of the patients showed any evidence of ischemic heart disease, musculoskeletal disorders, or other disabling disorders that could limit participation in the rehabilitation program. All patients agreed to participate in the rehabilitation program and the study. This study was approved by the ethics review board of the institution.

2.2. Intervention

The pulmonary rehabilitation program was conducted twice weekly for 3 hours for 4 weeks with 2 - 4 participants in each session and supervised by a pulmonologist, physiotherapist, nutritionist and psychiatrist. The exercise program as mainly a symptom-limited walking-based protocol with 30 minutes each session to aim for a Borg's dyspnea score of 4 - 5 along with upper and lower limb resistance training. Breathing re-training & dyspnea-relieving techniques were also included in the sessions. Education interventions, nutrition and psychologic counselling, and occupational or activities of daily living adjustments were integral in

the program. A home exercise program and the use of a diary of activities and an action plan for exacerbations were emphasized.

2.3. Outcome Measurements

Resting Lung Function: Post-bronchodilator FEV1, FVC, and FEV1/FVC were measured before and after completion of the PRP with the best of three efforts selected for each parameter. The Microlab spirometer was used.

Exercise capacity as measured by the 6-Minute Walk Test: The distance the patient was able to walk in 6 minutes was determined in a measured corridor while the patient was instructed to walk at his fastest pace and longest possible distance under direct supervision of the investigator. This was performed before and after completion of PRP.

Dyspnea and Health Related Quality of Life: St. George's Respiratory Questionnaire is a self-administered Health Related Quality of Life measure containing 50 items and 76 weighted responses divided into the three domains of symptoms, activity, and impacts. SGRQ is a valid measure for bronchiectasis in that it can distinguish between different levels of impaired health and appears to be sensitive to spontaneous changes in health over a 6-month period [15] [16] [17]. The SGRQ was administered before and after undergoing the PRP.

2.4. Statistical Analysis

The relevant features of the patients were reported in percentages. The lung function test values were reported as percent of predicted for the normal Filipino population while the SGRQ scores and 6 MWT values were in their actual unit measures.

The paired t-test was utilized to evaluate the effect of PRP before and after its administration for the different outcome measures established in this study. A p value of <0.05 was considered to be significant.

3. Results

A total of fourteen patients, six males and eight females, age ranged from 28 - 72 years old, were included in the study (**Table 1**). Consent was given by all the patients. They all underwent the pulmonary rehabilitation program and completed eight sessions. There were four ex-smokers and ten non-smokers. Ninety-three percent of the patients had significant occupational exposure to dust or chemicals. Concomitant chronic respiratory illnesses were noted of which four had COPD and five had bronchial asthma. Sixty-four percent among the patients had an inhaled corticosteroid-containing treatment while 71% were given an inhaled bronchodilator. Twenty-eight percent of the patients were not on any form of inhaled medication.

Baseline means lung function of the patients showed a post-bronchodilator moderate degree of airflow obstruction that would qualify also these patients under the definition of COPD. The mean baseline 6 MWT test value of 355.5 ± 94.9

Table 1. Baseline characteristics of the study subjects with Post-TB bronchiectasis.

Feature	No. of subjects (% from total of 14 subjects)
Gender:	
Male	6 (43%)
Female	8 (57%)
Age, range (years)	28 - 72 years
Previous smoking history	4 (28%)
COPD, doctor-diagnosed	4 (28.6%)
Asthma, doctor-diagnosed	1 (35.7%)
Current occupation:	
Mechanic, driver	2 (14.2%)
Beautician, domestic worker	2 (14.2%)
Factory worker	7 (50%)
Farmer	1 (7.14%)
Office worker	1 (7.14%)
None	1 (7.14%)
Number of patients currently on pharmacologic regimen:	
Inhaled corticosteroid-long-acting beta-2 agonist combination (ICS-LABA)	8 (57.1%)
Inhaled short-acting beta-2agonist-anti-muscarinic combination (SABA-SAMA)	1 (7.14%)
Combination ICS-LABA and LAMA	1 (7.14%)
None	4 (28.6%)

meters is lower than reference values utilized in other studies, reflecting an impairment of exercise capacity (**Table 2**). The baseline means SGRQ score of the patients was 39.0 ± 18.8 units which reflect a generally poor quality of life if the threshold 25 units and above is also adopted for bronchiectasis, similar to COPD [17]. All the domains of symptoms, activity and impacts ranked low for the patients in the study (**Table 3**).

