Original Article

Physiology Section

Autonomic Nervous System Changes in Chronic Obstructive Pulmonary Disease (Copd) Patients

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ABSTRACT

Introduction: In the patho-physiology of chronic obstructive pulmonary disease (COPD), changes in the autonomic control of the cardiopulmonary functions are important. The quantification of the para-sympathetic and the sympathetic activity may be useful in treating COPD patients.

Aims And Objectives: To observe the changes in the autonomic activity in COPD patients.

Material And Methods: The present study was conducted on 90 (male) COPD patients and 30 controls. The para-sympathetic activity tests i.e. the heart rate variation with deep respiration, the valsalva manoeuver, the standing to lying ratio and postural changes (30:15) and the sympathetic activity tests i.e. orthostasis, the cold pressor test (CPT) and the blood pressure response to a sustained hand grip were conducted. An FEV_1 which was >80% was the criteria for the healthy control subjects.

Results: The heart rate variation to the para-sympathetic stimuli was less in the COPD patients as compared to that in the healthy subjects. The fall in systolic blood pressure (SBP) in response to standing was lesser while the rise in diastolic blood pressure in response to a sustained hand grip was higher in the COPD patients. A significant rise in the SBP in response to CPT was observed.

Conclusion: The cardiac para-sympathetic activity was significantly reduced in COPD, while there was sympatho-excitation.

Key Words: COPD, Valsalva manoeuver, 30:15 ratio, S/L ratio, DBT, CPT, HGT, Orthostasis

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) broadly consists of two pathological conditions i.e. emphysema and chronic bronchitis. These two conditions are clinically grouped together and are referred to as COPD, since many patients have the overlapping features of damage both at the acinar and the bronchial levels [1]. Over the past decade, there has been a growing consensus that COPD includes airway obstruction that is not completely reversible [2]. The term "partial reversibility" defines patients who in fact have "reversibility" in response to a therapy with corticosteroids or a bronchodilator and yet their best FEV1 and FEV1/FVC ratios classify them as having airflow limitation [3]. Globally, by 2020, COPD is expected to rise to the 3rd position as a cause of death and to the 5th position as a cause of loss of disability adjusted life years (DALYs) according to the baseline projections which were made in the Global Burden of Disease Study (GBDS) [4].

Autonomic abnormalities have consistently been found in COPD. These span from a reduction in the heart rate variability, a reduction in the respiratory sinus arrhythmia and a reduction in the baroreflex sensitivity, together with a direct increase in the muscle sympathetic nerve activity [5]. COPD is an independent risk factor for cardiovascular disease. Given the established negative connotations of the neurohumoral activation for cardiovascular morbidity and mortality, it is reasonable to hypothesize that the neurohumoral activation in COPD exposes the COPD patients to an increased cardiovascular risk [6].

MATERIALS AND METHODS

The present study was conducted in the department of Physiology, Government Medical College, Amritsar. It was carried out on 90 male chronic obstructive pulmonary disease (COPD) patients and 30 healthy controls and these were designated as group-I and group-II, respectively.

The study group subjects (COPD), were selected from the TB and Chest hospital, Amritsar. Thirty healthy controls subjects were selected from the general population. A written informed consent was obtained from the subjects after fully explaining to them the elements which were contained in the research protocol.

A detailed history of the subjects was taken and a physical examination of all the subjects and the patients was carried out. An ECG for autonomic function testing was done by using a Recorder and Medicare System, Chandigarh, by using a standard limb, lead-II. The blood pressure was recorded by using a mercury sphygmomanometer.

Because the anatomic location of the cardiovascular autonomic nervous system renders it inaccessible to simple direct physiological testing, a group of clinical tests for measuring the cardiovascular autonomic functions was employed to circumvent this problem. These tests measure the end organ response to various physiological manoeuvres. Based on the cardiovascular reflexes, simple tests of autonomic function that were performed were:

TESTS FOR THE PARASYMPATHETIC SYSTEM:

1. The heart rate response to postural change (30:15 ratio)

Procedure

The subject is made to lie quietly on a couch while the heart rate is continuously monitored on an electrocardiograph. The subject is

then asked to stand unaided and the point at the starting to stand is marked on the electrocardiograph. The shortest R-R interval at or around the 15th beat is measured, while the longest R-R interval at around the 30th beat after standing is measured. A ratio of less than or equal to 1 is considered as abnormal.

