Six Minute Walk Test as a Monitoring tool in Chronic Obstructive Pulmonary Disease on Pulmonary Rehabilitation

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ABSTRACT

Background and Aims- The six minute walk test is widely used as an outcome measure in pulmonary rehabilitation programs. The objective of this study is to report the magnitude of change in the six minute walk test with test repetition in patients with chronic obstructive pulmonary disease on pulmonary rehabilitation program.

Methods: A prospective study of 51 patients with moderate to very severe COPD was carried out. Clinical examination, spirometry, six minute walk distance were done. All were advised regular follow up visits at three, six and twelve months.

Results: Four (8%) very severe cases completed all visits and one in those showed improvement in Forced Expiratory Volume in 1 second by 6% and six minute walk distance by 71 metres. Seven (31.37%) severe cases completed all visits; showed improvement in Forced Expiratory Volume in 1 second by 2.5%; the distance walked was a mean 381.5 metres and this was 2.5 % improvement over base line walking distance. Six (11%) moderately severe cases completed the study; the mean distance walked at the end of the study was 451 metres, which is an improvement of 53% and the mean change in Forced expiratory volume in 1 second was <2%. Totally, the mean of modified Burden of Lung disease Dyspnoea scale was 1.7 (baseline) and 4 (after the test).

Conclusions: These findings support the recommendation of practice six minute walk test at baseline assessment in order to provide an accurate measure of the effects of rehabilitation on six minute walk distance.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is currently a major global health problem. In the developed world, in contrast to other big killer diseases like coronary artery disease, cancer, cerebro-vascular accidents, there has been steady increase in cases of COPD. World health organization (WHO) statistics show that COPD is currently 4th leading cause of death in the world [5.8%] and its prevalence rates were 11.8% for men and 8.5% in women.[1] According to Burden of Lung Disease (BOLD) study,[2] 10% of COPD cases belong to stage II (GOLD criteria)[1] and higher in terms of severity. Developing countries have higher prevalence of COPD than higher income countries. On an average, Indian COPD patient spends about 15% of his income on smoking products and up to 30 percent on disease management [3]. The Indian data suggests that the overall prevalence rates of COPD was 5% in males and 2.7% in females aged in those above 30 years.[4] Tobacco smoking remains the most important risk factor of COPD [5]. Since all chronic smokers do not get COPD, a genetic predisposition may have a role.[3] In developing countries such as India, indoor pollution from cooking fire smoke is associated with COPD especially in women.[6] Global Initiative for Chronic Obstructive Lung Disease (GOLD) [7] defined

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COPD as a "preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity of the disease in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles and gasses". The diagnosis of COPD is suggested by history, clinical examination and confirmed by Spirometry.[8] The clinical symptoms of COPD include persistent progressive dyspnoea, chronic cough, chronic sputum production, wheeze, reduced exercise tolerance, fatigue, malaise, pedal oedema. The signs of severe COPD include central cyanosis, barrel shaped chest, use of accessory muscles for respiration, tachypnoea, pursued lip breathing etc. But none of the symptoms or findings is specific for COPD.

Smoking cessation is the only effective measure in altering the progression of COPD and quitting smoking at any age reduces the overall mortality.[9] The management of COPD include supplemental oxygen, bronchodilators and glucocorticoids. Pulmonary rehabilitation is indicated whenever there is moderately severe or severe COPD. Controlled breathing techniques such as pursed lip breathing, slow prolonged expiration reduce the respiratory rate and enhance expiratory tidal volume thereby decreasing air trapping. Currently, Spirometry and Walk tests (Six minute walk test, Twelve minute walk test, Shuttle walk test) are available for monitoring the progress of COPD. The 6-min walk test (6MWT) has historically been used to characterise the functional status of COPD (COPD) patients. The 6MWT is a sub-maximal exercise test that can be performed by a patient not tolerating maximum exercise tests.[10] It is a reproducible test and is considered safe because patients can stop by themselves during exercise. American thoracic society (ATS) proposed guidelines for the 6MWT. However, over the past few years, the 6MWT has assumed a more central role in the assessment and management of COPD. Much of the attraction of the 6MWT as an assessment tool in COPD is due to its simplicity of performance, inexpensiveness, responsiveness to standardisation and embodiment of an important functional task (i.e. ambulation). The impact of a learning effect on the distance walked during a 6MWT in COPD has been the focus of multiple small studies over the past three decades. Leach et al., attributed a 14.9% improvement in subsequent 6MWT performances in 30 hypoxemic patients with COPD and/or restrictive diseases to a learning effect.[11] Swinburn et al., reported a 16% increase in 6MWTs conducted in 17 COPD subjects who performed four successive 12-min walks over a period of 1 week.[12] Stevens et al.,[13] performed three 6-min walks in 21 COPD patients on separate days and found a mean increase of 10% on the second test and a further 3% increase in distance walked on the third test. In a retrospective observational study, the researchers studied the reproducibility of two 6MWTs performed on subsequent days in 1,514 COPD patients (Forced Expiratory Volume in 1 second 45±18% predicted; 41% female). 82% of the patients improved in the second test. Reasons for the improved performance in the second 6MWTs are not entirely known but may include motivational factors, better pacing, or familiarity with the 6MWT process or course layout.[14] It is reassuring that the two largest trials that have looked at reproducibility with the 6-min walk, one a large multicentre trial of severe emphysema patients and the other an observational report conducted in COPD patients with a range of severity, report the same magnitude of improvement on the subsequent test: 7% in both studies.[15] Moreover, both studies demonstrated that the majority of patients (70% and 82 %) had an improved 6-min walk distance on the second test.[16] With this context, the current study was carried out to observe the outcome of 6MWT in patients with COPD undergoing rehabilitation program.