Upon comparing the baseline and post rehabilitation values of the patients, there was a statistically significant improvement in the exercise capacity using the 6 MWT (p value = 0.0001) and in the quality of life of the patients, based on the SGRQ score (p value = 0.008) (**Table 2** and **Table 3** and **Figure 1**). The mean improvement of 114.6 meters in the 6 MWT after the 4 weeks of PRP is a substantial improvement above the minimal clinically important difference (MCID)

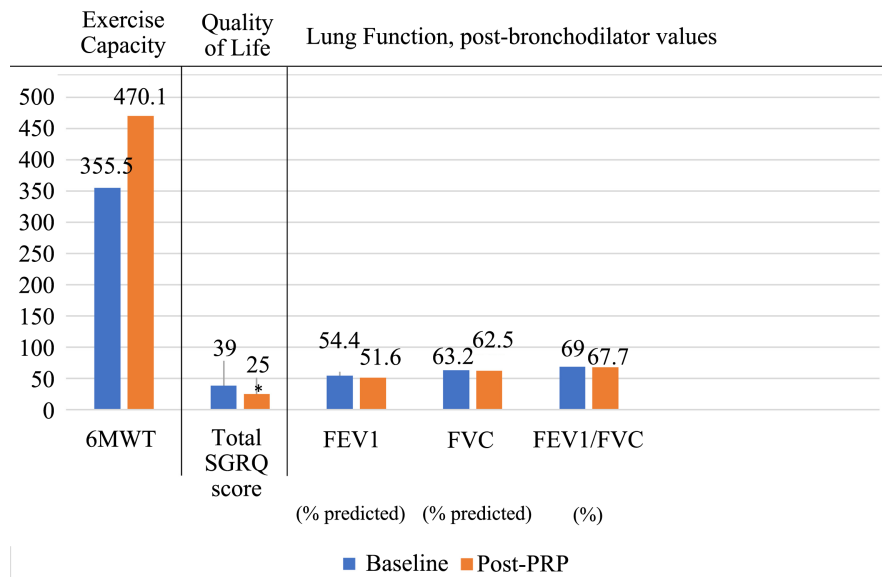


Figure 1. Summary of outcome parameters of study subjects before and after 4-week pulmonary rehabilitation, (n = 14 post-TB Bronchiectasis patients). *p < 0.05: statistically significant difference and above minimal clinically important difference. 6 MWT: 6-minute walk test; SGRQ: St. George Respiratory Disease Questionnaire; FEV1: Forced expiratory volume at 1 second; FVC: Forced vital capacity.

Table 2. Lung function test post-bronchodilator and exercise capacity results of study patients at baseline and after a 4-week Pulmonary Rehabilitation Program (PRP), (n = 14 post-TB Bronchiectasis patients).

Lung Function Test & Exercise Capacity Parameter	Mean	Standard deviation	Median	Range	p-value
FEV1 (% predicted)					0.14
Baseline	54.4	24.0	51.0	22 - 91	
Post-PRP	51.6	21.9	51.5	22 - 91	
FVC (% predicted)					0.64
Baseline	63.2	19.7	60	28 - 95	
Post-PRP	62.5	18.4	62.5	27 - 90	
FEV1/FVC (post-bronchodilator %)					0.50
Baseline	69.0	15.2	68.5	42 - 88	
Post-PRP	67.7	15.3	72.0	41 - 88	
Exercise Capacity by the 6 MWT (6 MWT (meters))					0.0001*
Baseline	355.5	94.9	358.5	147.6 - 482.5	
Post-PRP	470.1	76.9	462.3	348.9 - 645.3	

*p value < 0.05 is considered as statistically significant. FEV1: Forced expiratory volume at 1 second; FVC: Forced vital capacity; 6 MWT: 6-Minute walk test.

Table 3. Quality of life or the St. George's Respiratory Questionnaire (SGRQ) Scores of study subjects at baseline and after 4 weeks of pulmonary rehabilitation program, (n = 14 post-TB Bronchiectasis patients).

