Original Article

Outcome of Pulmonary Rehabilitation in Patients after Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Abstract

Background. Pulmonary rehabilitation (PR) is an evidence-based intervention in patients with chronic obstructive pulmonary disease (COPD) which improves the exercise capacity and quality of life (QoL).

Methods. We studied 60 patients after an episode of acute exacerbation of COPD (AECOPD). They were randomised to receive conventional treatment without pulmonary rehabilitation (CTWPR) (n=30) or, standard treatment plus a 12-week post-exacerbation pulmonary rehabilitation (PEPR) programme in addition. Assessment of exercise capacity by six minute walk test (6MWT) and QoL measured by St George's Respiratory Questionnaire (SGRQ) were carried out initially and at the end of three months.

Results. The baseline characteristics of both the groups were found to be similar. There was a statistically significant increase in the six minute walk distance (6MWD) (increase by 37.9 meters, $p< 0.001$) and a significant decline in the total SGRQ score (by 3.8 units $p< 0.001$) in the PEPR group compared to CTWPR group.

Conclusion. Early pulmonary rehabilitation in patients with an AECOPD has significant benefits on the QoL and exercise capacity. **[Indian J Chest Dis Allied Sci 2014;56:7-12]**

Key words: Pulmonary rehabilitation, COPD, Acute exacerbation, Quality of life.

Introduction

Chronic obstructive pulmonary disease (COPD) is a disease state characterised by progressive airflow limitation that is not fully reversible. COPD affects 6%-10% of the adult population and is a leading cause of morbidity and mortality responsible for 5.1% of all deaths worldwide.[1,2]

COPD is strongly associated with impaired exercise performance and functional capacity. As the airflow obstruction progresses, COPD patients typically become increasingly sedentary, leading to muscular and cardiovascular deconditioning. The exercise capacity, quality of life (QoL) and participation in activities of daily living are often impaired out of proportion to the lung function impairment.[3-5] Increasing physical disability contributes to social isolation and depression, which are highly prevalent in patients with severe COPD.[6] Exercise limitation has been traditionally explained by the increased work of breathing and dynamic hyperinflation that results from the airflow limitation. The skeletal muscle dysfunction (SMD) is a major contributor to the exercise limitation.[7] Corticosteroids used in the treatment of COPD are known to add to the myopathy.[8] Pulmonary rehabilitation (PR) aims at strengthening essential muscle groups, improving overall oxygen utilisation and enhancing body's cardiovascular response to physical activity.

Acute exacerbation of COPD (AECOPD) is defined as "an event in the natural course of the disease characterised by a change in the patient's baseline dyspnoea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD".[9] Exacerbations are the most common cause of hospitalisation among COPD patients. The methods of reducing exacerbations have been the focus of numerous pharmacological[3,9,10] and non-pharmacological interventional trials.[11-13] Patients' knowledge about the disease and recognition of early signs of an exacerbation are important to achieve this target. PR aims at teaching the patient about his disease state with due stress to areas like energy conservation techniques, managing activities of daily living with little dyspnoea provocation and planning complex activities to minimise distress associated.

PR is a multi-disciplinary programme of care for patients with chronic respiratory impairment that is individually tailored and designed to optimise physical and social performance and autonomy. The primary goal of PR is to reverse muscular and cardiovascular

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dysfunction. It improves patients' exercise capacity, reduces dyspnoea, improves the QoL, and reduces the number and duration of hospitalisations related to respiratory disease.[11]

Limited data are available in the literature on the role of early PR following an acute exacerbation in COPD patients. After hospitalisation for an acute exacerbation, patients typically remain inactive for several weeks. Quadriceps muscle strength commonly falls during exacerbation and may further deteriorate due to inactivity. Early rehabilitation may help in improving muscle power and retards the muscle atrophy, prevent re-exacerbation and improve QoL. Little published data are available from India on this topic. The present study was designed to evaluate the benefits of PR on the exercise capacity and QoL in the patients with AECOPD from the North India.

