Original article:

Impact of nutritional support on quality of life in stable chronic obstructive pulmonary disease patients

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ABSTRACT-

COPD is a state of systemic inflammation that causes changes in body composition, metabolism and immune status. These systemic effects contribute to weight loss and skeletal muscle wasting limiting the exercise capacity of these patients. Thus individuals with low weight(low BMI) have more gas trapping, lower diffusion capacity and lower exercise capacity than those with similar pulmonary mechanics but with normal weight.

The present study is undertaken in stable but malnourished moderate to severe COPD patients with aims and objectives (1) to evaluate the impact of nutritional support on quality of life and (2) to evaluate the impact of nutritional support on pulmonary support on pulmonary function and exercise capacity using 6MWT.

Patients with nutritional support showed improvement in BMI associated with high hopes of improvement in quality of life. Parallel improvement in lung and exercise capacity was not **seen.**

INTRODUCTION

COPD is a state of systemic inflammation that causes changes in body composition, metabolism, and immune status. These systemic effects contribute to weight loss and skeletal muscle wasting, limiting the exercise capacity of these patients, and worsening the prognosis, independent of their pulmonary function status.[1]Malnutrition varies between 20% and 70% among different patient groups with COPD.[2] BMI is a simple and accurate indicator of nutritional status in these patients. Nutritional status of these patients was found to correlate with their exercise capacity regardless of pulmonary functions. Thus, individuals with low weight have more gas trapping, lower diffusing capacity, and lower exercise capacity than those with similar pulmonary mechanics but with normal weight[3].

Although nutritional repletion in some ambulatory COPD patients resulted in improvements in respiratory and limb muscle function.[2,3,4,5] but this has not always been the case.[6,7] Nutritional improvements in association with anabolic stimuli have been associated with better muscle functioning, quality of life and 15-month survival, but failed to show a clinically significant increase in 6MWT[8]. Quality of life (QoL) is thought to be associated with severity of

disease[9] and can be represent exercise tolerance but it has been rarely reported. Nutritional intervention may improve exercise tolerance and thereby QoL, in these malnourished COPD patients.

Materials and Methods:

All patients attending the out-patient department of TB & Respiratory Diseases of NIMS Hospital with clinical history consistent with COPD as per GOLD[10] guidelines (2014), during December 2015 to October 2017, formed the study material. A written informed consent was taken from all the patients after explaining the study protocol.

All the included subjects were then evaluated as under: -

1. A detailed present & past clinical history & physical examination
2. Peripheral blood tests for TLC, DLC, ESR, TEC, Hb%, RBS, Urea, Creatinine and SGOT/PT, urine routine exam, X-ray chest PA view, ECG, Spirometry.
3. Height in centimeters, weight in kilograms

All COPD patients with irreversible airway obstruction i.e. <12% post bronchodilator (salbutamol) reversibility in spirometery, were recruited in the study subject to the following inclusion and exclusion criteria:-

Inclusion criteria:-

1. Moderate to severe COPD as per GOLD guidelines (2014)[12].
2. BMI<18.5 kg/M^2
3. No history of exacerbation in the previous 2 months.

Exclusion criteria:-

1. Other illnesses like active pulmonary tuberculosis, Malignancy, Diabetes mellitus, Coronary artery disease, Stroke, Renal or Hepatic disease.
2. Oxygen saturation < 90 %.

Study design: Interventional, randomized study of 30 days.

The study patients was randomly divided in 2 groups as under:-

The Intervention group patients received 30gm of a commercially available nutritional powder with 1 glass of milk* in addition to the usual diet and standard pharmacotherapy.

The Control group patients will receive the usual diet and standard pharmacotherapy only.

*100gm of the commercially available nutritional powder is comprised of 14.8gm proteins, 25gm carbohydrates, and 22.1gm fats, and is fortified with various minerals and nutrients. 100gm of this powder provide 355 Kcal. The dose used in the study is 30gm per day (equivalent 106.5 Kcal) in 2 divided doses with 1 glass of milk (250 ml) each (equivalent 110 Kcal each).