2. The S/L (standing to lying) ratio

Procedure

In this test, the subject is asked to stand quietly and to then lie down without help, while a continuous electrocardiogram is recorded from 20 beats and 60 beats after lying down. The S/L ratio is taken as the ratio of the longest R-R interval during the 5 beats before lying down to the shortest R-R interval during the 10 beats after lying down.

3. Heart rate response to the valsalva manoeuvre (Valsalva ratio)

Procedure

The subject is asked to exhale into the mouth piece which is connected to a mercury manometer, while holding it at a pressure of 40 mmHg for 15 sec. During this manoeuvre and 45 seconds subsequent to this, the ECG is recorded and the vaslava ratio is calculated, which is the ratio between the maximal R-R interval (after the release of the strain) and the minimal R-R interval (during the strain). A ratio of less than or equal to 1.10 is considered as abnormal.

4. Heart rate variation with deep respiration

Procedure

Deep breathing at six breaths a minute is the most convenient and reproducible technique. In this test, the subject is asked to breathe deeply at six breaths per minute i.e. five seconds in and five seconds out for one minute. The ECG is recorded throughout the period of deep breathing with a marker which is used to indicate the onset of each inspiration and expiration. The maximum and the minimal R-R intervals during each breathing cycle are measured by using a ruler and these are converted to beats per minute. The results of this test are expressed as the mean of the difference between the maximum and minimum heart rates for the six measured cycles in beats per minute. A value of less than or equal to 10 beats per minute is considered as abnormal.

TESTS FOR THE SYMPATHETIC SYSTEM:

Orthostasis i.e. B.P response to standing and lying

Procedure

This test is performed by measuring the subject's blood pressure with a sphygmomanometer while he is lying down quietly and one minute after he is made to stand up. The postural fall in B.P. is taken as the difference between the systolic blood pressure while lying and the systolic blood pressure on standing. A fall in the systolic blood pressure of more than or equal to 30 mm is considered as abnormal

Blood pressure response to a sustained hand grip (HGT)

Procedure

A sustained isometric muscle contraction causes a reflex rise in the blood pressure and the heart rate. The subject is asked to apply pressure on a standardized handgrip at his maximum voluntary contraction for one minute. A diastolic blood pressure increase of less than 15 mm Hg is considered as normal.

The cold pressor test (CPT)

Procedure

In this test, the subject is asked to place his hand in cold water (4°C) for one minute while his blood pressure is recorded before the test, during the test and after the test, every 30 seconds, till the blood pressure returns to the pre-test level. An increase in the systolic blood pressure of greater than or equal to 15 mm Hg is considered as normal

The pre-test heart rate, the respiratory rate, the pulse, the temperature and the FEV_1 were recorded in the healthy subjects as well as in the patients.

STATISTICS

The statistical analysis of all the autonomic function tests was done by using the unpaired t-test to compare the autonomic nervous system activity of the chronic obstructive pulmonary disease patients and the normal healthy controls. A p value of <0.05 was taken as significant.

RESULTS

1) In all the subjects, the pre-test pulse rate, the respiratory rate and the systolic and diastolic blood pressures were recorded. The values of all these recordings were found to be significantly higher in group-I (COPD patients) than in group-II (normal subjects) [Table/Fig-1].

2) The results of the tests for the assessment of the sympathetic nervous system activity:

   (a) Changes in systolic blood pressure (SBP) in response to the cold pressor Test (CPT); b) Changes in systolic blood pressure (SBP) in response to standing and c) Changes in diastolic blood pressure (DBP) in response to the hand grip test (HGT) showed a significant rise in the sympathetic nervous activity in the COPD patients (group-I) as compared to that in the normal subjects (group-II) [Table/Fig-2].

