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Research Article

SEF Staging: A Novel Approach to Optimal COPD Management

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Abstract

Considering the limitations of FEV1, presence of complications (respiratory failure, other comorbidities), frequency of exacerbations and impact of disease on patients' life, a new management plan for COPD has been formulated which is proposed to be more effective than Gold management plan. A modified staging and management of COPD is formulated which is based on symptoms (S) frequency of exacerbations (E) and Function (Lung Function, i.e. FEV1). Depending on these three parameters, SEF (symptom, exacerbation and Function) classification has been coined. According to SEF classification, COPD patients are divided into four stages on the basis of FEV1 and each stage is again sub-classified on the basis of symptoms (a) and exacerbation (b).

Results: 153 COPD stable patients included initially in SEF Study. 12 patients were excluded since they were not true COPD. 111 (72.6%) patient responded to treatment and 27 (17.6%) patient not responded to treatment and 3 (2.0%) patient died during treatment. Out of 141 patents, 51 responder patients and 14 non-responder patient completed 1-year full face to face follow up and necessary investigations. Lack of Family support (26.7%) and improvement of physical condition (45.0%) were major reason of failure to follow up in responder group. Major cause of failure to respond was default in completion to treatment. Finally, 65 patients completed full follow up. Significant improvement of total impact factor was observed in responder group and it was 9.19 ± 1.99 before SEF based treatment and after one year 6.01 ± 1.15 (P = 0.0001) versus no significant improvement in non-responder group before SEF based treatment 9.64 ± 1.15 and after one year 10.92 ± 1.31 (P = 0.30). Exacerbation Per patient/year in responder group before SEF based treatment 0.784 ± 1.08 and after 1 year 0.431 ± 0.60 (P = 0.03) which was significant versus in non-responder group before SEF based treatment 0.571 ± 1.09 and after 1 Yr 1.0714 ± 0.92 (p = 0.20) which was not significant. So, reduction of exacerbation rate and significant improvement of total impact factor was observed in responder group.

Conclusion: SEF Staging based treatment approach may be alternative to the FEV1 based staging of COPD patient's and need additional study with adequate sample and follow up.

Keywords: *SEF Staging; COPD; FEV1*

Introduction

Chronic Obstructive Lung Diseases (COPD) is a rapidly increasing troublesome non-communicable disease prevalent throughout the world [1-2]. It is one of the most common respiratory ailments encountered by the physicians. This disease is a burden for both developed and developing countries. In 2007, a study on COPD known as BOLD-BD (Burden of Obstructed Lung Disease in Bangladesh) revealed the prevalence of COPD in general population to be 4.32% [6-12].

COPD results from long-standing lung inflammation of smoldering nature causing narrowing of small airways, which is sometimes not properly represented by FEV1 measurements [3]. Though FEV1 correlates well with exertional dyspnea, it does not reflect the effects of chronic productive cough even when associated with wheeze [4]. Patients with chronic productive cough are more prone to exacerbations in COPD than the patients having emphysema [5]. CAT [6] score is not so friendly for Bangladeshi patient as 80% COPD patients are less educated and poor [7]. Optimal management of COPD must be based on symptoms and exacerbations as well as FEV1 results. In GOLD classification of COPD, ABCD sub-classification is not user-friendly for the GPs [7].

According to GOLD guidelines, the primary outcome of therapeutic intervention is measurement of FEV1 (Forced Vital Capacity in 1st second) but this has several limitations [13,14]. The systemic inflammatory component and multisystem nature are also not adequately addressed by spirometry measurement [8]. Moreover, FEV1 is not always correlated well with exertional dyspnea, and with chronic productive cough even with wheeze. Patients with chronic productive cough are more prone to exacerbations than emphysema patient, so management of COPD depends on both symptoms and exacerbations besides FEV1 [4,12].

