Volume : 5 | Issue : 9 | September 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Original Research Paper

Study of Pulmonary Functions, Arterial Blood Gases and Autonomic Functions in Chronic Obstructive Pulmonary Disease and its Comparison Between Young and Elderly Patients

Medical Science

KEYWORDS : Chronic obstructive pulmonary disease, autonomic nervous system, Arterial blood gas, pulmonary function

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ABSTRACT

Purpose of the study: *Chronic Obstructive Pulmonary Disease (COPD) is one of the most important causes of morbidity and mortality worldwide. Purpose of this study is to compare the Pulmonary functions, Autonomic functions and Arterial Blood Gases (ABG) between young and elderly COPD patients and to determine association if any between severity of the disease and autonomic dysfunctions.*

Methods: *In this cross sectional study a total of hundred male patients attending medical OPD (Fifty young and fifty Old) who has diagnosis of COPD were included. This study was carried out in the outpatient setting in a tertiary referral Mathura Das Mathur Hospital, Jodhpur. Spirometry, arterial blood gas analysis and autonomic functions were assessed.*

Result: *The severity of COPD was more among elderly population as compared to young patients. The risk of development of co-morbidities and acute exacerbations also was more among the elderly. The study also demonstrated a high prevalence (97%) of early and definite cardiac autonomic neuropathy among patients suffering from COPD. The autonomic dysfunction developed independent of the age of the patients suggesting that COPD is responsible for earlier onset of cardiac autonomic neuropathy. The autonomic dysfunction does not depend upon the degree of airway limitation (FEV1). The prevalence of autonomic dysfunction did not show any significant correlation with the presence of hypoxia.*

Introduction

Currently, COPD is one of the most important causes of morbidity and mortality worldwide, causing both a significant economic impact on public health systems. Worldwide it is estimated that over 600 million patients suffer from COPD, this condition affecting about 2.5% of the population over 30 years in Europe [2, 3].

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease, characterized by persistent respiratory airflow obstruction, usually progressive, associated with chronic inflammatory response of the airways and lungs, due to the action of noxious particles or gases. Inflammation causes a combination of inflammatory lesions in the small bronchi and lung parenchyma. It increases the destruction of alveolar septa and causes pulmonary emphysema [1].

Autonomic dysfunction leading to orthostatic hypotension has been a major cause of falls in elderly population, leading to increased morbidity. Autonomic dysfunction is common in elderly population and its incidence is increased due to various diseases and drugs. It has been recognized that chronic obstructive pulmonary disease (COPD) is a systemic disease which has been shown to negatively affect the cardiovascular and autonomic nerve system. The autonomic nervous system (ANS) innervates the entire neuraxis and influences all organ systems. It regulates blood pressure (BP), heart rate, sleep, and bladder and bowel function. Gross et al studied maximum increase in forced expiratory volume in one second (FEV1) following administration of atropine methionitrate and showed that cholinergic tone in chronic obstructive pulmonary disease (COPD) was increased in proportion to the severity of airway disease. [3] It is therefore likely that abnormal activity of autonomic nerves innervations can contribute to airway narrowing in COPD and may be relevant to the pathogenesis of COPD. The complexity of the physiologic basis by which autonomic dysfunction occurs in patients with COPD is considerable and the knowledge in this field remains elementary.

In COPD patients the activity of sympathetic nerves may be affected by recurrent hypoxemia, hypercapnia, increased intrathoracic pressure swings due to airway obstruction, increased respiratory effort, systemic inflammation and the use of beta sympathomimetics. The insight into sympathovagal imbalance as a pathological phenomenon in COPD may be important in understanding the pathophysiology of COPD and may have a potential clinically importance for improving risk stratification and treatment of patients with COPD, because autonomic dysfunction has been attributed as a cause for endothelial dysfunction, increased arterial stiffness, left ventricular remodelling and supraventricular and ventricular arrhythmias. [18] .

The purpose of this study is to evaluate and determine an association if any between the Arterial Blood Gas, Pulmonary function test and Autonomic function if any among the patients suffering from Chronic Obstructive Pulmonary Disease.

Material and Methods

This study was conducted at Department of Medicine, M.D.M. hospital, Dr SN Medical College, Jodhpur.

Study Design:

Cross sectional study

Sample size:

100 patients (50 > 60 years and 50< 60 years) with known Chronic Obstructive Pulmonary Disease were evaluated. Mean age of 61.17 years with the youngest patient being 40 years and oldest being 85 years (Table 1).

Inclusion Criteria:

All known cases of Chronic Obstructive Pulmonary Disease attending Medicine outdoor.

Exclusion Criteria:

Patients with acute exacerbation of COPD.

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Patients with clinical cor pulmonale, congenital, rheumatic or any valvular heart disease, systemic hypertension, coronary artery disease and any other past or concurrent pulmonary disease, diabetes mellitus, renal failure, carcinoma, connective tissue disorder and liver disease.