METHODS

Study design: Hospital based prospective study carried out from July 2010 to September 2011at Respiratory ward of Narayana Medical College Hospital, Nellore, Andhrapradesh.

Inclusion criteria:

1. Stable COPD patients with moderate to severe obstruction as per GOLD criteria on pulmonary rehabilitation programme.
2. Those on optimum treatment (combination therapy with long acting beta2 agonists plus budesonide/ fluticasone and long acting anticholinergic (tiotropium bromide)

Exclusion criteria:

1. Patients with acute exacerbation.
2. Unstable angina, Myocardial infarction during last four weeks, life threatening cardiac arrhythmias,
3. Baseline heart rate greater than 120 beats/min, Systolic BP greater than 180 mm Hg and diastolic greater than 100 mm Hg.
4. Unwilling patient
5. Active rheumatologic disease, Diabetes mellitus, Neurological diseases

- The study was approved by the Institutional Ethics Committee and an informed written consent was obtained from all patients before enrolment into the study. A total of 51 patients with a mean age of 63 years with moderate

to very severe COPD were included in the study. Their smoking habits were documented.

- All patients were subjected to clinical examination followed by urine and blood investigations. Arterial blood gas analysis was done in severe and very severe cases of COPD. The diagnosis of moderate to very severe COPD was made through the pre-determined values in spirometry. All the patients had chest High resolution computerised tomography (HRCT) done before being included in the study.
- Anthropometric data including Body Mass Index (BMI) was measured in all the subjects. Electro cardiogram (ECG) and 2D Echocardiogram were obtained through cardiac consultations. Subjects with significant cardiac dysfunction were excluded from the study. After establishing the diagnosis of COPD and grading the severity, the patients were initiated on medical therapy based on GOLD guidelines. The patient's risk factors were identified and counselling done to avoid them.
- The patient with moderately severe (n:16), severe (n:26) and very severe COPD (n:9) were treated with combination of inhaled long acting beta2 agonists like salmeterol and corticosteroids like budesonide along with other non-pharmacologic treatment like pulmonary rehabilitation. The 6MWT was conducted according to American Thoracic Guidelines[18] and was supervised by the investigator.
- Modified Borg CR10 (BORG) score was obtained before and after 6MWT. The oxygen saturation was monitored before, during and after the 6MWT using a portable finger pulse oximeter (Contec Medical systems). The subjects were asked to walk at their own pace along a 30meter long, straight closed hallway in the hospital. The turnaround points were marked with a cone. The patient was positioned at the start line with investigator by his side.
- The timer was started once the patient began to walk. No encouragement was offered but the patient was informed of remaining time using standardized phrases. The patient was allowed to use support while walking if necessary. The patient was allowed to stop if significant distress occurred and he could resume as soon as possible if he could. If the patient stopped walking during the test; timer was left running for rest of the time. When the timer was 15 seconds from completion, the patient was instructed to. The number of laps completed was recorded and the distance covered was calculated. The patient was asked to rest on a couch and his vital parameters including oxygen saturation were-recorded. The patients were observed for 60 minutes after the test for any complaints.
- The 6MWT was immediately discontinued in the patients who had following symptoms: Chest pain; Intolerable dyspnoea; Leg cramps; Staggering; Diaphoresis; Ashen appearance
- All the patients were advised to continue inhalation therapy (MDI through spacer) and pulmonary rehabilitation. They were advised regular follow up visits at three, six and twelve months. Clinical examination, spirometry, 6MWT was done on each of the subsequent visits. At 3 months of follow up, 30 patients (58.9%) were available and at six months of follow up only 21 patients (41 .17%) remained. Only 17 (33.33%) patients completed 12 months follow up period. The patients were divided into responders (6 minute walk distance improved) and non responders (6 minute walk distance not improved)

