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Cognitive Domain Impaired In COPD Patients And Its Correlation With Exercise Capacity In COPD Patients.

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ABSTRACT

Cognitive dysfunction is an important systemic effect of COPD affecting various cognitive domains in these patients. The purpose of the present study was to assess type cognitive skills affected in COPD patients in comparison with healthy controls and to correlate the impaired cognitive skills with exercise capacity in COPD patients. In a hospital based prospective case control study, we examined fifty consecutive COPD patients and age, IQ and education matched fifty healthy controls. All the subjects were assessed for cognitive skills of orientation, attention, memory, visuo-perceptual abilities and executive functions by neuropsychological battery of tests and 6 minute walking test was used for exercise capacity. We found that COPD patients showed impairment in trial making B, Digital substitution ($p<0.001$) compared to the controls. They also performed poorly than controls on MOCA, MMSE and Trial making B($p<0.001$) . Absolute 6MWD was less in COPD patients than controls. Cognitive impairment was found to be associated with decreased exercise capacity. Cognitive skills of executive functioning are mostly affected in patients of COPD .The impairment of cognition is also observed to correlate with decreased exercise capacity affecting functional status of COPD patients.

Keywords: COPD, Cognitive dysfunction, 6MWD (6Minute Walking Distance)

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation that is usually progressive and not fully reversible (1). Although defined by abnormal spirometry, COPD is well recognized as more than a respiratory disease. Indeed, extra pulmonary features and co-morbidities occur frequently in patients with COPD and include, for example, decreased muscle mass, cardiovascular disease, anemia and osteoporosis. Furthermore, psychological problems and cognitive impairment are common in patients with COPD. (2)

Since COPD often develops in long-time smokers in middle age, patients often have a variety of other diseases related to either smoking or aging. Cognitive and nutritional abnormalities are very common in COPD patients (3, 4).

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 impaired cognition, nutritional impairment, altered exercise capacity of the patient of COPD influences the quality of life (5, 6). It is clear that COPD is a multisystem disorder, although it remains unclear whether individual cognitive function influences exercise capacity.

The goal of this study is to find out different cognitive domains affected in COPD patients in comparison to age matched healthy controls. Second aim was to find out if there was any correlation in cognitive impairment and exercise capacity in COPD patients. Decreased cognitive flexibility can lead to problems with patient compliance with drug treatment, smoking abstinence and functional independence, thus making pulmonary rehabilitation challenging.

MATERIALS AND METHODS

A hospital based prospective study was done on fifty COPD patients and fifty healthy controls. Controls were matched with COPD patients for age, level of education, IQ and socioeconomic background. Institutional ethical clearance was obtained for study by institutional review board. The purpose of the study was explained to both the groups and explicit written consent was obtained thereof.

The inclusion criteria for cases were

- Stable COPD patients who were diagnosed and staged as per GOLD (2013) guidelines(7) with no exacerbation for past two months.
- Age of 30-60 years.
- At least Primary School Education.

The controls were enrolled during the same study period as COPD patients, with normal spirometric pulmonary functions and without any lung disease (present or any time in past). Both the groups underwent a thorough clinical examination to rule out psychopathology, chronic debilitating medical disorders, endocrinal disorders, history of alcohol/drug abuse and any medication known to affect cognition and any co morbidity and/or complications of COPD.

All the patients were subjected to post-bronchodilator spirometry (Vitalograph Compact Buckingham, England) and were staged as per GOLD guidelines, .2013(7)The spirometric parameters recorded were FEV1 (litres), FVC (litres), FEV1/FVC ratio (percent predicted), FEF 25%-75% (liters/sec) and peak expiratory flow (PEFR) (liter/sec).

Cognitive impairment was evaluated by validated psychometric questionnaire.

These neuropsychological tests assessed cognitive domains of memory, verbal tasks, attention, executive functioning and mental flexibility. A Psychometric Test Battery was performed in a fixed sequence and lasted for approximately 50 minutes.

- Montreal Cognitive Assessment Test (MOCA)(8)
- Standardized Mini Mental Status Examination (MMSE) (9)
- Digit Symbol Substitution Test of Wesher Adult Intelligence Scale (10)
- Trail Making Test B of Haldstead Reirtan B (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. Pearson correlation was used to assess correlation of the cognitive battery of tests with the exercise capacity. Statistical significance was accepted at a p value of <0.05. Statistical analysis was done using SPSS version 16, statistical software (SPSS, Inc., Chicago, IL, USA).

RESULTS

The spirometry, anthropometry, body composition & exercise capacity 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 demographic characteristics in the COPD patients and control group.

Variable	COPD Patients	Healthy Controls	p value
	(N=50)	(N=50)	
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	0.69

*p<0.05 is statistical significant.

Table 2: Comparison of Exercise Capacity and Cognitive Parameters in COPD patients with Healthy Controls.

