Original Article

The Effect of a Short-Term Pulmonary Rehabilitation on Exercise Capacity and Quality of Life in Patients Hospitalised with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Abstract

Background. Recent research shows that pulmonary rehabilitation (PR) programmes in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), reduced dyspnoea, improved exercise capacity, and prevented occurrence of further exacerbations.

Objective. To evaluate the utility of a 3-week PR programme in patients with AECOPD.

Methods. Patients admitted with AECOPD, following clinical stabilisation in the respiratroy intensive care unit (RICU), were alternately assigned to intervention (n=15); and control groups (n=15), respectively. Baseline assessment included spirometry, six-minute walk test (6MWT), symptom limited cardiopulmonary exercise test (CPET), health-related quality of life (HRQoL) assessment by generic questionnaire medical outcomes study short form (S-F 36) questionnaire and dyspnoea evaluation by Borg score. The intervention group patients were treated with usual care plus PR exercises in the form of 20 minutes each of walking, bicycle ergometry and resistance exercises, thrice-weekly for three weeks. The control group patients were treated with only the usual care. After discharge from hospital the treatment regimens were continued on alternate days on outpatient basis, for a total of three weeks. The assessment was repeated in both the groups after three weeks.

Results. Nine sessions of PR exercises produced statistically significant improvement in general well-being, forced expiratory volume in the first second (FEV_1), 6MWT parameters, exercise capacity, peak oxygen uptake and volume of oxygen consumption (VO_2)/Watts slope on CPET in patients with AECOPD.

Conclusion. Short duration PR programmes appear to be helpful in the management of AECOPD.

[Indian J Chest Dis Allied Sci 2014;56:13-19]

Key words: Pulmonary rehabilitation, COPD, Cardiopulmonary exercise test, 6MWT.

Introduction

Chronic obstructive pulmonary disease (COPD) is an inflammatory disease of lungs and pulmonary vessels, with destruction of alveolar septa and enlargement of air-spaces, characterised by progressive airflow limitation which is not fully reversible. There are persistent symptoms of cough, expectoration, wheezing and progressive dyspnoea, which is further accentuated by static and dynamic hyperinflation of lungs. As the disease advances, ventilation/perfusion mismatch results in hypoxaemia, respiratory acidosis, pulmonary hypertension and heart failure, culminating in death.[1,2]

COPD is also complicated by profound systemic effects.[3-5] High levels of circulating proinflammatory cytokines produce a chronic catabolic state in 20%-40% patients, resulting in weight loss, skeletal muscle wasting and chronic fatigue; a low body mass index (BMI; Kg/m^2) is an independent predictor of mortality. Deconditioning and weakness of respiratory muscles adversely affect pulmonary disability and promote respiratory failure.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) Report 2011[6] over-rides its 2006 Report[1] in some important aspects. The staging of severity of COPD on the basis of forced expiratory volume in the first second (FEV_1) is replaced by grading of disease based upon symptom burden, activity limitation, risk of exacerbations, co-morbidities and health-related quality of life (HRQoL) including social isolation and depression. The FEV_1 alone is no longer considered a reliable marker of the severity of the disease.[6]

During the clinical course of COPD, 2-3 acute exacerbations per year are known to occur. These are often precipitated by upper and/or lower respiratory tract infections, exposure to environmental pollution and in one-third of the cases no cause is apparent. Each exacerbation may leave the patient with worsening of symptoms and greater vulnerability to further exacerbations and development of respiratory failure and pulmonary hypertension.[7-10] Long-term follow-up studies show that in-hospital mortality in

[Received: April 17, 2013; accepted after revision: November 11, 2013]

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COPD patients with type 2 respiratory failure is approximately 10%; reaches 40% in mechanically ventilated patients at one year after discharge and 49% from all causes at three years.[11-13]

An official statement from the American Thoracic Society (ATS) in 1999,[14] further reinforced by ATS/European Respiratory Society (ERS),[15] advocated pulmonary rehabilitation (PR) as 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". All COPD patients, including those after acute exacerbations, appear to benefit from PR programmes with significant improvement in exercise tolerance and relief from dyspnoea and fatigue (Evidence level A).[16] The available data from several studies suggest that improved physical endurance occurs even after a single PR programme,[17-19] if exercise training is maintained at home. Early institution of PR programmes in patients hospitalised with acute exacerbation was found to be feasible, effective and safe.[20] The present study was undertaken to evaluate the results of a short-term PR programme on the exercise capacity and quality of life (QoL) in COPD patients hospitalised with acute exacerbations.