Quality of Life based on SGRQ Score	SGRQ Scores, unit		p-value
	Mean (Standard Deviation)		
	Baseline	Post-rehab	
Domain: Symptoms	40.7 (25.9)	26.6 (21.7)	0.04*
Domain: Activity	46.7 (16.4)	36.9 (19.9)	0.03*
Domain: Impact	34.1 (22.4)	17.8 (10.7)	0.007*
Total Score	39.0 (18.8)	25.0 (12.6)	0.008*

*p value < 0.05 is considered as statistically significant. SGRQ: Saint George Respiratory Disease Questionnaire.

of 70 meters established for patients with chronic lung diseases [18]. The decrease in the SGRQ score among the subjects by 14 units after PRP is also above the MCID of 4 units identified for patients with chronic lung diseases [19]. This significant improvement in quality of life was consistent among the three domains of symptoms, activity and impacts.

After 4 weeks of the PRP, the lung function of the patients did not significantly change based on the FEV1 (p = 0.14), FVC (p = 0.64), and FEV1/FVC (p = 0.50) values (Table 2 and Figure 1).

4. Discussion

This study in a low-to-middle-income country with a high burden of tuberculosis, such as the Philippines, shows similar efficacy of pulmonary rehabilitation as other studies among patients with post-tuberculosis bronchiectasis in improving their exercise capacity and quality life [9] [10] [11] [12] [13]. This improvement is well above the established minimal clinically important difference levels [18] [19]. It is notable that all the subjects manifested with a persistently significant airflow obstruction which would place them under the diagnosis of COPD. These patients were also pharmacologically treated by their physicians as having chronic airflow obstruction. This highlights the heterogeneity and overlap of the different pathologies present in post-tuberculosis lung disease (PTLD) that is still currently being investigated as a distinct clinical syndrome [20]. Allwood et al emphasize that the host-pathogen interaction is extremely complex with the extent of eventual lung damage reliant on the processes of granuloma formation and recovery, the interplay of the T and B lymphocytes, cytokines, tumor necrosis factor alpha, interleukins and matrix metalloproteinases and the genetic predisposition to incur such lung pathologic sequelae [20]. Tuberculosis as a risk factor for the development of COPD is acknowledged and this was similarly observed in the Philippine Burden of Lung Disease (BOLD) study with the history of TB increasing the odds ratio of having the diagnosis of COPD at 6.31 (95% confidence interval 2.67% - 15.0%) [21].

In the study of Jones *et al.*, they utilized the additional screening criterion of MRC (Medical Research Council) dyspnea scale 2 or above that would indicate significant dyspnea prior to enrolling the patients with post-TB bronchiectasis for pulmonary rehabilitation [11]. This current study did not limit its enrollment to the PRP to symptomatic patients although the mean symptom SGRQ score of the subject population indicates high symptomatology.

Pulmonary rehabilitation benefits patients with bronchiectasis by improving their exercise capacity though the increase in aerobic capacity of peripheral muscles, improved disease management and quality of life [2] [3]. These mechanisms probably were operational in the improvement seen in this study's subject population. The PRP was shorter and utilized simple interventions that can readily be performed in resource-limited settings but, nevertheless, resulted to the improvement in the pre-determined patient-related outcomes.

The synergy of pharmacologic management of airflow obstruction and non-pharmacologic PRP to improve the exercise capacity and quality of life of COPD patients should similarly be adopted in the management of PTLD [8]. The patients in this study all showed chronic airflow obstruction which majority of the attending physicians recognized and managed pharmacologically as well.

Lung function test values have not been shown to improve with PRP among patients with COPD and bronchiectasis and are not the appropriate outcomes targeted for treatment with PRP [2] [3]. Similarly, the studies on PRP among post-TB bronchiectasis also did not show improvement in lung function test values as also observed in this study.

The standards of care for rehabilitation of PTLD patients established by the consensus panel of The Union's First Symposium are timely in setting the bar for adequate PRP interventions [14]. These standards also provide a unified approach and common language in managing this newly identified and complex syndrome of PTLD. Study results will be easier to interpret with the common standards and identified outcome indicators.

This study had several limitations with a small number of subjects and exacerbations not being accounted for. Severity of bronchiectasis was also not determined. A randomized trial on PRP in PTLD is urgently needed.

5. Conclusion

Pulmonary rehabilitation program led to a significant improvement in exercise capacity and health-related quality of life among patients with post-tuberculosis bronchiectasis when compared to baseline in a low-to-middle-income country setting. Larger and randomized studies are needed to firmly establish the role of pulmonary rehabilitation not only for post-tuberculosis bronchiectasis but for the large number of patients affected by post-tuberculosis lung disease (PTLD) as well.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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