3) The results of the tests for the assessment of the para-sympathetic nervous system activity:

   (a) The 30:15 ratio; (b) The Standing/Lying ratio; (c) The Valsalva Ratio and d) The Deep Breathing Test (DBT) showed a significant reduction in the parasympathetic nervous system activity in patients of COPD (group-I) as compared to that in the normal healthy subjects (group-II) [Table/Fig-3].

DISCUSSION

Chronic obstructive pulmonary disease has a chronic long-lasting course which is characterized by an irreversible decline of FEV1 (forced expiratory volume in the first second), an increasing presence of dyspnoea and other respiratory symptoms and a progressive deterioration of the health status [7].

COPD is frequently under-diagnosed and under-treated. The pathogenesis and the clinical manifestations of COPD are not restricted to pulmonary inflammation and structural remodelling. Rather, this disorder is also associated with clinically significant systemic alterations in the biochemical and organ functions.

Abnormalities in both the para-sympathetic and the sympathetic nervous systems in the COPD patients were demonstrated in

Parameters	Group-I (COPD)		Group-II (Normal)		p-value
	Mean	±SD	Mean	±SD	
Pulse rate (beats/min)	93.1	12.92	74.53	2.50	<0.001***
Respiratory rate (breaths/min)	18.9	1.6	13.8	1.35	<0.001***
Systolic blood pressure (mmHg)	138.27	11.16	130.27	3.92	<0.001***
Diastolic blood pressure (mmHg)	87.20	5.93	80.67	3.54	<0.001***

[Table/Fig-1]: Comparison of pre-test values of Pulse Rate, Respiratory Rate, Systolic Blood Pressure and Diastolic Blood Pressure (Mean ± SD) between COPD patients & Normal subjects

***p < 0.001 Highly Significant

Parameters	Group-I (COPD)		Group-II (Normal)		p-value
	Mean	±SD	Mean	±SD	
CPT (Rise in SBP) (mmHg)	18.96	1.95	17.67	1.75	0.002**
HGT (Rise in DBP) (mmHg)	19.02	1.85	18.07	1.7	0.014*
SBP fall on standing (mmHg)	9.73	1.17	10.6	0.93	<0.001***

[Table/Fig-2]: A Comparative data of Sympathetic Nervous System activity in COPD patients (group-I) & Normal healthy controls (group-II)

*p<0.05 Significant, **p<0.01 Significant at 1% significance level, ***p<0.001 Highly Significant

Parameters	Group-I (COPD)		Group-II (Normal)		p-value
	Mean	±SD	Mean	±SD	
30:15 Ratio	1.05	0.06	1.07	0.04	0.033*
S/L Ratio	1.05	0.07	1.17	0.05	<0.001***
Valsalva Ratio	1.11	0.07	1.25	0.03	<0.001***
DBT	8.59	2.65	17.57	1.96	<0.001***

[Table/Fig-3]: A Comparative data of Para-sympathetic Nervous System activity in COPD patients (group-I) & Normal healthy subjects (group-II)

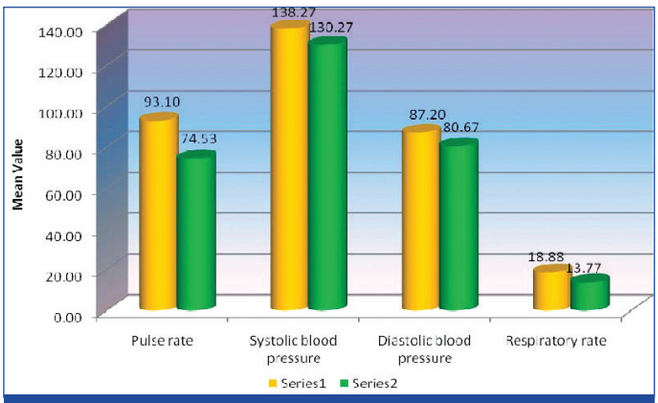
*p<0.05 Significant at 5% significance level
***p<0.001 Highly Significant

many studies [8]. In COPD, the sympathetic activation and the vagal withdrawal is at least as pronounced as in other chronic conditions, such as severe heart failure [9].