Material and Methods

The present study was carried out at the Metro Centre for Respiratory Diseases of the Metro Group of Hospitals, NOIDA. As per the guidelines of the Indian Council of Medical Research on Biomedical Research on Humans[21] as well as the mandatory practice of the hospital, the patient or his/her legal guardian was explained the purpose and procedures to be used in the study. Informed consent was also taken in writing.

All COPD patients admitted with an acute exacerbation in the respiratory intensive care unit (RICU) were given usual treatment as per the standard protocol,[1] including conventional chest physiotherapy with postural drainage, huffing and coughing, diaphragmatic breathing, and inhaled bronchodilators. An acute exacerbation meant an event resulting in increase in the patients' symptoms of cough, sputum and breathlessness which was beyond the normal day to day variations, was acute in onset and warranted a change in the routine treatment of COPD.[6] As the patients improved, they were alternately assigned to intervention group (n=15) and control group (n=15), respectively. The inclusion criteria consisted of: COPD – GOLD stage II to IV[1]; either gender; age 40 – 70 years; currently non-smoker; no history of atopy and a firm commitment to co-operate through the study period. Patients with evidence of persistent sepsis, haemoglobin less than 10 g/dL, heart or renal failure, tuberculosis or lung cancer were excluded.

All patients were assessed within 24 hours of clinical stabilisation. Relevant findings of in-depth clinical history and thorough physical examination were recorded. Laboratory investigations included, chest radiograph, routine tests and arterial blood gas analysis. Special investigations included: spirometry with Morgan Spiro – 232 as per the ATS guidelines[22]; assessment of functional exercise capacity by six minute walk test (6MWT)[23] and maximal exercise capacity by symptom limited cardio-pulmonary exercise testing (CPET);[24] HRQoL by generic questionnaire medical outcomes study short form (SF-36)[25] and dyspnoea assessment on modified Borg scale.[26]

Symptom limited CPET was performed as per ATS guidelines,[24] on an electronically braked cycle ergometer (ERGOSELECT 200P/200K; Ergoselect, Germany) with seat adjusted to avoid maximal extension of knee during biking. Incremental exercise protocol was used with 3-minute resting, followed by 3-minute warm up phase at 0-Watt and increased by 10 Watts in 60 seconds during the exercise phase until the patient reached volitional exhaustion, followed by three minutes of recovery phase. The patient was constantly exhorted to maintain a pedalling frequency of 60 rpm monitored by digital display.

Pulmonary Rehabilitation Programme for Intervention Group

PR programme consisted of self management education specifically related to COPD[27] and three different types of exercises: (i) walking; (ii) biking; and (iii) resistance exercises. Adequate break periods were allowed before and after each of the three modes of exercises.[28] The intervention group patients were administered nine sessions (three sessions per week for three weeks). The 20-minute walk consisted of 5 minutes walking followed by 2 minutes rest to begin with; the rest interval was reduced till the patient could complete 20 minutes walk without interruption.

Short-term intensive training programmes have been shown to be effective. Our short-term PR programmes was aimed at achieving maximal physiologic training effects in nine sessions. Hence, this was modified for interval training at an intensity of 75% of maximum work load achieved during the symptom terminated baseline CPET. This was well tolerated by the patients and was used throughout the study. The patient performed resistance exercises[28] for 20 minutes thrice weekly for three weeks. These consisted of dynamic strengthening of abductors, flexors, elevators and depressor muscles of shoulders, against the load of hand-held dumbbells. The quadriceps muscle strengthening was performed with weight cuffs. 1-Repetition maximum (1-RM) was calculated by Brzychi equation for strength training.[29] The patient started at 70% of initial one repetition maximum in the first week (3 x 8 repetitions). Every week the load was increased by 5% of the 1RM. The same progression pattern was used gradually for all muscle groups.

