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Association between Nutrition Status and Cognitive Impairment among COPD Patients and age Matched Healthy Controls.

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ABSTRACT

Background: Nutritional abnormalities & Cognitive decline are frequent systemic manifestations associated with COPD. The study aimed to investigate and compare the cognitive & nutritive parameters in COPD with age matched healthy controls, and to find association between cognitive impairment & nutrition parameters. **Methods:** 100 subjects were recruited, and divided into two groups. Group I consisted of fifty consecutive physician diagnosed COPD patients & Group II included fifty healthy volunteers respectively. The spirometric parameters recorded were FEV1 (Liters), FVC (liters), FEV1/FVC ratio(% predicted),FEF 25%75%(liters/sec). Anthropometric measurements included Body Weight, Height and BMI measurements. Nutritional status was assessed using mini nutritional questionnaire (MNA). Body composition was assessed by four-frequency bioelectric impedance analysis (BODY STAT, QUADSCAN, USA). The following parameters were calculated: FFM, FFMI & FMI. The exercise capacity was assessed by the six minute walking distance test (6MWD). MMSE (mini mental state examination) and MOCA (montreal cognitive assessment) were used for cognitive function. All the recordings were compared within and between groups and correlation was also computed between MMSE, MOCA and MNA score. Results were analyzed using SPSS,version 16 & Pearson correlation coefficient. **Results:** We found out that COPD patients showed decline in all the parameters as compared to healthy controls. And, great strength of association was found between MNA & MOCA in COPD patients. **Conclusion:** Thus our study indicates that COPD patients have age independent loss of muscle mass as well as cognition, and loss of cognition is associated with decline in nutritional parameters or vice versa.

Keywords: Chronic Obstructive Pulmonary Disease, body mass index, bioelectric impedance analysis, fat mass index, fat free mass index, six minute walking distance, neuropsychological tests and mini nutritional assessment.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation with many recognized systemic side effects.[1] Since COPD often develops in long-time smokers in middle age, patients often have variety of other diseases related to either smoking or aging. COPD itself also has significant extra pulmonary (systemic) effects that lead to co-morbid conditions. Amongst these nutritional abnormalities are also very common in COPD patients.[2,3]

During the progression of the disease, physical strenuous activities and performing everyday actions become increasingly difficult. The problems experienced in everyday life negatively influence the social lives and emotional states of patients. It's possible that the nutritional impairment, decreased cognitive abilities & altered exercise capacity of the patient of COPD influences the quality of life.[4,5] Proper nutrition is important for cognitive function. Recently several studies have been conducted in older population (80-90 years) demonstrating the relationship of nutritional status with cognitive impairment, although it remains unclear how individual nutritional status influences cognitive function.[6,7] Cognitive impairment can also result in nutritional risk. The association of nutritional status with cognitive impairment has been confirmed in older population, but there are no relevant data from COPD patients and age matched healthy controls.

The goal of our study is to investigate whether nutritional and cognitive impairment in COPD patients is same with age matched controls. And, to study whether there is a correlation between the nutritional status and cognitive impairment seen in COPD patients.

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MATERIALS AND METHODS

Sample

The present study was conducted in outpatient clinic of department of Pulmonary Medicine, Indira Gandhi Medical College and Hospital, Shimla from August 2017 to November 2016. Institutional ethical clearance was obtained for the study by institutional review board. For this study we recruited hundred subjects, divided into two groups. A sample size of hundred subjects was calculated by PASS statistical software.

Group I consisted of fifty consecutive physician diagnosed COPD patients with at least primary school education & Group II included fifty healthy volunteers matched with COPD patients for age, level of education, IQ & socioeconomic background. The COPD patients consisted of 28 males and 22 females (30-70years; mean age 64.8 years).

All the patients were screened by a detailed history and physical examination as per inclusion and exclusion criteria. Enrolment criteria were:

1. Moderate to severe patients of COPD as per GOLD guidelines, 2013.[3]
2. Stable patients of moderate to severe COPD with no acute exacerbation for the past six week according to GOLD guidelines, 2013.[3]
3. COPD patients with baseline SpO2≥90%.

Control group consisted of 35 males and 15 females (30-70 years of age; mean age 62 years), recruited on the basis of same criteria for age and smoking history. They were current or past smokers who did not suffer from pulmonary diseases either now or in the past. Neither lung symptoms nor physical examination deviations were stated in their cases. The results of spirometry tests in these subjects were normal.