The patients were monitored initially and then fortnightly as under:-

1. Height (in cm) and weight (in kg)
2. Spirometery
3. St George's Respiratory Questionnaire (SGRQ)
4. 6MWT
5. Average daily calorie intake*

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Outcome measures: The primary endpoint was improvement in quality of life. Secondary endpoints will be improvement in BMI, pulmonary function and exercise tolerance.

Body mass index (BMI): BMI will be expressed as kilograms per square meter. It will calculated initially and at each of the follow visits.

St George's Respiratory Questionnaire (SGRQ): The SGRQ is designed to measure health impairment in patients with asthma, COPD, bronchiectasis, kyphoscoliosis and sarcoidosis. It has 17 questions. A Total score is produced. While in a quiet area, free from distraction, subjects must answer every question in supervised self-administration. Hindi version of SGRQ has been validated.[11]

Six minute walk test (6MWT): Subjects were instructed to walk from end to end at one of the corridor of the hospital which is 40 m long at their own pace, while attempting to cover as much distance as possible in the allotted 6 min without supplemental oxygen. A research assistant timed the walk and recorded the total distance traveled. The research assistant offered verbal encouragement to each subjects. Test was terminated if the patient exhausts of fatigue legs and/or the dyspnea or requests to stop.

Average daily calorie intake: Average daily calorie intake will be calculated by charting the patient's oral intake in past 3 days and the taking an average of the calorie intake in those 3 days. Calorie value of foods will be calculated using value provided by using standard charts from Indian food ministry*.

Data management and Statistical analysis

The data collected will be analyzed for validity using student's t test and X^2 test as applicable. Level of significance used will be $P \leq 0.05$.

*The average daily calorie intake will be calculated by recording the patient's oral intake in past 3 days at inclusion and at every follow up.

RESULTS & OBSERVATIONS

150 OPD patients having symptoms suggestive of COPD were recruited for the study. Of these 110 patients fulfilled the study criteria. These patients were then divided in 2 groups of 55 patients each namely the Intervention group and the Control group. Table - 1 Shows the age and sex distribution of the patients. Mean age of patients in the Intervention group was 61.64 $\pm$ 7.23 years and the mean age of patients in the Control group was 61.80 $\pm$ 6.93 years. The difference was statistically insignificant (F = 0.38, P = 0.45). Calorie intake at baseline in the Intervention group was 1655.64 $\pm$ 232.68 and in the Control group was 1658 $\pm$ 125.99 (F = 0.47, P = 0.28).

Table 1 - Distribution according to Age and Sex

Age (years)	**Intervention group**		**Control group**	
	M	F	M	F
41 – 50	4	1	3	1
51 – 60	13	7	15	5
61 – 70	17	6	20	5
71 – 80	7	0	3	3
Mean $\pm$ SD	61.64 $\pm$ 7.23		61.80 $\pm$ 6.93	

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(F = 0.38, P = 0.45) Table 8 - shows the Mean Spirometery values at Day 0 in the 2 groups. The values were similar in both groups. Mean FEV1 at baseline in the Intervention group was 0.88 ± 0.37 and in the Control group was 0.86 ± 0.24. No significant difference was seen in the mean FEV1 between the two groups (P=0.34).

Table 2 - Mean Spirometery values on Day 0

Spirometry values	Intervention group	Control group	P value
Mean FEV1	0.88 ± 0.37	0.86 ± 0.24	0.34
Mean FVC	1.69 ± 0.55	1.68 ± 0.39	0.47
Mean FEV1/FVC	51.00 ± 8.92	50.96 ± 7.68	0.49
Mean Post broncho-dilator FEV1	0.94 ± 0.36	0.95 ± 0.25	0.39

Table 3 – Shows distribution of patients according to base line FEV1 (Day 0). The distribution of the patients according to baseline FEV1 in the 2 groups was also fair.