Variable		COPD Patients		Healthy Controls		p value
		(N=50)		(N=50)		
DST		28.42±2.24		47.14±1.12		0.0001

TMT		223.44±26.56		94±52.24		0.0001
MMSE		23.26±3.186		27.06±2.004		0.0001
MOCA		22.16±3.599		26.98±1.942		0.0001
6MWD (meters)		392.30±124.856		425.20±224.122		0.69

*p<0.05 is statistical significant

Table 2 summarizes that the cognitive scores for Digital Substitution Test, Trail Making Test, MOCA and MMSE scores were significantly lower in COPD patients as compared to controls. 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 3: Correlation between cognitive parameters and exercise capacity in COPD patients

cognitive parameters			6MWD	
			correlation	p value
MMSE			0.41	(0.00)
MOCA			0.30	(0.03)
TMT			0.33	(0.02)
DST			0.34	(0.02)

*p<0.05 is statistical significant

The strength of association of neuropsychological battery of tests and exercise capacity was done by Pearson correlation coefficient. The correlation of 6MWT with the cognitive battery of tests revealed that there was statistically significant association between cognitive functioning (as assessed by DST(r=0.34), TMT(r=0.33), and MOCA(r=0.30) & MMSE(r=0.41)) and exercise capacity in COPD patients.

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) 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.(12-16) 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. (17)

The main goal of our study was to find the major domains of cognition impaired with COPD and to correlate the impaired cognition with exercise capacity .In our study we tested for cognitive function of attention, language, memory and executive functions. We observed that although all the domains of cognition were variably affected psychomotor processing with visuospatial and motor constructional abilities were most affected functions such as copying a clock, trail making test. Stuss et al. reported that hypoxia in COPD results in impaired performance in tasks requiring attention allocation.(18) Further, an impairment of executive motor constructive tasks can also be attributed to muscle weakness frequently seen in COPD patients. Patients also scored less on MOCA & MMSE scores. A lower performance can be due to contributing factors like oxidative stress, systemic inflammation, tissue hypoxia and direct toxic effects of nicotine. (19,20)We didn't find significant differences in 6MWT between controls and COPD patients, although the 6MWD was less in COPD patients. COPD influences aspects related to body composition & muscle structure. And both these factors adversely affect the exercise capacity. Whether loss of skeletal muscle mass leads to decreased exercise capacity or it is a multi-factorial process, because of severe obstruction (exercise intolerance), airflow limitation (dyspnoea) or high resting energy expenditure is debatable. It is possible that decreased functional exercise capacity might be related to tendency to ignore more often, given guidelines or instructions because of cognitive impairment. We found significant correlation in cognitive parameters and exercise capacity, impaired memory or executive functioning might lead to decreased exercise capacity, affecting the functional status and pulmonary rehabilitation of COPD patients. Also, Roncero and colleagues found an association between cognitive functioning and health related quality of life.(21) In view of this, we believe that detecting patients with CI may improve overall care processes by for example including cognitive training strategies which can be divided into restorative and compensatory strategies.(22) Restorative strategies attempt to improve functioning in specific cognitive domains or domains of functioning, such as ADLs, social skills, and behavioral disturbances. Compensatory cognitive strategies, such as incorporating daily routines with fewer tasks and/or pacing tasks, and providing the patient with electronic notes, reminders, calendars, or planners to keep track of activities and appointments, (23) can be used to minimize functional and psychological problems experienced by patients. Health-care professionals should be aware of cognitive deficits in order to tailor clinical interventions to the individual patient and to determine the required type of assistance and environmental modification. Compensatory strategies have been applied in other patients, such as Alzheimer, multiple sclerosis, and patients with brain injuries.(23,24) Evaluation of these cognitive training strategies in COPD is needed to explore which are beneficial and should be incorporated in the overall care. Since we found that patients with COPD have cognitive impairment, and an intellectually stimulating atmosphere may boost cognitive performance, longitudinal studies are needed to assess premorbid cognitive ability and to incorporate cognitive reserve and cognitive loss over time in relation to clinical characteristics of this study population. Our study had several limitations that should be acknowledged. First, our sample size was small, which may partially account for weak association between some measures in our study. Although participants were stringently selected to avoid the influence of possible confounding variables, such as diabetes, cerebro-vascular disease and major chronic diseases, there is a possibility that other chronic or subclinical diseases which were not included in the analysis may also have contributed to cognitive decline. We did not perform neuro-imaging studies in our study population to identify regions of brain which play a critical role in the neural control of cognitive function. However, it was costly and is not usually recommended for COPD patients. Future studies should assess how many neuropsychological tests are needed to do a first cognitive screening in clinical practice with a comparable sensitivity in order to detect both general and domain-specific CI.

CONCLUSIONS

Cognitive impairment in patients with COPD is prevalent, irrespective of clinical characteristics. In the present study, we found a highly significant lower performance in cognitive tests like trail making, copying landmark, MMSE score, MOCA score in COPD patients as compared to controls . Thus suggesting that low lung functioning may contribute to cognitive disorders. The decreased cognitive function was related to exercise capacity which could affect functionality of patients. Based on our observation; we would like to suggest that a routine inclusion of the neuropsychological battery of test can be helpful for planning therapeutic and optimal care programs for COPD patients with cognitive impairment. We hope that our study help to implicate the importance of the assessment of cognition in subjects suffering from COPD.

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