The exclusion criteria for all the subjects were:

1. Those subjects with historic or clinical evidence of pulmonary diseases other than COPD.
2. Subjects with active or past diseases that could affect nutritional state disorders (diseases of heart, liver, kidney, diabetes, neoplasm's) as well as those subjects using steroids, diuretics were excluded from the study.
3. Subjects who were symptomatic for neuromuscular, musculoskeletal, peripheral vascular diseases, cardiovascular diseases which limited their capacity to perform six minute walk test.
4. Diagnosis of major neurological or psychotic disorders, taking medication affecting central nervous system. No visual and hearing impairment.
5. Major clinical illness that could affect cognitive functioning (cancer, diabetes mellitus, chronic heart failure).

The purpose of the study was explained to the subjects and written consent was obtained thereof. Institutional ethical clearance was obtained for the study by institutional review board. All the patients as well as controls were subject to detailed demographic history, occupational history, history of smoking habits, biomass exposure, history of disease with treatment history and history of any co-morbidities and complications. All the selected patients & controls were subjected to thorough medical examination and various routine investigations such as complete blood count, lipid profile, blood sugar, serum protein, blood urea, serum creatinine, serum electrolyte profile, ankle brachial ratio. Plain chest radiograph, resting electrocardiogram and echocardiography were also performed to rule out any co morbidity and complications of COPD.

Spirometry

All the patients performed post-bronchodilator spirometry with an electronic portable PC based spirometer with printer (Vitalograph Compact Buckingham, England) which fulfilled the accuracy and precision criteria as per American Thoracic Society/ ERS.[8] The patients were staged as per GOLD guidelines, 2013 (post bronchodilator FEV1/FVC ratio<70% predicted),[4] mild (FEV1≥ 80% predicted), moderate (50%≤FEV1<80% predicted), severe (30%≤FEV1<50% predicted), and very severe (FEV1<30% predicted) or FEV1<50% predicted plus the presence of signs of chronic respiratory failure. Spirometric parameters were recorded as absolute measurements and percent predicted for race, age, gender and height. The spirometric parameters recorded were FEV1 (Liters), FVC (Liters), FEV1/FVC ratio (percent predicted), FEF 25%75% (Liters/sec).

Anthropometry

Body weight was measured on a calibrated balance to the nearest 0.1 kg while patients were barefoot and wearing light clothing. Body height was measured to the nearest 0.5 cm while patients were barefoot and standing with their backs and heels touching a vertical bar. BMI was calculated as weight divided by height squared (kg/m2).

Nutritional assessment

Body composition was assessed by four-frequency bioelectrical impedance analysis (BODY STAT, QUAD SCAN, and USA). All body composition measurements were performed between noon and 2 p.m. The patients fasted on the day that the measurement was performed and did not ingest coffee, tea, chocolate or alcoholic beverages for 48 h prior to the measurement. During the measurement, patients lay in a supine position with their limbs slightly apart from their bodies. Two electrodes were positioned on the dorsal surface of the right hand, and two additional electrodes were positioned on the dorsal surface of the right foot. The FFM was calculated using an equation that has been

specifically validated for patients with respiratory diseases. FM was calculated as total body weight minus FFM. FFM index (FFMI) and FM index (FMI) were calculated by dividing the body weight (in kg) of FFM and FM, respectively, by height (in m) squared in order to adjust for body surface area. Under these conditions, bioelectrical impedance analysis measurements are considered accurate and comparable to other techniques used to assess body composition. The following parameters were calculated: FFM (kg), FFMI (kg/m2), FM (kg) and FMI (kg/m2).

MNA

MNA was used to assess the nutritional status along with body composition and anthropometric measurements. The MNA questionnaire explores the three domains of the nutritional status: body composition, energy intake and body functionality.[9] It consists of 18 items: four explore the body composition (BMI, arm and calf circumferences, and weight loss in the previous 3 months), six explore the energy intake (number of total, proteic and vegetable- and fruit-based daily meals, reduction of appetite, hydration, and feeding autonomy) and eight explore the body functionality (number of drugs, acute events, autonomy in daily life and in transfers, pressure ulcers, cognitive status, patient's perception of his/her own nutritional status and own health status compared to the other elderly persons) (9). The MNA questionnaire was completed according to the developers' instructions (www.mna-elderly.com). Participants are classified by MNA scores as follows: normal nutritional state (score of 24-30); at risk of malnutrition (score 17-23.5); and malnutrition (score <17).