Table 3– Distribution of patients according to FEV1 at baseline

FEV1 (L)	Intervention group	Control group	Total
≤ 0.5	5	4	9
>0.5 - ≤ 1	35	41	76
>1 - ≤ 1.5	11	9	20
>1.5 - ≤ 2	4	1	5

Table 4 – Shows the distribution of patients according to FEV1 at Day15. Mean FEV1 in the Intervention group was 0.92 ± 0.37. Mean FEV1 in the Control group was 0.92 ± 0.25. No significant difference was seen in the mean FEV1 between the two groups (P=0.48). Mean FEV1 was slightly higher at day 15 as compared to day 0 (0.92 ± 0.37 vs. 0.92 ± 0.25).

Table 4 - Distribution of patients according to FEV1 at Day 15.

FEV1 (L)	Intervention group	Control group	Total
< 0.5	4	2	6
>0.5 - < 1	34	39	73
>1 - < 1.5	12	12	24
>1.5 - < 2	5	2	7
Mean	0.92 + 0.37	0.92 + 0.25	-

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Table 5 - Shows the distribution of patients according to FEV1 at Day 30. Mean FEV1 in the Intervention group was 0.99 + 0.39. Mean FEV1 in the Control group was 0.92 + 0.25. No significant difference was seen in the mean FEV1 between the two groups (P=0.13).

Table 5- Distribution of patients according to FEV1 at Day 30.

FEV1 (L)	Intervention group	Control group	Total
≤ 0.5	3	2	5
>0.5 - ≤ 1	31	39	70
>1 - ≤ 1.5	12	12	24
>1.5 - ≤ 2	9	2	11
Mean	0.99 ± 0.39	0.92 ± 0.25	-

Table 6 – shows distribution of patients according to SGRQ score at baseline. There was no significant difference seen between Intervention and control groups (F=0.16, P= 0.23).

Table 6– Distribution according to SGRQ score at baseline (Day 0)

SGRQ score	Intervention group	Control group	Total
< 40	12	15	27
>40 - < 45	33	33	66
>45 - ≤ 50	10	07	17
Mean ± SD	42.27 ± 2.93	41.43 ± 2.14	-

(F=0.16, P= 0.23)

Table 7 – shows distribution of SGRQ score at Day 15. Intervention group had a mean SGRQ score of 37.39 ± 3.50. Control group had a mean SGRQ score of 41.33 ± 1.98. Mean SGRQ score was significantly lower in the Intervention group as compared to control (F<0.0001, P<0.0001).

Table 7 – Distribution according to SGRQ score at Day 15

SGRQ score	Intervention group	Control group	Total
≤ 35	7	0	7
>35 - ≤ 40	45	18	53
>40 - ≤ 45	11	34	45
>45 - ≤ 50	0	3	3
Mean ± SD	37.39 ± 3.50	41.33 ± 1.98	-

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Table 8– shows distribution of SGRQ score at Day 30. Intervention group had a mean SGRQ score of 37.39 ± 3.50. Control group had a mean SGRQ score of 41.33 ± 1.98. Mean SGRQ score was significantly lower in the Intervention group a compared to control (P<0.0001, F<0.0001).

Table 8 – Distribution according to SGRQ score at Day 30

SGRQ score	Intervention group	Control group	Total
< 35	38	0	38
>35 - < 40	14	18	32
>40 - < 45	2	34	36
>45 - < 50	0	3	3
Mean + SD	31.90 + 4.65	41.33 + 1.98	-

Following figure shows the Calorie intake at baseline. It was similar in both groups (Intervention group 1655.64 + 232.68; Control group 1658.73 + 125.99). Calorie intake was higher in Intervention group as compared to Control group on day 15 (1990 ± 193.10 Calories/day as compared to 1658.73 ± 125.99 Calories/day) and day 30 (1990.73 ± 193.49 Calories/day as compared to 1667.09 ± 123.39 Calories/day), as shown below. This was due to additive nutritional therapy given to the patients in the interventional group.