Material and Methods

This was a prospective randomised controlled study conducted in the department of Pulmonary Medicine at Government Medical College Hospital, Chandigarh (GMCH) from September 2010 to September 2012. Consecutive patients who were admitted with an AECOPD and were discharged from the hospital who fulfilled the study criteria were included in the study. Severely ill patients who were unable to walk, or patients with unstable cardiovascular disease (unstable angina or recent acute myocardial infarction), had cognitive impairment, disabling arthritis, and severe neurological disease were excluded from the study.

Study Design

Participants were evaluated and randomised into two groups within two weeks of discharge from the hospital. They were assigned to receive either post-exacerbation pulmonary rehabilitation (PEPR) or conventional treatment without pulmonary rehabilitation (CTWPR). An informed consent was obtained from each patient. Randomisation was done by block randomisation technique.

Diagnosis of COPD

Spirometry was used for diagnosis and staging of COPD as per the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. It was performed using the Pulmonary Function Test (PFT) Machine (Morgan transfer test model, USA). Forced vital capacity (FVC), i.e., maximal volume of air forcibly exhaled from the point of maximal inhalation; forced expiratory volume in the first second (FEV_1), and the ratio of these two measurements (FEV_1/FVC) was evaluated. The presence of a post-bronchodilator FEV_1/FVC less than 70% confirmed the presence of airflow limitation that is not fully reversible. Severity of airflow obstruction was classified according to the GOLD staging into mild (FEV_1 ³ 80% predicted), moderate (50% £ FEV_1 <80% predicted), severe (30% £ FEV_1 <50% predicted) and very severe (FEV_1 <30% predicted, or FEV_1 <50% predicted plus chronic respiratory failure) was done.

Pulmonary Rehabilitation

Components of PEPR consisted of patient assessment, exercise testing, exercise training, education, nutrition and psycho-social rehabilitation.[14] The patients were educated about the disease state, respiratory physiology, drugs used in the treatment, their usage techniques and side effects. Chest physiotherapy was used for drainage of secretions. Breathing retraining techniques, like diaphragmatic and pursed lip breathing, were used for the symptom control and reduction of hyperinflation. Psycho-social support was extended to the patients attending the rehabilitation programme. They were taught about techniques to control dyspnoea using energy conservation techniques. Exercise sessions lasted upto two hours, with adequate rest as required in between. Exercises were a mixture of limb strengthening and aerobic activities, tailored to individual baseline function. In addition, they were educated about the disease, behaviour modification, and interventions to improve social and psychological functioning. During each session, a physiotherapist and a doctor from the Department of Pulmonary Medicine supervised the activities.

Baseline Investigations

Spirometry and measurement of FEV_1, FVC, peak expiratory flow rate (PEFR) and reversibility to bronchodilator was performed according to recommended guidelines following administration of inhaled salbutamol using nebuliser.[15-17] Patients were allowed to use their inhaled long-acting bronchodilator therapy on the day of testing. Measurements were taken before initiation of PR and after three months. Non-attendance within three weeks of the designated follow-up time was deemed failure to attend. Arterial blood samples were obtained for measurement of arterial oxygen tension and arterial carbon dioxide tension.

The level of dyspnoea was assessed using the modified Medical Research Council (mMRC) Breathlessness Scale.[18] It consists of five statements describing the range of respiratory impairment in each patient.

Six Minute Walk Test

The six minute walk test (6MWT) is a simple test used to measure the functional capacity of patients with respiratory disorders. The test measures the distance (6MWD; metres) that a patient can quickly walk on a flat hard surface in a period of six minutes.[19] Each patient was explained about the procedure prior to the test. The test was performed on a hospital hallway measuring 100 feet in length. The turnaround points were marked with cones. The patient was seated at the

test site 10 minutes before commencement. Baseline measurements of pulse, blood pressure, oxygen saturation was done during this time period. The phrases of encouragement used during the test were according to the American Thoracic Society (ATS) guidelines. Patients in need of supplemental oxygen were provided with it during the test. The distance covered was recorded at the end of the test.