Assessment of cognitive function

The neuropsychological tests assessed cognitive domains of memory, verbal tasks, attention, executive functioning and mental flexibility. A psychometric battery was performed in a fixed sequence and included:

Montreal Cognitive Assessment test (MOCA) (10)

Standardized Mini Mental Status Examination (MMSE) (11)

Exercise Capacity

The exercise capacity was assessed by the six-minute walking distance test (6MWD), which is validated and reliable for evaluation of the exercise capacity of patients with COPD. The 6MWT was performed according to the ATS guidelines, 2002(5). Subjects were asked to walk as fast as they can, along a 30 m long and straight hospital hallway marked at intervals of meter each. All of the patients were familiarized with the test procedure prior to testing. Patients were instructed to walk as fast as possible, aiming to complete the longest possible distance in the allotted time. At each full minute during the test, the patients were verbally encouraged with a standardized incentive phrase. The patient was allowed to stop if symptoms of significant distress occurred, like severe dyspnea, chest pain, dizziness, diaphoresis, or leg cramps. However, the patient was asked to resume walking as soon as possible, if he or she could. At the end of six minutes, the patient was asked to stop. Each patient's result was expressed as an absolute value (meters).

Statistical Analysis

Statistical analysis was done using SPSS version 16, statistical software. Bivariate comparison between COPD patients and healthy controls was done by independent student t-test. The distribution of data is presented as Means ±Standard Deviation. The association between the indicators of cognitive function and MNA score was assessed using Pearson correlation analysis.

RESULTS

The spirometry, anthropometry, body composition, exercise capacity & cognitive parameter results are presented in Table 1, in which comparison is shown between the study and control group. There were no statistically significant differences among the groups in age, height and smoking history. As per inclusion criteria control group has normal spirometric data whereas most of the COPD patients fall in II & III stage according to Gold staging.

Table 1: Comparison of socio-demographic, BIA measurements and 6MWD in COPD patients with Healthy Controls.

Variable	COPD Patients (N=50)	Healthy Controls (N=50)	p value
Age (years)	64.8	62	0.08
Sex (M/F)	28/22	35/15	0.43
Education (1-6)	4	4	0.56
Smoking (packs/yr)	39.5±18.46	36.45±14.48	0.06
BMI (kg/m2)	19.68±1.28	20.13±0.74	0.01
FEV1 (liters)	1.09±0.78	2.84±0.46	0.004
PEFR (liters/min)	3.46±1.67	6.84±1.24	0.06
FVC (liters)	1.75±0.11	3.64±0.38	0.006
FEV1/FVC %	60.52±6.352	73.04±4.228	0.003
FMI (kg/m2)	6.992±2.4006	8.644±3.2236	0.84
FFMI (kg/m2)	13.36±0.37	20.18±0.18	0.001
6MWD (meters)	392.30±124.856	425.20±224.122	0.84

*p<0.05 is statistical significant.

Body composition: Body weight: The study was conducted in Shimla (Himachal Pradesh), where due to difficult terrain & lifestyle it is very difficult to enroll overweight/ obese subjects for study (in control as well as study group). BMI: The calculated BMI in the study and control group were 19.68±1.28

& 20.13±0.74 respectively. The BMI (p<0.01) was significantly higher in control group. Bioelectrical Impedance Analysis: FM, FFM, FMI & FFMI were found to be significantly lower in COPD patients as compared to healthy controls. FMI: The average fat mass index in both groups was calculated & compared. Mean FMI was 6.99±2.4in pts and 8.64±3.2 in control group. The control group had higher fat mass as compared to patients. (p<0.84) FFMI: Average FFMI in the patients and control group were found to be13.36±0.37 & 20.18±0.21 respectively. Comparison analysis was made in both groups. A significant difference of FFMI between the groups was found. In the study group FFMI (p<0.001) was significantly lower than in controls. Exercise capacity: Exercise capacity was assessed using 6MWD test. Walking distance in absolute values (meters) was found to be 392.30±124.85& 425.20±224.12 respectively in the COPD & control group. Walking distance was found to significantly lower in the patients of COPD.

Table 2: Comparison of nutrition and cognitive parameters in COPD patients with Healthy Controls.

Variable	COPD Patients (N=50)	Healthy Controls (N=50)	p value
MNA	17.96±3.630	22.29±2.285	0.0001
BMI	19.68±1.28	20.13±0.74	0.01
FFMI	13.36±0.37	20.18±0.18	0.001
MMSE	23.26±3.186	27.06±2.004	0.0001
MOCA	22.16±3.599	26.98±1.942	0.0001

*p<0.05 is statistical significant

[Table 2] shows the comparison of cognitive and nutritional parameters in COPD patients with controls. All the parameters are significantly higher in healthy controls as compared to COPD patients, showing altered nutrition as well as cognition in COPD patients.

Table 3: Correlation between cognitive parameters and nutrition in COPD patients.

	MNA Score Correlation	p value
MMSE	0.1782	0.2157
MOCA	0.2722	0.055

Table 4: Correlation between cognitive parameters and nutrition in Contols.

