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A Correlation between Parasympathetic activity and Chronic Obstructive Pulmonary Disease

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ABSTRACT

Background: Chronic Obstructive pulmonary disease is a chronic inflammatory lung disease that causes obstructed airflow from the lungs. It consists of a group of chronic and slowly progressive respiratory disorders characterized by decreased expiratory flow during forced exhalation. COPD broadly consists of two pathological conditions- Emphysema and chronic bronchitis. Autonomic abnormalities have been consistently found in COPD. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases.

Aims and Objective: This study was done to study changes in parasympathetic activity in patients of COPD and to compare them with normal subjects.

Methods: The study was carried out on 60 male COPD patients and 40 healthy subjects as controls. For testing parasympathetic activity heart rate variation with postural change, valsalva manoeuvre and deep breathing were recorded.

Results: The mean values of 30:15 ratio showed significant decline in COPD patients as compared to normal subjects. The variation in heart rate in response to valsalva manoeuvre and in response to deep breathing was highly significant between the two groups.

Conclusion: From the results thus obtained, it can be concluded that there is significant decrease of parasympathetic nervous system activity in patients of COPD as compared to controls.

Key words: Chronic Obstructive Pulmonary Disease, parasympathetic activity, valsalva manoeuvre, deep breathing test, heart rate variation.

INTRODUCTION

COPD is a common, preventable, and treatable chronic lung disease effecting small airways of the lungs leading to limitation of airflow in and out of the lungs. A number of processes cause the airways to become narrow, like - destruction of parts of the lung, mucus blocking the airways, and inflammation and swelling of the airway lining. Chronic obstructive pulmonary disease is characterized by irreversible decline of FEV_1 (forced expiratory volume in first second), dyspnoea and progressive deterioration of health status. It is the third leading cause of death worldwide, causing 3.23 million deaths in 2019.Over 80% of these deaths occurred in low- and middle-income countries. [1] Forced expiratory volume in 1st second is the spirometric index most commonly used to detect the presence of COPD, to mark its severity and to determine bronchodilator response.[2] Air pollution both outdoor and indoor, tobacco smoking (active and passive), biomass fuel, asthma in childhood and occupational hazards are major risk factors for

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COPD due to which it has been on the rise in India.[1,3] The systemic effects of COPD include oxidative stress and altered circulating levels of inflammatory mediators and acute phase proteins.[4] Cardiovascular disease is one of the important causes of death and hospitalization among patients with COPD.[5] Neurohumoral activation has been shown to be present in hypoxic patients with COPD which may have negative consequences namely inflammation, cachexia, skeletal muscle dysfunction and cardiovascular disease.[6] Abnormalities in both parasympathetic and sympathetic nervous system in COPD patients have been demonstrated in many studies.[7] so the present study was conducted to record changes in parasympathetic activity in male patients with COPD and findings compared to observations recorded in normal subjects.

MATERIAL AND METHODS

The study was carried out on 60 male Chronic Obstructive Pulmonary disease patients and 40 healthy controls and these were designated as group-I and group-II, respectively. Study group subjects were taken from TB and Chest department of the institute and healthy controls were taken from the general population. Written informed consent was taken from all the subjects. Permission for the study was taken from the institutional ethical committee. Patients with coronary artery disease,hypertension, encephalopathy and diabetic neuropathy were excluded from the study. Patients taking medications likely to interfere with the tests, such as vasodilators, angiotensin-converting enzyme inhibitors, and antihypertensive agents, were also excluded. Detailed history and physical examination of all the subjects and patients was carried out. For testing parasympathetic system following tests were done:

1. Heart rate response to postural change (30:15 ratio).
   The subject was made to lie quietly on the couch and the heart rate was continuously monitored on the electrocardiograph. The subject was then asked to stand unaided and the point at starting to stand was marked on electrocardiograph.The shortest R-R interval at or around 15^{th} beat and the longest R-R interval at around the 30^{th} beat after standing was measured. Ratio of 1 or less than one is considered abnormal.
   30:15 ratio= Longest R-R interval at beat 30 after standing/shortest R-R interval at beat 15 after standing.
2. Heart rate response to valsalva manoeuvre (Valsalva ratio)
   The subject was asked to exhale into the mouth piece connected to mercury manometer and holding it at a pressure of 40mmHg for 15sec. during this manoeuvre and 45 seconds subsequent to this, ECG was recorded and valsalva ratio calculated, which is the ratio between maximal R-R interval and minimal R-R interval. Ratio of less than one or equal to 1.10 is considered as abnormal.
3. Heart rate variation with deep respiration
   Deep breathing at six breaths a minute is the most convenient and reproducible technique. In this test the subject was asked to breathe deeply at six breaths per minute i.e. five seconds in and five seconds out for one minute. ECG was recorded throughout the period of deep breathing. The results of this test were expressed as the mean of the difference between maximum and minimum heart rates for the six measured cycles in beats per minute. Value of less than or equal to 10 beats per minute is considered as abnormal.