Health-related QoL (HRQoL) of the patient was assessed using the St. George's Respiratory Questionnaire (SGRQ) version- 2.3. The responses to its 50 items were aggregated into an overall score and three subscores for symptoms, activity, and impact. A change of four units or more was accepted as significant.[20]

Statistical Analysis

Discrete categorical data are presented as number (%); continuous data are presented as mean ± standard deviation (SD) and median. Normality of quantitative data was checked by means of Kolmogorov Smirnov test. Mann-Whitney U-test was used for statistical analysis of skewed continuous variables. All statistical tests were two-tailed; a p-value less than 0.05 was considered significant. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) for Windows (version 15.0; SPSS Inc., Chicago, IL, USA).

Results

We enrolled 60 patients and randomised them to PEPR (mean age 58.4±6.8 years; 28 males) and CTWPR (mean age 59.4±6.7 years; 28 males) groups. The case and control groups had a 43.1 and 33.9 mean pack years of smoking, respectively. According to the above data the stages of COPD in both the groups were found to be similar and comparable statistically.

The mean FEV_1% in the case and control group was 53.3±18.4 and 46.7±14.8, respectively. The mMRC Breathlessness Scale in the two groups during the initial assessment was found to be similar (Tables 1 and 2). The mMRC status was compared within the groups at baseline and at three months. The PEPR group showed a significant improvement with regard to the mMRC at the end of study (p=0.013) while the CTWPR group showed no significant change (p=0.102).

Six Minute Walk Distance

The six minute walking distance by stage of disease in PEPR and CTWPR groups is shown in tables 3 and 4.

Table 1. mMRC breathlessness scale status by stage (PEPR group)

	Stage I		Stage II		Stage III		Stage IV	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Number	3	2	12	12	13	12	2	2
mMRC	1.33±0.57	1.50±0.70	2.08±1	1.92±1	2.15±0.98	1.75±0.96	3.0±1.41	3.0±1.41

Definitions of abbreviations: mMRC=Modified Medical Research Council Breathlessness Scale; PEPR=Post-exacerbation pulmonary rehabilitation

Table 2. mMRC breathlessness scale status by stage (CTWPR group)

	Stage I		Stage II		Stage III		Stage IV	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Number	1	1	1	2	14	13	3	3
mMRC	1±1	2±2	1.58±0.66	1.82±0.60	1.93±1.14	1.92±1.15	2.67±0.57	3.0±1.0

Definitions of abbreviations: mMRC=Modified Medical Research Council Breathlessness Scale; CTWPR=Conventional treatment without pulmonary rehabilitation

Table 3. 6MWD by stage of disease (PEPR group)

	Stage I		Stage II		Stage III		Stage IV	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Number	3	2	12	12	13	12	2	2
6MWD (metres)	397.9±72.45	425.2±62.5	328.60±85.58	364.14±77.23	289.63±84.92	324.05±75.37	228.61±64.67	210.37±101.27

Definitions of abbreviations: 6MWD=Six minute walking distance; PEPR=Post-exacerbation pulmonary rehabilitation (PEPR)

Table 4. 6MWD by stage of disease (CTWPR group)

	Stage I		Stage II		Stage III		Stage IV	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Number	1	1	12	11	14	13	3	3
6MWD (metres)	410.00±0	323.09±0	327.73±54.69	301.55±55.26	264.64±108.60	248.26±113.36	197.72±65.79	137.49±90.82

Definitions of abbreviations: 6MWD=Six minute walking distance; CTWPR=Conventional treatment without pulmonary rehabilitation

The mean 6MWD in the PEPR group during the initial evaluation was 303.05±84.49 metres; however at the end of three months it significantly improved to 340.34±86.16 metres (p< 0.001). The results also showed an increase of 6MWD above the minimum clinically important difference (MCID) among the 32.1% of the cases who underwent PR programme (Table 5).

The mean 6MWT in the CTWPR group during the baseline evaluation was found to be 288.0± 94.8, however at the end of three months the value decreased to 260.0±100.2 and the change was statistically significant (p <0.001) (Table 6). The above values showed a significant improvement in the PEPR group with regard to their 6MWT after the three-month of rehabilitation programme in comparison to the CTWPR group.