A new "question and scoring" module for staging and management of COPD is formulated which is based on symptoms (S) frequency of exacerbations (E) and Function (Lung Function = FEV1) and depending on these three parameters, SEF (symptom, exacerbation and Function) staging has been made. According to SEF classification, COPD patients are divided into four stages on the basis of FEV1 and each stage is again sub-classified on the basis of symptoms (a) and exacerbation (b) into Stage-a or b.

Methodology

A case control cross over SEF (Symptoms-Exacerbations-Function) trial of COPD was conducted in a private Hospital in Dhaka Bangladesh, from July 2011 to December 2012. This Staging based treatment was developed as trial and error basis in Principal Investigators chamber primarily based on GOLD guideline 2010. It was pre-tested for 6 months from July –December 2011 and final classification based treatment was applied during 2012. All COPD patients digitized previous prescriptions were examined scrupulously. All previously diagnosed COPD patients were re-evaluated and if the diagnosis was reconfirmed, the patient was included in the study as a case.

Age, sex and economic status matched controls were recruited. They were assessed for previous Symptoms, Impact of COPD score, rate of exacerbations last 12 months and previous and current FEV1were compiled during face to face interview. Then baseline investigations were done. If investigations were suggestive of COPD, then the control was crossed-over as a case. SEF classification based treatment was meticulously calculated by a trained Respiratory Physician and recalculated randomly by the principal investigator. Then the patient was prescribed for COPD treatment and difference between previous prescriptions was noted in data sheet. Every 2 months' interval Telephone follow up and every 4 months' interval Spirometry with face to face follow up was done for one year. At follow up reduction of symptoms, frequency of exacerbations, improvement of MRC Dyspnea Scale, Impact of COPD in life and FEV1 change were monitored. All data were recorded, tabulated and analyzed. According to SEF Staging, COPD patients are dividing into four stages on the basis of FEV1 and each stage is again sub-classified on the basis of symptoms and/or exacerbation (Category a or b).

FEV1 (F) Score: (Post –Bronchodilator FEV1)

FEV1= ≥ 80% = score 0

FEV1= < 80% ≥ 50% = score 1

FEV1= < 50% ≥ 30% = score 2

FEV1= < 30% = score 3

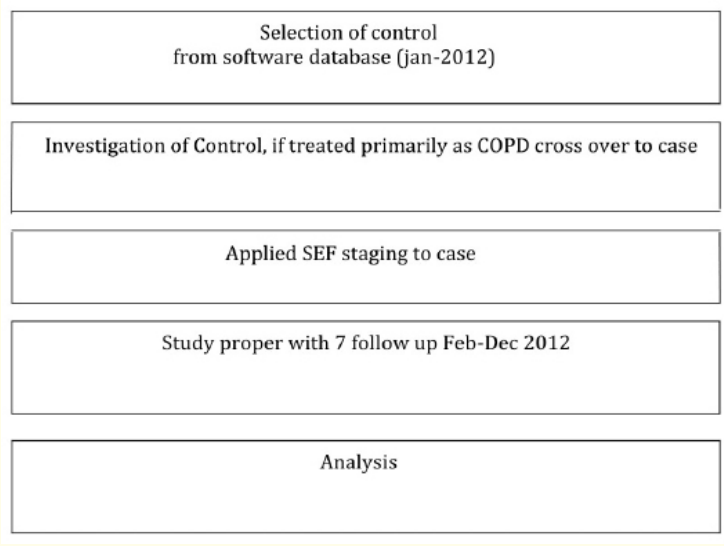

Figure 1: *Flow chart of Methodology.*

We calculated -Symptoms score 0-2, Exacerbation score 0-1 & FEV1 score separately 0-3, Summation of SEF SCORE = 0-6

Score	SPUTUM/Phlegm production (NOT SALIVA or watery secretion) with/without Breathlessness
0	None
0	Few/Mild/Scanty
0	1 TSF Sputum daily or no need to stop to catch breath while walking at least 1 flight of stair
1	More than 1 TSF up to 6 TSF or 1/2 cup a day and /or need to stop to catch breath while walking at least 1 flight of stair

Table 1: *Classification of Symptoms used for SEF based treatment plan.*

Exacerbations means more than two-fold increase sputum from stable stage and/or change of color of sputum, increased cough and/ or dyspnea.