Usual Care for Control Group

Three to four days after starting the programme, patients in both the groups were discharged from the hospital. They continued with the usual care at home for further three weeks. The intervention group patients reported to the hospital every alternate day to perform PR exercises to complete the prescribed period of three weeks. The control group patients were not administered PR exercises. They were simply given the usual care and kept under observation on outpatient basis. Patients were again assessed at three weeks as at the baseline and underwent clinical evaluation, spirometry, 6MWT, CPET, QoL and modified Borg dyspnoea score.

Statistical Analysis

The participants were assessed at baseline, within 24 hours of stabilisation from acute exacerbation and then at end of three weeks of PR programme. The variables considered for statistical analysis included modified Borg score (for assessment of dyspnoea); functional exercise capacity by six minute walk distance (6MWD); CPET to evaluate maximal exercise capacity; spirometry test values and SF – 36 questionnaires for HRQoL. Variables were compared between the intervention and the control groups, using Mann-Whitney U-test. Within group analysis was done using Wilcoxon Signed Rank test. The tests were applied at 95% confidence interval and alpha values set at 0.05; p-value <0.05 was considered statistically significant. Analysis was carried out by using the Statistical Package for the Social Sciences (SPSS) for Windows (release 16: SPSS: Chicago, IL, USA).

Results

The distribution of mean values for age and BMI in the two groups did not show any statistically significant difference (Table 1). Male to female ratios in the intervention and control groups were 11: 4 and 13: 2, respectively. The severity of COPD based on staging in the intervention and control groups were: Stage II – 5/6; stage III – 7/4 and stage IV – 3/5, respectively. Baseline values of spirometry, arterial oxygen tension (PaO_2), arterial carbon dioxide tension ($PaCO_2$) and bicarbonate in the two groups were similar; baseline values of arterial blood pH were statistically significantly higher in the control group than the intervention group patients (Table 2).

After three weeks of PR, the intervention group patients showed a small but statistically significant improvement in FEV_1, FEV_1 (% predicted) and FEV_1/FVC (%). In the control group, on the other hand, after three weeks of usual care, there was a reduction, though statistically not significant, in these parameters. The change in FEV_1 (% predicted) between baseline and three weeks PR in the intervention group was statistically significant when compared with the change in the control group. The change in other parameters in the two groups were statistically not significant (Table 2).

Table 1. Physical characteristics and severity of COPD data in intervention group and control group patients

Parameter	Intervention Group (n=15)	Control Group (n=15)	p-value
Age (years)	63.4±7.31	63.8±9.16	0.201
BMI (kg/m^2)	22.87±5.81	22.09±5.37	0.705
ABG on admission	N=11	N=12	
PaO_2	73.53±25.12	83.47±22.4	0.814
$PaCO_2$	40.68±7.89	41.11±12.1	0.72
pH	7.414±0.046	7.450±0.03	0.051
$HCO3^-$	25.93±6.82	27.34±6.83	0.53

Data are presented as mean ± standard deviation
Definitions of abbreviations: ABG=Arterial blood gas; PaO_2=Arterial oxygen tension; $PaCO_2$=Arterial carbon dioxide tension; HCO_3^-=Bicarbonate; COPD=Chronic obstructive pulmonary disease

Administration of PR programme in COPD with acute exacerbations significantly improved exercise capacity (Table 3). Baseline values of 6MWD, pulsatile oxygen saturation (SpO_2), lowest SpO_2, end SpO_2 and dyspnoea – Borg scale in the intervention and control group patients did not show any statistically significant difference (data not shown). After three weeks of PR exercises, there was a significant improvement in 6MWD (p=0.0001) and SpO_2 (p = 0.04) in the intervention group patients. By contrast, three weeks of usual care alone in the control group patients produced only a small improvement which was statistically not significant (Table 3). The mean change between baseline and 3-week PR in 6MWD in the intervention group was significantly better than control group patients. The 6MWT produced considerable arterial desaturation in both study group patients but with no statistically significant difference between them (Table 3). Dyspnoea (Borg score) in both the groups did not show any significant change. Mean delta changes in SpO_2, lowest SpO_2 and end SpO_2 in the two groups were not found statistically significant.