RESULTS

Table no. I depicts the comparison of age between the two groups. It shows that the average age in group-I (COPD patients) is 54.31±2.11 and in group-II (healthy controls) is 53.21±1.11years.

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The two groups were age matched, so difference of age statistically non-significant (p>0.05) in the two groups.

Table I: Comparison of Age (Mean±SD) between the COPD patients and Normal subjects

Groups	Mean	± SD	P value
COPD patients (Group-I)	54.31	2.11	0.083
Controls (Group-II)	53.21	1.11	

Table no. 2 shows the comparative values of parameters of parasympathetic nervous system activity in COPD patients and healthy controls. The mean values of 30:15 ratio during evaluation of Parasympathetic functions, in group-I (COPD) was 1.03±0.05 as compared to mean value of 1.05±0.04 in group-II (Normal subjects). The variation was significant at 5%significance level (p<0.05).

Table 2: A comparative data of Parasympathetic Nervous System activity in COPD patients (group-I) & Normal healthy subjects (group-II)

Parameters	Group-I (COPD)		Group-II (Normal)		p-value
	Mean	±SD	Mean	±SD	
30:15 Ratio	1.03	0.05	1.05	0.04	<0.05
Valsalva ratio	1.12	0.06	1.26	0.02	<0.001
DBT	8.66	2.56	17.79	1.82	<0.001

P<0.05 Significant at 5%significance level
P<0.001 Highly Significant

The mean values of Valsalva ratio in group-I (COPD) & in group-II (Normal subjects) were 1.12±0.06 and 1.26±0.02, respectively, showing again statistically highly significant (p<0.001) variation.

The mean value of heart rate variation during Deep Breathing Test (DBT) in group-I (COPD) was 8.66±2.56 whereas it was 17.79±1.82 in group-II(Normal subjects). The variation was again statistically highly significant (p<0.001).

From the results shown above it is observed that there is significant reduction in parasympathetic activity in patients of COPD (group-I) as compared to that in normal healthy subjects (group-II).

DISCUSSION

COPD is not just one disorder but consists of different conditions. Chronic bronchitis and emphysema which most of the times occur in association are grouped under the umbrella term COPD.[8] COPD is not restricted to pulmonary inflammation and structural remodeling, but systemic alterations in the biochemical and organ function too. Persistent hypoxia may be associated with autonomic dysfunction in COPD patients.[9] This study was done on males because smoking is most prevalent in males and thus causing higher incidence of COPD in them.[10] The 30:15 ratio findings of our study are consistent with another study done on hypoxic COPD patients. It was observed that patients with autonomic neuropathy had a heart rate which continued to rise throughout the observed time and thus had a ratio of ≤1.[11] valsalva ratio another tool to assess parasympathetic activity, showed highly significant variation between two study groups. Our results are in accordance with another study done on 35 patients with hypoxaemic COPD and seven age matched normal subjects.[12] Another study showed depressed heart rate

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variation in the heart rate response to different stimuli, such as the Valsalva manoeuvre in COPD patients.[13]

Heart rate variation with deep breathing showed a highly significant variation, supported by another study by Stewart AG etal., who observed that patients with an autonomic neuropathy lose this heart rate variability. [12] These findings were consistent with some other studies as well.[14,15] The vagus nerve modulates the rate of sinoatrial discharge. The possibility exists that an abnormality in the parasympathetic control of airway caliber may be reflected by a parallel change in the control of heart rate.We found that in patients with COPD, there was a shift in autonomic nervous system activity that suggests a relative increase in parasympathetic tone. Intrathoracic pressure, increased by breathing against resistance, can affect cardiac function and blood pressure. Large intrathoracic pressure swings, such as those that occur in obstructed breathing, may cause fluctuation in cardiac performance and arterial blood pressure.[16] Reduction in the parasympathetic variability may be explained by the demonstration that the adrenergic system may have a modulatory influence on cholinergic neurotransmission.[17]

CONCLUSION

This can be concluded that there is significant decrease of parasympathetic activity in patients of chronic obstructive pulmonary disease as compared to normal subjects. Study of autonomic cardiopulmonary control in patients with COPD may have important implications with regard to prognosis in this condition. A further research work to probe the autonomic nervous system dysfunction in COPD patients in relation to the duration of the disease and the variation in incidence of COPD among males and females is recommended, which is the limitation of our study.

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