Question to categorize COPD stage a or b	
1. Every day do you cough up 1 to 6 teaspoons of sticky/ mucoid/ purulent sputum.	Yes = score 1 No= score 0 (applicable for stage -1-4)
More than 1/2 cup Sputum (consider other cause: e.g. associated or as separate disease like Bronchiectasis) Note: Give one sputum cup to measure all sputum of whole day with avoiding swallow of sputum	
2. When you walk 1 flight of stair, do you need to stop for a while to catch your breath?	Yes = score 1 No= score 0 (applicable for stage -2-4)

3. In the last 12 months, for increased cough, sputum or dyspnea, did you have to take two courses of antibiotics and rescue medications (Antibiotics with Bronchodilators with or without Corticosteroids, ABC) or seek hospital admission at least once?	Exacerbation Yes = score 1 No= score 0
All 3 Questions negative, i.e. score 0 COPD category a	All 3 Questions Any one positive, i.e. score 1-3 COPD category b

Table 2: *Most important 3 questions to categorize COPD.*

Patients Score on the basis of SEF Classification: Total SEF Score: 0-6

Impact of disease on patient's life: 0-5

➢**Work:** Missed work / Change work /Loss work - (yes = 1, no = 0)

➢**Visit:** Failed to visit family, friends/ recreation/shopping/ or failed to go Regular at Masque or Temple or Market --(yes=1, no=0)

➢**Mental:** Suffering from Anxiety/Depression - (yes = 1, no = 0)

➢**Income:** Family Income = Decreased/ No income - (yes = 1, no = 0)

➢**Family Expenditure** = Increased due to illness - (yes = 1, no = 0)

So, Total SEF Score and Impact Factor was calculated as 11.

Symptoms	Exacerbations	Function	Score SEF Class	Stage
S0 = No Sputum or upto 1TSF /day	E0 = no or 1 exacerbation/ Year	F0 = FEV1 ≥ 80%	0	1a
S0 = No Sputum or up to 1TSF /day	E0 = no or 1 exacerbation/ Year	F1 = FEV1< 80% ≥ 50%	S0E0F1	2a
S1= Sputum more than 1TSF to 1/2 cup/day/ SOB 1 flight	E1 = 2 exacerbations or more/ Year or 1 hospitalization	F1= FEV1< 80% ≥ 50%	S1-2 &/or E1 F1	2b
S0 = No Sputum or upto 1TSF /day	E0 = no or 1 exacerbation/ Year or 1 hospitalization	F2 = FEV1 < 50% ≥ 30%	S0E0F2	3a
S1= Sputum more than 1TSF to ½ cup/day/ SOB 1 flight	E1= 2 exacerbations or more/ Year or 1 hospitalization	F2 = FEV1 < 50% ≥ 30%	S1-2 &/or E1 F2	3b
S0 = No Sputum or to 1TSF /day	E0 = no or 1 exacerbation/ Year or 1 hospitalization	F3 = FEV1< 30%	S0E0F3 = 3	4a
S1 = Sputum more than 1TSF to ½ cup/day/ SOB 1 flight	E1= 2 exacerbations or more/ Year or 1 hospitalization	F3 = FEV1< 30%	S1-2 &/or E1 F3	4b

Table 3: *COPD stage according to SEF with Proposed treatment plan.*

We define Primary outcome as treatment improvement, i.e. COPD Responder means reduction in total score (SEF Score + Impact score) with or without reduce exacerbation rate with or without improvement of FEV1. Non-responder COPD means no reduction of total score whatever rate of exacerbation and FEV1 changes.