STATISTICAL ANALYSIS

Data was analyzed using Graphpadprism Software Version-4 USA. Intention to treat plus last observation carried forward principle was used to analyze the data. The patient who came for third month follow-up, his data was used for ITT analysis and the third month data of 6MWT was carried forward to final analysis. Data was presented as Mean±SD. One way non parametric Friedman's repeated measures ANOVA followed by Dunn's Multiple Comparison of change from baseline walking distance, since the data did not follow normal distribution pattern. Spearman Correlation analysis was performed between baseline FEV1 and 6MWT.

RESULTS

Of the 51 subjects included in this study, 29 (56%) were Bidi smokers, 17(33%) subjects smoked cigarettes and the remaining 5(10%) subjects smoked both cigarettes and Bidis. About 78% of the included subjects were either illiterates or discontinued at primary level. Out of 51 patients, 30 (59%) patients remained after first visit and 21 patients (41%) completed second visit. Only 17 (33%) members completed all visits. Out of 9 cases of very severe COPD, 4(8%) completed study, and out of 26 cases of severe COPD 7(31%) completed the study successfully. Out of 16 moderately severe COPD 6 (11%) completed the study. There were large number of cases (n: 34) who didn't complete the study. Of the total number of subjects, 31% of the moderately severe COPD, 50.98% severe COPD and 17% very severe COPD completed the study. There were 2 deaths (4%); 10(20%) hospital admissions with acute exacerbations of COPD. Two patients opted out of walk test as they developed severe breathlessness. Two patients developed hypertension during the study and were excluded. Rest of the subjects (n=18) didn't complete the study as they did not follow the treatment protocol and could not be followed up.

The clinical characteristics and baseline test results are shown in Table.1.

TABLE 1 : Showing the Baseline characteristics (Mean)

Characteristics	Mean value
Age	63
Smoking Index	29
BMI	18.6
FEV1	42.5
SMWD	322
Pulse rate(beats per minute)	82
Systolic Blood pressure(mm Hg)	130
Diastolic Blood pressure(mm Hg)	73
Modified Borg Score	1.7
Oxygen saturation %	98

At the end of study, only one of the 4 cases of very severe COPD showed improvement in FEV1 by 6% and 6MWT by 71 meters. The remaining four cases showed an average of 1.5% decrease in FEV1 and 25 meters of walking distance. Seven patients with severe COPD, the distance walked was a mean 381 meters and this was 2.5% improvement over base like walking distance. However there mean difference in FEV1 was 2.5% only. In moderately severe COPD group, the mean distance walked at the end of study was 451 meters which is an improvement of 53%. However the mean change in FEV1 was less than 2%. The details are mentioned in Table 1-6 and Figure 1 and 2.

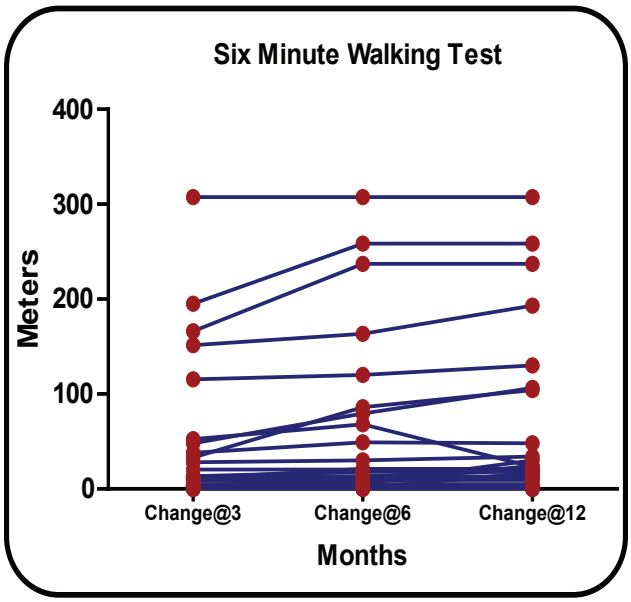

Figure 1 : *Showing changes or improvement in 6 minute walking distance (Metres) according to 3rd, 6th and 12th month respective follow-ups.*