CALORIE INTAKE

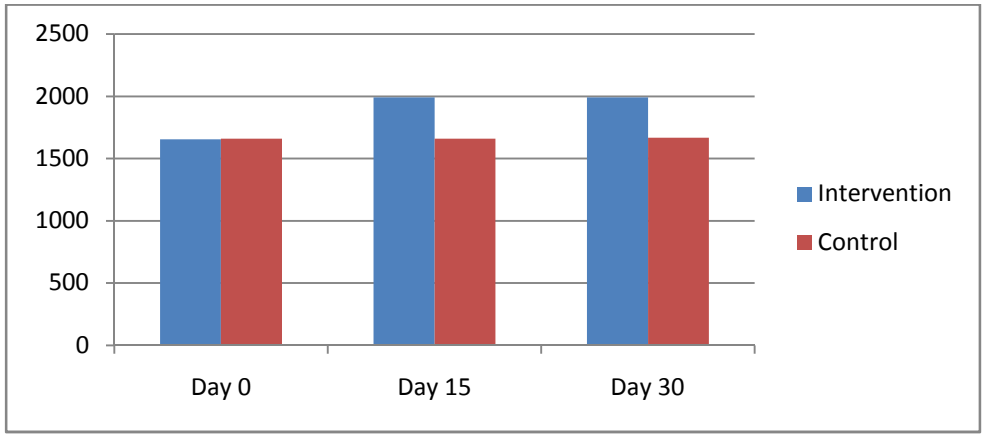

Table 9– shows distribution of Body Mass Index (BMI in kg per meter^2) at day 0. All recruited patients had BMI less than 18 as per the inclusion criteria.

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Table 9:- Distribution of Body Mass Index at day 0.

BMI	Intervention group	Control group	Total
≤ 14	3	4	7
>14 - ≤ 16	28	27	55
>16 - <18	24	24	48
Mean	15.54 ± 1.09	15.55 ± 1.07	-

(F=0.44, P=0.49)

At baseline, mean BMI in Intervention group was 15.54 ± 1.09, and in Control group was 15.55 ± 1.07. Thus it was similar in both groups without any significant difference.

Table 10 – shows distribution of Body Mass Index (BMI) at day 15.

Table 10:- Distribution of Body Mass Index (BMI) at day 15

BMI	Intervention group	Control group	Total
≤ 14	2	4	6
>14 - ≤ 16	27	27	54
>16 - <18	26	24	50
Mean	15.75 ± 1.14	15.55 ± 1.07	-

(F=0.31, P=0.16)

At day 15, an increase in BMI in the Interventional group was seen while there was no change in BMI in the Control group. However the difference in BMI at day 15 was not significant (15.75 ± 1.14 vs. 15.55 + 1.07).

Table 11:- Distribution of Body Mass Index (BMI) at day 30

BMI	Intervention group	Control group	Total
≤ 14	1	4	5
>14 - ≤ 16	24	27	51
>16 - <18	30	24	54
Mean	16.07 ± 1.12	15.55 ± 1.07	-

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(F=0.36, P=0.0069)

At day 30, an increase in BMI in the Interventional group was seen while there was no change in BMI in the Control group. The difference in BMI at day 30 was statistically significant (P=0.0069) in intervention group (16.07 ± 1.12 vs. 15.55 ± 1.07).

Table 12 – Shows mean number of lapses in 6MWT in both Intervention and Control groups. Each lap was of 40 meters in length.

Table 12:- Distribution of mean 6MWT at day 15 and 30

Day	Intervention group	Control group	P value
0	4.50 ± 1.49	4.50 ± 0.84	0.5
15	4.58 ± 1.62	4.51± 0.75	0.37
30	4.68 ± 1.73	4.52± 0.79	0.24

No change in 6-minute walk distance was seen in the Control group. There was little increase in 6-minute walk distance in the Intervention group on day 15 as well as day 30. No significant difference was seen in 6-minute walk distance on any follow up.

Table 13:- Difference in mean SGRQ score from day 0 to day 15, day 0 to day 30, and day 15 to day 30.