	MNA Score Correlation	p value
MMSE	-0.0863	0.5513
MOCA	0.1047	0.4692

*p<0.05 is statistical significant

[Table 3&4] correlations between cognitive function and indicators of nutrition are shown in [Table 3&4] in COPD patients and controls respectively. MNA scores significantly correlated with MOCA scores in COPD patients. We didn't find significant correlation with the other indicators.

DISCUSSION

Although COPD is primarily a disease reflecting lungs, it produces wide ranging systemic consequences such as nutritional changes, skeletal muscular dysfunction, cardiovascular and neurological effects.[6] Impaired cognitive status and Malnutrition are a frequent complication in COPD and an important predictor of functional capacity, mortality and morbidity. 7Malnutrition is associated with structural and metabolic changes in peripheral and respiratory muscles, thereby aggravating preexisting dyspnoea and exercise intolerance.[12,13] Cognitive dysfunction reduces the level of functioning assessed by activities of daily living and is associated with poor compliance with both medication and oxygen therapy.[14] Many studies have confirmed declines in number of cognitive functions, such as memory, reaction time, abstract reasoning skills and complex visuomotor processes in COPD patients. Several studies have confirmed lower values of body composition parameters (BMI, FMI, FFMI) in COPD patients and the change in these parameters keeps on increasing with increased severity of disease.[15] But, loss of skeletal muscle mass is described not only in patients with COPD and other consuming diseases,[16] but also in healthy elderly.[17] Thus, the main goal of our study was to compare the nutrition status parameters, exercise capacity and cognitive parameters of COPD patients with age matched healthy controls.

And whether there is an association between cognition and nutrition. In the present study we used body weight, BMI, FMI, FFMI and MNA score as indicators for assessment of nutrition & MMSE, MOCA for cognitive function. We found significant difference in body mass of subjects on basis of body weight and BMI assessment between the study and control group. In other studies, malnutrition estimated by BMI assessment was seen in 3.9% (18), 6.6 % & 23 % patients.[19,20] In several studies BMI in range of 18.5- 25 kg/m2 is considered normal, consequently the % of subjects with malnutrition decreased in these studies. Surrogate measures such as BMI alone give no indication of body composition, muscle mass or nutritional state. Thus, malnutrition requiring intervention can exist in spite of normal to high BMI.[21] In a study by Spanish researchers (Soller & colleagues), in 62.9%of patients without loss of complete body mass (20.7% of them with over nutrition & obesity), nutritional status disorders were confirmed.[22] In a study by Schols. et al, 14.8% of patients with normal body mass , had significant FFMI loss.18 Analysis of body composition by BIA is simple, quick & non-invasive technique which provides the assessment of body composition by division into components (FM& FFM).[21] BIA provides qualitative information on body composition that is it can detect where loss is occurring (fat/muscle) & pathogenesis of weight loss.[23] In current study, the body composition parameters FM& FFM showed well defined differences of nutritional status between the two groups. Significant difference was found in

FFMI ($p<0.001$) between COPD patients and control group. COPD patients more frequently lost muscle mass, whereas for those from control group greater muscle was characteristic. Although BMI was lower in COPD patients as compared to controls, we found significantly worse results concerning muscle mass and body composition among the study group compared to controls. The mechanisms leading to muscle wasting in COPD are still uncertain. Accelerated muscle proteolysis is considered the primary cause of the loss of lean body mass, not only in COPD, but also in many other chronic disorders.[16] Physical inactivity, hormonal dysfunction, increased levels of cytokines play important roles in muscle wasting.[18] In current study, we found that exercise capacity ($p<0.84$) assessed by 6MWD was lower in COPD patients as compared control group. A significant strength of association was also found between decreased MOCA score & MNA score in COPD patients. The correlation between cognitive parameters and nutritional status in controls was insignificant. Thus, cognitive decline might affect the nutritional parameters in COPD patients, decreasing functionality of the patient group and vice versa. Our, findings suggest that COPD patients show a significant decrease in BMI, FFMI, MNA score, MMSE, MOCA score and exercise capacity as compared to healthy controls.

In conclusion, So, nutritional intervention, increase use of load bearing capacity through increase in physical exercise and mental ability exercises (like Sudoku, meditation) can be incorporated in treatment regimen of COPD patients, to improve body functionality, quality of life in these patients.

CONCLUSION

In the present study we found a highly significant decrease in nutritional as well as cognitive parameters in COPD patients as compared to age matched healthy controls. Also we found a significant correlation of MOCA score with MNA score in COPD patients. Thus, suggesting that decreasing cognitive and nutritive parameters in COPD patients may contribute to reduced functional capacity, morbidity & mortality.

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