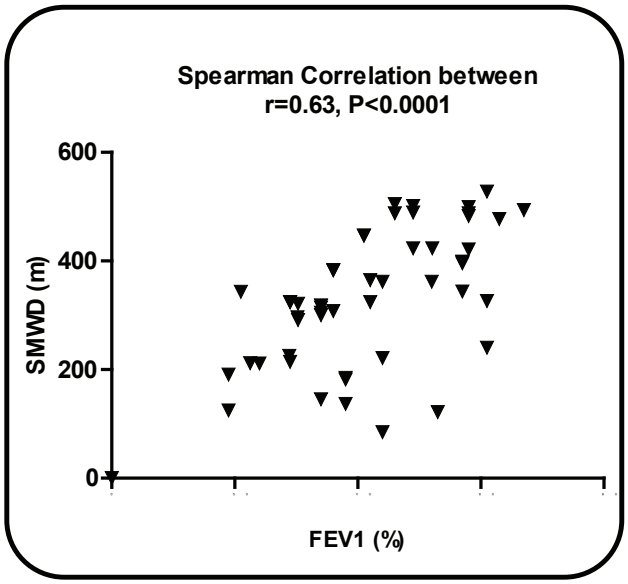

Figure 2 : *Showing spearman correlation of % of FEV1 versus 6 minutes walk distance (SMWD- indicate 6 minute walk distance* **in metres)**

The mean of modified Borg dyspnoea scale was 1.7 before and after the test the mean was 4. The details of Modified BORG scale is given in Figure 3 and Table 7.

TABLE 2 : Showing FEV1 according to day 0, 3rd, 6th and 12th month respective follow-ups

FEV1	0	3	6	12
No Of patients	30	30	30	30
Median	41	38	38	38
Mean	42.02	41	40.83	41.47
SD	14.37	13.77	13.96	13.76

TABLE 3 : Showing distance covered after 6MWT at day 0, 3rd, 6th and 12th month respective follow-ups

Mean± SD of the distance covered in 6 min walk test				
	SMWD0	SMWD3	SMWD6	SMWD12
Mean	335	355	364	367
Standard deviation	118.8	109	109.3	110.7

TABLE 4 : showing distance changes observed after 6MWT from baseline to respective follow-ups

Mean± SD-Change from baseline in walking distance in 6MWT			
	SMWD3	SMWD6	SMWD0
Mean	42.3	52	55.6
Standard deviation	11.2	13.2	20

TABLE 5 : Showing ratio of responders to non-responders according to 3rd, 6th and 12th month respective follow-ups

Responders to Non Responders ratio in 6MWT			
	SMWD3	SMWD6	SMWD12
Responders	6	8	7
Non Responders	24	22	23

TABLE 6 : Showing One way non parametric Friedman's repeated measures ANOVA followed by Dunn's Multiple Comparison of change from baseline walking distance (ns: not significant)

One way non parametric Friedman's repeated measures ANOVA followed by Dunn's Multiple Comparison of change from baseline walking distance		
6MWT	P < 0.05	Significant
Change@3 vs. Change@6	No	ns
Change@3 vs. Change@12	Yes	**
Change@6 vs. Change@12	No	ns

TABLE 7 : Showing Change of Modified BORG Score. C@0; C@3; C@6; C@12 Indicates Change At Baseline; 3rd Month; 6th Month; and 12th Month Respectively

Modified BORG Score Change	C@0	C@3	C@6	C@12
Number	30	30	30	30
Median	6	5.5	7	6
Mean	5.467	5.833	6.6	5.8
SD	2.24	1.663	1.476	1.955