Test	Condition of Patients	Use ICS
Reversibility test positive	FEV1 improvement more than FVC	As anti-inflammatory agent
Sputum Eosinophil 4% or more	In Stable COPD	As anti-inflammatory agent
ATOPY strong evidence	Allergic Rhinitis/ Allergy eye/skin with high IgE > 100 iu	As anti-inflammatory agent
Oral/Injectable Corticosteroids shows rapid (within 4 to 6 hours) improvement of Exacerbation	During acute exacerbations	As anti-inflammatory agent

Table 4: *Classification as 'Asthma COPD Overlapping Syndrome' (ACOS) and indications to use Inhaled corticosteroids (ICS) in COPD.*

Symptoms	Exacerbations	Function	Stage	Action
S0 = No Sputum or upto 1TSF /day Emphysema predominant	E0= no or 1 exacerbation/Year	F0 = FEV1 ≥ 80%	1a	Ipra + sal inhalerprn
S0 = Emphysema predominant	E0	F1=FEV1< 80% ≥ 50%	2a	+ any one continuous use of LAMA/LABA/Theo
S1= Sputum more Than 1TSF upto ½ cup/ day. Chronic Bronchitis Predominant	E1= 2 exacerbations or more or 1 hospitalization/ Year	F1 = FEV1< 80%≥ 50%	2b	+ any 2 of LAMA +LABA +Theo if ACOS consider ICS
S0 = No Sputum or upto 1TSF /day	E0 = no or 1 exacerbation/ Year	F2 = FEV1< 50% ≥ 30%	3a	Any 3-long actingbronchodilator (maximum Bronchodilation) if ACOS consider ICS
S1-2= Sputum more Than 1TSF upto 1/2 cup/day / SOB 1 flight	E1= 2 exacerbations or more/ Year	F2 = FEV1< 50% ≥ 30%	3b	Any 3-long acting bronchodilator (maximum Tolerable dose) + ICS +/- Prophylactic Azithromycin
S0 = No Sputum or upto 1TSF /day	E0 = no or 1 exacerbation/ Year	F3 = FEV1 < 30%	4a	3 long acting bronchodilator+ + NEB 2-4 TIMES BRONCHODILATORS
S1-2= Sputum more Than 1TSF upto 1/2 cup/day / SOB 1 flight	E1= 2 exacerbations or more/ Year	F3 = FEV1 < 30%	4b	+ COMBINE ALL For maximum improvement of Sx with minimum side effects to bother

Table 5: *Management of COPD on the basis of SEF Classification.*

Results

We recruited 153 stable COPD patients in the study. 12 patients were excluded from case series as investigation demonstrated primary disease was not COPD. 111 (72.6%) patient responded to treatment and 27 (17.6%) did not respond to treatment and 3 (2.0%) patients died during treatment.

Out of 141 patents, 51 responder patients and 14 non-responder patient completed full face to face follow up and necessary investigations over 1 year. Lack of family support (26.7%) and improvement of physical condition (45.0%) are major reason of failure to follow up

in responder group. Major cause of failure to response was default to continue to treatment.

Final data calculated from 65 patients, who completed full follow up are tabulated bellow:

	Responder group N = 51	Non-Responder group n = 14	
Age (Mean ± SD)	65.1 ± 10.7	60.6 ± 8.2	P = 0.15 N. S
Pack –Yr smoker (Mean ± SD)	27.3 ±13.4	30.8 ±12.9	P = 0.4 N. S
FEV1 Improvement Mean ± SD	42.2 ±15.6 after 1 Yr 45.1 ±15.5 (P = 0.34)	40.9 ± 9.5 after 1 Yr 38.1 ± 13.1 (P = 0.52)	P = 0.77 P = 0.13
Exacerbation Per Patient/ Year Mean ± SD	Before- 0.784 ±1.08 After 1 year 0.431 ± 0.60 (P = 0.03) OR 0.209 [95% CI 0.112 to 0.388]	Before 0.571 ±1.09 After 1 Yr 1.0714 ± 0.92 (p = 0.20) OR 1.288 [95% CI 0.808 to 2.053]	P = 0.52 P = 0.0027
Total Impact Factor Mean ± SD	Before – 9.19 ± 1.99 After -- 6.01 ± 1.15 P = 0.0001	Before – 9.64 ± 1.15 After – 10.92 ± 1.31 P = 0.30	P = 0.74 NS P = 0.0001

Table 6: *Population Characteristics and outcome of Responder and non-responder group, who completed full follow up.*

Mean FEV1 improvement in responder group versus non-responder group before SEF based treatment and after 1 year follow up was not significant; P = 0.77 vs 0.13. Exacerbation rate in Responder group versus non-responder group before and after SEF application showed significant improvement in responder group after 1 year. OR in responder group 0.209 [95% CI 0.112 to 0.388] and OR in non-responder group 1.288 [95% CI 0.808 to 2.053].