At baseline testing, CPET parameters in both the intervention and control group patients (Table 4) did not show any statistically significant difference. Repeat CPET at three weeks (Table 4) showed statistically significant improvement in all CPET parameters except anaerobic threshold (AT), heart rate and ventilatory equivalents for oxygen and carbon dioxide in intervention group. The findings indicate improved cardiovascular function as well as exercise capacity which can be attributed to PR programme. In the control group patients who received only the usual care for three weeks, on the other hand, none of the CPET parameters, except breathing reserve showed any

Table 2. Spirometry data in intervention and control group patients

Parameter	Intervention Group (n=15)			Control Group (n=15)			Change Between Pre- and Post-Values		
	Baseline (pre)	3-week (post)	p-value	Baseline (pre)	3-week (post)	p-value	Intervention Group	Control Group	p-value
FVC (L)	2.40±0.63	2.49±0.59	0.24	2.25±0.64	2.27±0.64	0.68	0.057±0.142	0.025±0.136	0.467
% Predicted	74.6±12.7	78.1±18.9	0.36	65.6±16.4	64.8±16.1	0.74	0.055±0.198	0.001±0.156	0.419
FEV_1(L)	1.36±0.58	1.45±0.56	0.02	1.18±0.47	1.16±0.53	0.781	0.081±0.122	- 0.010±19.5	0.221
% Predicted	46.3±20.8	51.5±27.9	0.04	44.64±17.7	40.8±14.8	0.10	0.100±0.16	-0.597±0.15	0.014
FEV_1/FVC%	53.37±15.53	57.51±16.7	0.04	53.1±12.8	50.36±13.59	0.256*	0.031±0.12	-0.30±0.17	0.250

Definitions of abbreviations: FVC=Forced vital capacity; FEV_1=Forced expiratory volume in the first second

Table 3. Six minute walk test (6MWT) and dyspnoea Borg Scale data in intervention and control group patients

Parameter	Intervention Group (n=15)			Control Group (n=15)			Change Between Pre- and Post-Values		
	Baseline (pre)	3-week (post)	p-value	Baseline (pre)	3-week (post)	p-value	Intervention Group	Control Group	p-value
6MWD (m)	291.1±124.9	363.5±85.6	0.0001	325.3±89.2	332.1±104.4	0.706	0.543±0.95	0.027±0.21	0.013
SpO_2 (%)	95.73±2.18	96.47±1.99	0.04	96.67±1.64	96.13±2.44	0.660	0.008±0.01	0.003±0.029	0.18
Lowest SpO_2	83.0±11.18	85.67±7.17	0.35	85.13±8.49	87.47±9.48	0.299	0.05±0.16	0.032±0.011	0.85
End SpO_2	88.33±9.75	90.4±7.78	0.25	89.47±6.64	90.53±10.24	0.528	0.03±0.09	0.01±0.08	0.92
Dyspnoea Borg scale	3.33±1.87	2.87±1.72	0.39	3.67±1.80	2.93±1.62	0.119	0.06±0.74	0.04±1.17	0.55

Definitions of abbreviations: 6MWD=Distance walked in six minutes; SpO_2 =Pulsatile oxygen saturation

Table 4. Cardio-pulmonary exercise test (CPET) data in intervention (pulmonary rehabilitation) and control group patients with intra- and inter-group comparisons