Table 5. Proportion of patients showing more than minimum clinically important difference for 6MWD

Change (metres)	Variable	PEPR Group	CTWPR Group
<54	Number	19	28
	% within group	67.9	100
>54	Number	9	0
	% within group	32.1	0

Definitions of abbreviations: 6MWD=Six minute walking distance; PEPR=Post-exacerbation pulmonary rehabilitation; CTWPR= Conventional treatment without pulmonary rehabilitation

The statistical analysis revealed that the groups were similar initially. No statistically significant difference was present between two groups before starting the study (p=0.372). The mean SGRQ (total) in the PEPR group at the baseline evaluation was 53.73±12.86; however, at the end of three months the value was 39.04±12.91 (Table 7). The reduction in the value observed was statistically significant (p<0.001). The mean SGRQ in the CTWPR group during the baseline evaluation was 57.27±18.54; however, at the end of three months, the value was 62.64±18.74. The change observed was also found to be significant (p=0.002) (Tables 8 and 9). The total SGRQ score revealed a significant reduction in the PEPR group when compared to the CTWPR group. There was a significant improvement in the QoL in PEPR group when compared to the CTWPR group. The SGRQ change of more than MCID was seen among 82.1% of the PEPR group who underwent the PR programme (Table 10).

Discussion

We assessed the feasibility and safety of an early pulmonary rehabilitation programme for outpatients and determined its effects on exercise capacity and QoL as compared with conventional treatment. In patients in the PEPR group, at the end of three months,

Table 6. The 6MWT at baseline and at the end of three months

Variable	PEPR Group		CTWPR Group	
	Pre	Post	Pre	Post
Number	28	28	28	28
6MWD	303.05±84.49	340.45±86.16	288.26±96.14	260.00±100.19
p-value	<0.001		<0.001	

Definitions of abbreviations: 6MWD=Six minute walking distance; PEPR=Post-exacerbation pulmonary rehabilitation (PEPR); CTWPR=Conventional treatment without pulmonary rehabilitation

Table 7. Comparisons of St George's Respiratory Questionnaire scores

St. George's Respiratory Questionnaire	Cases		Controls	
	Pre	Post	Pre	Post
Symptom	61.99±14.0	51.51±15.28	56.70±16.75	59.16±16.34
Activity	72.80±16.58	56.15±15.75	69.24±20.78	74.47±23.67
Impact	40.25±14.34	25.36±13.67	50.61±21.84	56.97±21.16
Total	**53.73±12.86**	**39.04±12.91**	**57.27±18.54**	**62.64±18.74**

Table 8. St. George's Respiratory Questionnaire (SGRQ) score by stage of disease (PEPR group)

	Stage I		Stage II		Stage III		Stage IV	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Number	3	2	12	12	13	12	2	2
SGRQ	29.93±13.7	14.16±8.59	55.77±7.7	39.12±9.1	55.92±10.42	41.28±11.44	59.07±3.24	63.26±18.93

Table 9. St. George's Respiratory Questionnaire (SGRQ) score by stage of disease (CTWPR group)

	Stage I		Stage II		Stage III		Stage IV	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Number	1	1	1	2	14	13	3	3
SGRQ	67.26±0	56.78±0	50.09±19.04	56.08±19.66	60.33±19.37	66.4±18.74	67.45±5.11	72.98±10.07

Table 10. Proportion of patients showing minimal clinically important difference for St. George's Respiratory Questionnaire (SGRQ) score

SGRQ Value Change		PEPR Group	CTWPR Group
Decrease < 4 points	Number	5	27
	% within group	17.9	96.4
Decrease > 4 points	Number	23	1
	% within group	82.1	3.6

Definitions of abbreviations: 6MWD=Six minute walking distance; PEPR=Post-exacerbation pulmonary rehabilitation; CTWPR= Conventional treatment without pulmonary rehabilitation

there was a significant improvement in the 6MWD and a significant reduction in SGRQ score as compared to the baseline values. However, the CTWPR group had a significantly higher SGRQ score at the end of the study when compared to the baseline value, indicating an improved QoL was evident only in the patients who underwent the rehabilitation programme (PEPR group). The dyspnoea as evaluated by the mMRC scale had improved significantly in the patients who underwent the rehabilitation programme (PEPR group) at the end of three months.