Significant Improvement of Total impact Score in responder group before and after 1 year treatment versus no significant improvement in non-responder group before SEF and after 1 year treatment; P < 0.0001 responder group versus non-responder group p = 0.74).

Lack of Family support	62.8 %
Poor Financial condition	11.1 %
Didn't come due good physical condition	14.8%
Refused to do free Spirometry test	11.1%
No time for follow up as busy for his own work	14.8%
Communication problem	3.2%
Own negligence for follow up	5.0%
Others	6.6%

Table 7: *Causes of failure of full follow up, n = 60, 43% of total 141 patient, even SEF based Treatment Responder Patients were as follows: n = 60(100%).*

Still smoker + drug defaulter + Only using reliever	42.6%
Poor inhalation technique	57.4%
Drug defaulter	51.8%
Difficult to treat asthma, improve after Omalizumab Inj	3.7%

Table 8: *Causes of reluctance to full follow up n = 27 (100%) SEF Non-Responder Patients are as follows.*

Lack of family help, still smoking, no use of regular medicine, poor inhalation technique is the major cause of reluctant to follow-up even after good education from our end.

No	Name of Medicine	Patient getting medicine Before SEF Treatment Plan Control N= (51)	Patient getting medicine after SEF Treatment Plan Control N = (51)	OR (95% CI)
1.	Salbutamol + Ipratropium	24 (47.1%)	46 (90.2%)	10.35 (3.53 to 30.30)
2.	Triotopium	33 (64.7%)	51 (100%)	52.03 (3.02 to 896.16)
3.	Fluticasone + Salmeterol	45 (86.3%)	26 (50.9%)	0.139 (0.05to 0.382)
4.	Montelukast	46 (90.2%)	15 (29.4%)	0.139 (0.05 to 0.382
5.	Theophylline	26 (50.9%)	48 (94.1%)	15.385 (4.239 to 55.842)
6.	Salbutamol	27 (52.9%)	5 (9.8%)	0.097(0.033 to 0.283)

Table 9: *Treatment difference 1 year after SEF classification based treatment in COPD Responder group.*

Significant improvement of Salbutamol plus Ipratropium inhaler use as reliever in responder group COPD patient and Triotopium and theophylline use also significantly increased as regular medicine and Fluticasone plus salmeterol and montelukast use decreased significantly after use SEF based classification in COPD responder group.

Discussion

The aim of pharmacotherapy in COPD is reduction of symptoms as well as lessening of morbidity and mortality by reduction of exacerbations and hospitalizations [15-27]. Unfortunately till now no medicine is fully effective to get these benefits on long term basis.

We developed SEF classification on trial and error basis during 2008-2009. These classification based treatment showed significant improvement of impact factor as well as reduction of hospitalizations although FEV1 improvement was not significant. Other study also demonstrated that dose related FEV1 improvement not always significant in true COPD patient [18, 20].

This study clearly showed that after application of SEF staging impact of disease on patients improved significantly than control and moreover proper use of medicine by physician also improve significantly. But even with maximum efforts, regular follow-up remains a great barrier to manage and to control COPD properly in developing country like Bangladesh. In this study, only 46% patient completed full follow-up at the end of study.

So, 'Community based home COPD care' based on SEF classification may be considered as an effective solution for total COPD management.

Conclusion

SEF Staging may be taken as a better alternative to the FEV1 based staging for COPD patients' management. Additional study with larger sample and longer follow up is warranted for proper evaluation of the proposed tool.

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