Parameter	Intervention Group (n=15)			Control Group (n=15)			Change Between Pre- and Post-Values		
	Baseline (pre)	3-week (post)	p-value	Baseline (pre)	3-week (post)	p-value	Intervention Group	Control Group	p-value
Exercise duration (sec)	185.3±82	242.0±65.8	0.014	202.0±99.6	216.0±96.6	0.16	0.478±0.47	0.156±0.58	0.03
Power (Watts)	36.67±14.9	43.33±14.0	0.038	38.0±18.2	40.0±16.48	0.85	0.263±0.32	0.169±0.64	0.20
VO_2 peak (mL/min)	895±302	1073±325	0.022	955±226	956±230	0.88	0.248±0.36	0.028±0.347	0.03
VO_2 peak (% predicted)	55.0±22.4	65.4±22.0	0.02	55.7±11.9	57.1±11.8	0.70	1.295±0.54	1.309±0.79	0.902
Anaerobic threshold	72.1±14.7	63.6±13.7	0.64	73.1±13.3	59.3±10.8	0.13	-0.083±0.46	-0.120±0.13	0.72
Breathing reserve (BR)	41.9±21.3	24.7±15.4	0.01	40.5±22.6	27.8±12.5	0.04	-0.277±0.43	-0.24±0.38	0.55
Heart rate (per min)	125.3±9.8	123±10.02	0.46	126±15.8	124±8.97	0.58	-0.12±0.08	-0.004±0.09	0.85
Heart rate reserve	19.6±6.4	20.7±5.2	0.51	18.1±0.6	19.7±5.4	0.43	0.16±0.50	1.04±3.34	0.34
VE/VCO_2 (L/min)	29.1±5.8	29.3±7.7	0.87	29.5±7.7	27.3±6.1	0.08	0.018±0.22	0.05±0.14	0.37
VE/VO_2 (L/min)	27.7±3.6	34.8±19.2	0.187	33.3±20.1	33.1±15.9	0.97	0.281±0.82	0.174±0.85	0.21
Tidal ventilation (L)	0.904±0.27	1.11±0.33	0.027	0.915±0.21	0.94±0.25	0.73	0.285±0.38	0.057±0.31	0.09
O_2 pulse ventilation (L)	7.07±2.15	8.71±2.88	0.039	7.60±1.83	7.69±2.02	0.88	0.279±0.43	0.036±0.28	0.03
VO_2/ W slope ventilation (L)	28.42±17	9.06±4.21	0.001	28.6±10.2	29.1±17.0	0.76	1.607±0.85	1.935±1.72	0.94

Definitions of abbreviations: VE/VO_2=Ventilatory equivalent/volume of expired oxygen; VE/VCO_2=Ventilatory equivalent/volume of expired carbon dioxide; O_2=Oxygen; VO_2/W=Volume of oxygen consumption/Watt

statistically significant improvement. The volume of oxygen consumption/watt (VO_2/W) slope, which reflects amount of oxygen consumed per unit work done, was steep at baseline in both groups of patients (28.42±16.99 and 28.56±10.18, respectively). After PR exercises for three weeks this dropped to 9.06±4.21 in the intervention group (p=0.0001) while there was no statistically significant improvement in the control group patients (p=0.762). This shows that PR exercises reduced the amount of oxygen consumed per unit work done. At baseline CPET, AT was achieved in three patients in the intervention group and five patients in the control group. At three weeks, the number increased to nine patients in the intervention group, but actually decreased to three patients in the control group. Overall, there was no statistically significant change in AT in the two groups of patients. Change between baseline and three week CPET values for duration of exercise, VO_2 uptake, and oxygen pulse was much more marked in the intervention group than the control group patients (Table 4).

Analysis of QoL data by SF-36 questionnaire at baseline compared with three weeks of PR or usual care revealed that there was a statistically significant improvement in both the groups of patients at the end of three weeks. Between-group analysis of data and delta changes in various domains, however, showed that the benefit was considerably more in favour of the intervention group patients who were administered PR exercises over the usual care provided to the control group patients (Table 5).

Discussion

The results of the present study clearly demonstrate that add-on therapy with PR programmes — even of short duration — play a definite role in the management of COPD patients with acute exacerbations. It definitely improves capacity and duration of exercise as well as general QoL of patients. The treatment modalities available for stable COPD are not entirely satisfactory as these not only fail to arrest the progression of disease and the accompanying disability, but also do not provide adequate relief of symptoms. The problem is further compounded with the development of systemic effects of the disease resulting in loss of weight, skeletal and respiratory muscle dysfunction with increasing disability and recurrent acute exacerbations. In the absence of specific anti-inflammatory therapy against COPD, a holistic approach to its management is the best option. In addition to the well-established treatment regimens with antibiotics, bronchodilators and corticosteroids,[6] administration of PR programmes is a relatively newer concept.[15-22] Such programmes are conventionally administered during a period of clinical stability, for six weeks or longer, followed by continued exercises at home for sustained effect.[30] Only a few studies have reported on the effects of 3-4-week duration programmes on stable COPD patients with varying results. It is noteworthy that in-patient PR programmes of two-week duration have been shown to produce significant improvement in exercise capacity.[31] Recently, administration of PR programmes has been shown to provide significant clinical benefits during or immediately after an acute exacerbation.[20, 32-34] In India the treating respiratory physicians do not seem to be aware of the benefits of PR as add-on therapy. A practical problem, however, is that to ensure better compliance by the patient, the duration of an effective PR programme needs to be as