In the present study, early pulmonary rehabilitation was done in patients with COPD after discharge from hospital following an acute exacerbation. One study[21] looked at the effects of an initial 10 days inpatient training programme, followed by six months of supervised home training, compared with usual care. In another study[22] assessing the effects of community based PR after an exacerbation of COPD revealed benefits with respect to the QoL and exercise capacity. In the present study, we found that though patients were more receptive to the concept of rehabilitation, they had difficulties in initiation of the exercise therapy.

The minimal clinically important change of 6MWD has been estimated to be 54 meters.[23] In the present study, we found that the mean 6MWD in the patients who underwent PR at the three months evaluation increased by 37.29 meters. This improvement though less than the clinically significant value was still found to be statistically significant. Our study results showed an increase of more than 54 meters on the 6MWD in 32.1% of the subjects who underwent PR programme. Exercise capacity in the patients with COPD post-PR was analysed by another study that found an increase of at least 54 meters in the 6MWD in 64% of the patients who underwent PR.[24] Another study[25] conducted to evaluate the benefits of outpatient PR in COPD patients revealed that the 6MWD increased more than 54 meters in the group which underwent PR.

A critical review and meta-analysis on the long-term effects of pulmonary rehabilitation in patients with asthma and COPD detected a significant improvement in the 6MWD after PR, corresponding to a mean value of 49 meters.[26] In a more recent Cochrane systematic review,[27] which included 16 trials, a similar but not significant increase of 48 meters was found. In both the cases the values were below the threshold of clinical significance. These support our findings of significant increase in the 6MWD in the patients of the PEPR group.

The improvement in the 6MWD in the study group could be due to reconditioning and retraining of the respiratory and skeletal muscle groups. Recent studies have shown that training can raise the anaerobic threshold of the musculature in these patients.[28] It lowers their ventilatory requirement and blood lactate levels leading to better functional capacity.[29] However, aerobic physical conditioning does not modify lung function.[7,30] Thus, we presume that these mechanisms may hold true in this study.

We assessed the effects of PR on the QoL of these patients at baseline and at three months. Barakat *et al*[25] evaluated the effects of outpatient PR in patients with COPD and SGRQ was assessed in the patients at baseline and at the end of 14 weeks. The results found were comparable with that of the present study. Griffiths *et al*[11] conducted a randomised controlled trial to assess the effects of PR programme in a group of patients with COPD. SGRQ values were monitored at six weeks intervals and found similar results. Cambach *et al*[26] analysed the effects of community-based PR programme on exercise tolerance and QoL using a randomised controlled crossover design. The study results found a significant improvement in QoL and the benefits were maintained over six months. Ergun *et al*[31] demonstrated positive outcomes of the comprehensive PR programme at all stages of the disease. In our study, similar benefits with respect to mMRC were observed.

The present study has found a significant benefit in the exercise capacity, QoL and dyspnoea scores in patients with COPD treated with PR in addition to the conventional management consisting of drug therapy.

The present study, however, has certain limitations. First, it was a single centre study. Secondly, the small sample size might not allow us to estimate the treatment effect very precisely. Thirdly, the results would have been more precise if the study could guide us regarding which stage of COPD benefitted maximally from the PR programme.

If rehabilitation is effective in both stable COPD and after exacerbations, then question arises, at what point in time should patients be referred for PR programme? An advantage of rehabilitation in patients soon after an exacerbation is that it provides a window of opportunity for patient education because patients may be more willing to change their health behaviour after recovery. Also, continuity of care is possible if patients are referred to PR at the earliest. The large improvements in exercise capacity indicate that it is superior compared with usual care alone in terms of prognosis and health-related QoL. Hence, the study results emphasise the importance of early PR in patients of COPD in the Indian set-up.

Conclusions

We conclude that pulmonary rehabilitation in patients with COPD after an acute exacerbation has significant benefits in their quality of life and exercise capacity. Pulmonary rehabilitation may be included in the standard management of patients with COPD and soon after recovery from an episode of acute exacerbation.

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