Group	Day 0-15	Day 0-30	Day 15-30
Intervention	-4.88 ± 1.75	-10.37 ± 3.26	-5.49 ± 2.02
Control	-0.54 ± 0.99	-0.64 ± 0.99	-0.10 ± 0.22

Mean Difference between SGRQ score at day 0 to day 15 in the Intervention group = -4.88 ± 1.75. All patients in the Intervention group show an improvement in the SGRQ score. Mean difference between SGRQ score at day 0 to day 30 in the Intervention group = -10.37 ± 3.26. All the patients in the Intervention group show improvement from day 0 to day 30. Mean Difference between SGRQ score at day 15 to day 30 in the Intervention group = -5.49 ± 2.02.

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All patients in the Intervention group show an improvement in the SGRQ score. Mean Difference between SGRQ score at day 0 to day 15 in the Control group = -0.54 ± 0.99. 22 out of 55 patients in the control group show a change in SGRQ score on day 0 to day 15. 20 of these 22 patients show an improvement in their SGRQ score, while the remaining 2 show deterioration in same. Mean Difference between SGRQ score at day 0 to day 30 in the Control group = -0.54 ± 0.99. This value is same as difference in day 0 to day 15. No further change is seen.

DISCUSSION

In our study we studied the impact of nutritional support, in the form of protein rich powder fortified with several vitamins and mineral on quality of life, BMI, pulmonary function and exercise tolerance in moderate to severe COPD patients with BMI less than 18 at the time of recruitment. In our study, 110 COPD patients were included after exclusion of bronchial asthma on the basis of history (wheeze, allergy, seasonal variation) and post bronchodilator improvement in FEV1% of >12%. Both Intervention and Control group had 55 patients each of which 41 patients were male and 14 patients were female in each. Mean age of patients in the Intervention group was 61.64 ± 7.23 years and the mean age of patients in the Control group was 61.80 ± 6.93 years. The difference was statistically insignificant (P = 0.45). Mean age in our study is in line with a study conducted by Elisabeth et al[13].

In our study, mean Forced Expiratory Volume (in Litres) in first second (FEV1) at baseline in the Intervention group was 0.88 ± 0.37 and in the Control group was 0.86 ± 0.24 (P=0.34). The distribution of the patients according to baseline FEV1 in the 2 groups was also fair. After recruitment, standard bronchodilator pharmacotherapy was initiated in both groups and nutritional supplementation was started only in the Intervention group. On day 15, mean FEV1 in the Intervention group was 0.92 ± 0.37 and mean FEV1 in the Control group was 0.92 ± 0.25. Thus an increase in FEV1 was seen in both groups, however there was no significant difference between them (P=0.48). This increase in FEV1 can be credited to the standard bronchodilator pharmacotherapy give to all the patients in our study. On day 30, mean FEV1 in the Intervention group further increased to 0.99 ± 0.39 while the mean FEV1 in Control group was 0.92+/- 0.25. But no significant difference was seen in the mean FEV1 between the two groups on day 30 (P=0.13). This further increase in FEV1 in the intervention group, although statistically insignificant, is possibly due to increased BMI as a result of nutritional supplementation given to patients in the intervention group.

In our study, all recruited patients had BMI less than 18 kg/m^2 as per the inclusion criteria. At baseline, mean BMI in Intervention and Control group was 15.54 ± 1.09 and 15.55 ± 1.07 kg/m^2, respectively. There was no significant difference between both groups (F=0.44, P=0.49) at the time of recruitment. As previously mentioned nutritional supplement was given only to patients in the intervention group. In an article by Angus Deaton and Jean Drèze titled 'Food and Nutrition in India: Facts and interpretations', they reported a gradual decline in daily calorie intake among rural population from 1983 (2240 Calories/day) to 2005 (2047 Calories/day) due to various social and economic factors.[15] They also suggested that a further decline may be expected due to increasing costs of food items. Hugli et al reported that in patients with COPD, resting energy expenditure was reported to be 15–20% above predicted values and the increased energy required for work of breathing was suspected to account for the difference. Under controlled conditions, the basal metabolic rate was found to be higher in patients with stable COPD although the daily total energy expenditure was normal.[16] It seems that the patients compensated by reducing their level of spontaneous physical activity and related energy expenditure. In contrast to aforementioned findings,