Table 5. Quality of life data-analysis of eight domains in SF 36 – in intervention (pulmonary rehabilitation) and control group patients with intra- and inter-group comparisons

Parameter	Intervention Group (n=15)			Control Group (n=15)			Change Between Pre- and Post-Values		
	Baseline (pre)	3-week (post)	p-value	Baseline (pre)	3-week (post)	p-value	Intervention Group	Control Group	p-value
Exercise	185.3±82	242.0±65.8	0.014	202.0±99.6	216.0±96.6	0.16	0.478±0.47	0.156±0.58	0.03
Physical functioning	19.3±18.6	82.7±9.7	0.0006	18.7±14.1	51.7±25.2	0.001	63.3±20.7	33.0±26.8	0.005
Role limitation									
Physical health	0.00±00	74.3±29.3	0.0005	5.0±10.4	30.0±41.4	0.048	74.3±29.3	25.0±46.3	0.005
Emotional problem	0.00±0.00	84.2±21.1	0.0005	15.4±21.2	44.4±43.1	0.041	84.2±21.1	29.0±53.2	0.008
Energy/fatigue	38.0±8.0	65.0±9.3	0.0005	45.3±10.3	53.3±12.9	0.076	27.0±12.1	8.0±14.9	0.001
Emotional well being	41.2±11.1	63.3±9.1	0.001	51.7±17.1	61.3±16.6	0.010	22.1±13.4	9.6±12.6	0.021
Social functioning	47.3±15.8	75.0±15.7	0.002	49.7±16.4	61.3±20.2	0.077	27.7±22.1	11.6±21.1	0.049
Pain	46.0±14.4	84.2±13.2	0.0006	53.2±13.2	81.4±14.1	0.0009	38.2±13.4	28.2±17.6	0.092
General health	40.2±8.9	54.0±12.3	0.008	42.0±13.7	53.5±13.0	0.008	13.8±15.9	11.5±16.8	0.785

short as possible. Thus, we were keen to tailor the PR to a total of nine sessions in three weeks which in our opinion would be effective.

The results of the present study instituting 3-week PR programme in COPD patients hospitalised with acute exacerbation are very encouraging. The 6MWT and CPET both showed significant improvements in 6MWD, duration of exercise, power output (Watts = W), peak oxygen uptake, and the VO_2 / W slope in the intervention group compared with the matched control group patients who were not administered PR exercise. It is likely that the deconditioned, wasted skeletal muscles in COPD especially after an acute exacerbation of disease used excessive oxygen per unit work done. PR exercise training for three weeks shifted the VO_2 / W slope to the right suggestive of improvement in skeletal and respiratory muscle efficiency.

There are several other issues which would influence the outcome of the PR programmes. Compliance by the patient is always difficult to achieve, especially when regular exercise at home for at least 20 minutes daily is mandatory to sustain the functional improvement achieved through PR. Issues related to malnutrition that is common especially in older individuals, use of supplementary oxygen need to be addressed. Other co-morbidities, especially diabetes, anxiety, depression and other mental health disorders must be promptly diagnosed and appropriately treated. Regular administration of pharmacotherapy to reduce the impact of airflow limitation is absolutely vital for successful implementation of PR programmes.

Frequent counselling of patients including self-management education also forms an integral part of COPD management. A recent multi-centric randomised clinical trial[35] has provided evidence that a multi-component, skill oriented self management programme– including an exacerbation action plan – reduced hospitalisations, emergency visits and improved HRQoL. These claims, however, were not substantiated in another comparable randomised study.[36] The beneficial effects of PR, i.e., symptom relief, improved physical endurance and enhanced HRQoL start declining towards baseline after 6-12 months of the PR programme.[37] Strategies to maintain the benefits of PR are yet not clear and more research in this area is needed. The management problems are population specific and the results of investigations carried out in other countries should not be extrapolated to Indian population in toto. Further research is needed to precisely define the role of PR programmes in AECOPD in India.

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