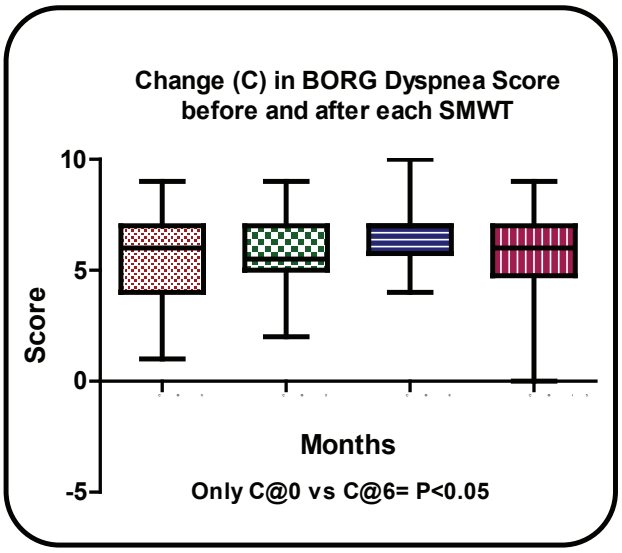

Figure 3 : *Showing Change in BORG dyspnoea score before and after SMWT*

DISCUSSION

We chose 6MWT for study of our patients as previous studies have evaluated other test like twelve minute walking test or shuttle walk test with regard to variability and reproducibility. Sherra S et al.,[17] performed an observational study on 52 studies examining measurement properties of various walk tests such as 2MWT, 6MWT, 12MWT and self paced walk test or shuttle walk test. They recommended that 6MWT is currently the test of choice when using a functional walk test for clinical or research purposes. The 6MWT is easy to administer, better tolerated and more reflective activities of daily living than other walk tests. In our study 33% of COPD cases of at least moderate severity completed the one year study period and 6MWT as a monitoring tool correlated well with clinical and spirometric data. The low completion rate in our study was because the natural course of COPD even with optimal treatment is progressive deterioration with varying speed and acute exacerbations.

In our study 19 % experienced acute exacerbations during study period and had to be withdrawn. Another Indian study evaluating the utility of 6MWT in varying severity of COPD revealed that the distance walked during the test was almost similar as in our study but the hospital admissions were higher (68%) in very sever COPD and 28% in severe COPD and the completion rate was (78%). In a study by Cassanova C et al.,[18] the 6MWT was evaluated in clinically stable COPD patients for five years and pulmonary function tests were done at each visit. The rate of decline in the distance walked correlated with the severity of COPD and spirometry values being maximum in very severe COPD. In our study the rate of decline in distance walked was not significant except in very severe COPD and spirometry values did not change significantly. Previous studies have confirmed the utility of six minute walking test in matching changes in spirometric values.

In 2005, Naghshin R et al.,[19] conducted a study to determine the association between 6MWT and spirometry parameters in 55 patients with COPD. All the patients underwent 6MWT within one hour of spirometry. The study showed statistically significant association between the results of 6MWT and spirometric values. Our study also revealed that the change in 6MWT is related to the values of FEV1.To know the long term results of 6MWT and spirometry in stable COPD patients , Casanova et al.,[18] studied 294 cases of COPD over a period of 5 years and revealed that decline in 6MWT correlated well with the degree of severity of COPD.

In our study all the patients who have been already started on pulmonary rehabilitation programme showed constant walking distance in severe and improved in moderately severe COPD. This may be due to pulmonary rehabilitation. The benefits of pulmonary rehabilitation were evaluated previously

in 59 subjects with moderate COPD and similar improvements in 6MWT were documented. Compared to spirometry, the technique of 6MWT is easy to understand even for those with primary education level or illiterates.

In our study there were 40 illiterate or primary education dropped out subjects. The 6MWT has been documented as simple and safe test for those with chronic pulmonary disease [20].In our study, there were only two dropouts from the 6MWT as result of worsening breathlessness and both recovered with rest. The mortality rate among COPD is influenced by severity, complications and comorbid conditions. In a one year study done by Agarwal SK et al., [21], 8% patients died during the study period. Most of the deaths were among those with very severe group.

In a two years study by Pinto VM et al.,[22], there were 42% deaths during the study period. These deaths were attributed to the age, low body mass index and co morbidities. In our study the mortality was 2(4%) deaths. This low mortality mainly because of exclusion of co morbidities and higher body mass index.

To conclude 6MWT is a simple, safe and inexpensive monitoring tool when compared to spirometry which is dependent on patient's cooperation and understanding. 6MWT may be recommended as a substitute for objective measurement of stable cases of COPD.

CONCLUSION

6MWT is a simple, safe, and quick monitoring tool of patients with COPD. The value of distance walked and FEV1 were related to severity of COPD. There is improvement in six minute walking distance in moderately severe COPD on treatment. The change in FEV1 is not significant among COPD patients with varying severity. The acute exacerbation in COPD is not related to the values of 6MWT and FEV1. 6MWT is a reliable and acceptable monitoring tool to illiterates and to all when spirometry is not available.

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