Baarends et al reported that independent of resting metabolic rate, the total energy expenditure was elevated in patients with COPD as measured by the doubly labeled water method.[17]

In our study, calorie intake at baseline was similar in both groups (Intervention group 1655.64 ± 232.68 Calories/day; Control group 1658.73 ± 125.99 Calories/day; P=0.46). Following protein rich nutritional supplementation, calorie intake was significantly higher in Intervention group as compared to Control group on day 15 (1990 ± 193.10 vs. 1658.73 ± 125.99 Calories/day; P= <0.0001) as well as day 30 (1990.73 ± 193.49 vs. 1667.09 ± 123.39 Calories/day; P= <0.0001). On first follow up at day 15, a slight increase in mean BMI of the intervention group of our study was observed, However, this change in BMI was not significant (F=0.31, P=0.16). No change in BMI was seen in the control group (15.75 ± 1.14 vs. 15.55 ± 1.07 kg/m^2).On second follow up at day 30, a further increase in BMI in the Intervention group was seen while the mean BMI in the Control group remained unchanged (16.07 ± 1.12 vs. 15.55 ± 1.07 kg/m^2). The difference in BMI at day 30 was statistically significant (P=0.0069). Hence suggesting that nutritional supplementation significantly increases calorie intake which leads to a significant increase in BMI. However, calorie intake has to be kept high consistently for approximately a month so as to significantly increase the BMI.

Katsura H et al[19], Miravitlles M et al[20], and Stojkovic J et al[21] have all reported that COPD patients with low BMI have a poorer quality of life/ health status as compared to patients with normal BMI. We used St. George's Respiratory Questionnaire (SGRQ) to assess quality of life in our patients. At baseline, mean total SGRQ scores in intervention and control group were higher but similar (42.27 ± 2.93 vs. 41.43 ± 2.14; F=0.16, P= 0.23) in our patients in line with other studies[19-21] and those of Shoup et al who assessed 50 COPD patients, and showed that underweight patients presented higher SGRQ scores (indicating lower quality of life) as compared to patients with normal body weight.[18]

On first follow up at day 15, we reassessed quality of life by administering SGRQ and highly significant improvement was seen in intervention group patients as compared to controls (37.39 ± 3.50 vs. 41.33 ± 1.98; F<0.0001, P<0.0001). Mean improvement in SGRQ score from day 0 to day 15 in the Intervention group was -4.88 ± 1.75. On second follow up at day 30, a further significant improvement was seen in the intervention group SGRQ scores while the score remained the same in the control group (31.90 ± 4.65 vs. 41.33 ± 1.98; F<0.0001, P<0.0001). Mean improvement in SGRQ score from day 15 to day 30 in the Intervention group was -5.49 ± 2.02. A total mean improvement in SGRQ score from day 0 to day 30 was -10.37 ± 3.26. All the patients in Intervention group showed significant improvement in quality of life. This improvement in quality of life was possibly due to an increase in BMI in intervention group as a result of nutritional supplementation or due to the positive impact of micronutrients. No other study is available, assessing the impact of nutritional supplementation on QoL in COPD patients to the best of our knowledge. In our study, 6-minute walk test was used as a test for exercise tolerance and distance covered was reported in laps. An improvement was seen in intervention group as compared to the control group but it was not significant. It is in line with previous study that was conducted on patients with chronic respiratory failure with primary endpoint of finding improvement in 6-minute walk test with nutritional support, but no significant change was seen.[22]Possibly a larger follow up may unravel the benefit of nutritional supplement.

CONCLUSION

To conclude, it was observed from the study that malnutrition is frequently associated with moderate to severe COPD, leading to a poor health related quality of life. Further, nutritional supplementation is associated with high hopes of improvement in quality of life. Parallel improvements in lung function and exercise capacity may or may not be seen. Major limitations of this study are lack of double blinding and small number of patients. Larger multicentre studies of a longer duration are required to confirm the effects of nutritional therapy on parameters like QoL, lung functions and exercise capacity.

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