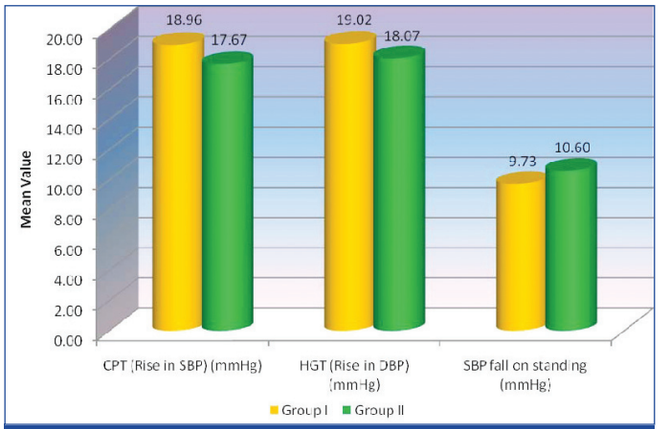
The present study was conducted to record the changes in the autonomic nervous system activity in male patients with COPD (N=90) and those findings were compared to the observations which were recorded in normal subjects (N=30).

The demographic data was comparable among the two groups. The pulse rate, the respiratory rate and the blood pressure of each subject were recorded before the commencement of the autonomic function testing. The statistical analysis showed that the mean values of the pulse rate were higher in the COPD patients (93.1±12.92/min) than in the normal subjects (74.53±2.50/min). The difference of the pulse rate between the COPD patients and the normal subjects was statistically highly significant (p<0.001).

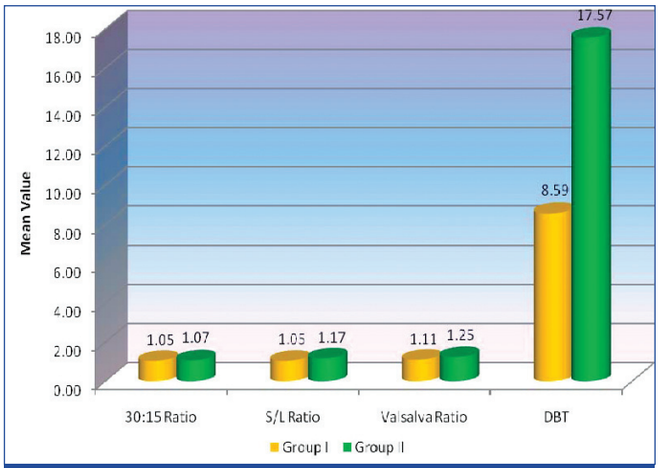
The mean pre-test respiratory rate in the COPD patients was 18.9 ± 1.6/min, whereas its value in the normal subjects was 13.8±1.35/min. The variation between the two values was statistically highly significant (p<0.001). Our findings were consistent with the observations of many other studies which showed the presence of tachypnoea and dyspnoea in the COPD patients [10].



[Table/Fig-4]: Comparison of pre-test values of pulse rate, systolic blood pressure amd diastolic blood pressure (Mean + SD) between COPD patients & Normal subjects



[Table/Fig-5]: Comparison of sympathetic function between the COPD patients & normal subjects



[Table/Fig-6]: Comparison of parasympethic function between the COPD patients and normal subjects

The mean pre-test systolic blood pressure recording in the COPD patients was 138.27±11.16 mmHg, as compared to 130.27±3.92 mmHg in the normal subjects. The variation in the systolic blood pressure was highly significant (p<0.001). The mean pre-test diastolic blood pressure recording in the COPD patients was 87.20±5.93 mmHg, whereas it was 80.67±3.54 mmHg in the normal subjects. The variation in the diastolic blood pressure was highly significant (p<0.001).

Variations in the blood pressure in response to CPT and HGT were significantly higher in the COPD patients as compared to those in the normal healthy controls. A fall in the systolic blood pressure in response to standing was also significantly lower in the patients

of COPD than in the normal subjects. Thus, an overall increased sympathetic activity was seen in the COPD patients. On the contrary, the tests of the parasympathetic nervous activity i.e. the 30:15 ratio, the S/L ratio, the valsalva ratio and the DBT showed a marked decreased activity in patients of COPD in contrast to those in the normal healthy controls. This finding was consistent with those of a number of studies which were conducted earlier [11,12].

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