Indoor patients.
Methodology:
Hundred male patients diagnosed as COPD were included in this cross-sectional study carried out in the outpatient setting in a tertiary referral hospital, Mathura Das Mathur Hospital, Jodhpur. The study was approved by the Ethical committee and informed consent was taken from all the participants.

The diagnosis of COPD was based on the criteria of the Global Initiative for Chronic Obstructive Lung Diseases (GOLD) and established by a history of smoking, cough with expectoration accompanied by progressively increasing dyspnoea on exertion. Asthma was excluded clinically. Only stable patients requiring no change in their medication in the previous 4 weeks and not having an acute exacerbation in that period were included. The inclusion criteria included an FEV_1/FVC ratio of less than 70% and a post-bronchodilator increase in FEV_1 of less than 12% and 200ml from the initial value. The severity of COPD was categorized on the basis of FEV_1% predicted as per the GOLD criteria.

Spirometry was performed on dry, rolling-seal spirometer of the Transfer Test C model lung function machine (P.K. Morgan, Kent, UK). Maximal expiratory flow volume (MEFV) curves were obtained. Three acceptable and at least two reproducible curves were obtained in each subject. The highest FEV_1 obtained was recorded. Reference equations for north Indian adults were used to calculate the percent-predicted values.

Arterial blood gas analysis was carried out on a sample drawn from the radial artery in a heparinzed syringe and measured in Instrumentation Laboratory machine.

Autonomic functions were assessed by CAN Win Analysis System. The following non-invasive autonomic function tests were performed by CAN Win Analysis System.

Tests of predominantly parasympathetic function:-
Resting Heart Rate.

Heart Rate variation during deep breathing (Expiration/Inspiration ratio).

Heart-rate response to standing (30:15 ratios).

Heart-rate response to Valsalva manoeuvre (VM ratio).

B. Tests of predominantly sympathetic function:-
Blood-pressure response to standing.

2. Blood pressure response to Sustained handgrip (SHG).

Discussion
Chronic obstructive pulmonary disease has a long lasting course which is characterized by an irreversible decline of FEV1 [forced expiratory volume in the first second], an increasing levels of dyspnoea, other respiratory symptoms and a progressive deterioration of the health status [4].

Abnormalities in both the para-sympathetic and the sympathetic nervous systems in the COPD patients were demonstrated in many studies [5]. In COPD, the sympathetic activation and the vagal withdrawal is at least as pronounced as in other chronic conditions, such as severe heart failure [6].

The pulse rate, the respiratory rate and the blood pressure of each subject were recorded before the commencement of testing. Haemoglobin levels were obtained prior to testing to rule out anaemia as it can lead to autonomic dysfunction.

The present study had a total of 100 patients of which 50 were young and 50 were elderly. Mean age of 61.17 years with the youngest patient being 40 years and oldest being 85 years (Table 1). All the subjects enrolled in the study were male which can be explained because of high prevalence of smoking habit among the male population.

The study demonstrated that the severity of disease as determined by spirometry and the risk of development of comorbidities as per the GOLD 2014 guidelines correlates with the age of patient. This is similar to the finding of Elisabeth Stall et al [8] which concluded that health related quality of life in COPD deteriorates with age.

Cukic V[8] et al studied the pulmonary functions of 199 COPD patients prospectively over a period of 4 years and concluded that airflow limitation in COPD is progressive; both FVC and FEV1 showed the statistically significant decrease during follow-up period of 4 years.

Among the study populations 11 patients belonged to group A (low risk, less symptoms), 24 belonged to group B (low risk, more symptoms), 7 belonged to group C (high risk, less symptoms) and 58 subjects belonged to group D (high risk, more symptoms).

On comparison among the young and elderly age groups, we found that among the young population 18% (n=9) subjects belonged to group A, 28% (n=14) belonged to group B, 12% (n=6) belonged to group C and 21% (n=42) belonged to group D. similarly for the elderly, 4% (n=2) subjects belonged to group A, 20% (n=10) belonged to group B, 2% (n=1) belonged to group C and 74% (n=37) belonged to group D. Chi-Square test the between the two groups was statistically significant ($p<0.05$) (Figure 1).

Table 2 illustrates a comparison of the various parameters of spirometry, ABG and Autonomic functions among Young and Elderly population. It shows that on comparing the ABG values of young and elderly population the difference in pO_2 values was statistically significant ($p<0.05$) with a higher mean pO_2 in young subjects (79.29) as compared to that among elderly patients (70.16), where as the difference for pCO_2, pH and s pO_2 was found to be statistically insignificant.

The degree of airway limitation as determined by FEV1 values showed no significant difference among young (mean FEV1= 44.78) and elderly (mean FEV1 = 43.78) with a p value of 0.724. Other spirometry indices like FVC and FEV1/FVC also showed no significant statistical difference (Table 2).

Abnormalities in both the para-sympathetic and the sympathetic nervous systems in the COPD patients were demonstrated in many studies. In COPD, the sympathetic activation and the vagal withdrawal is at least as pronounced as in other chronic conditions, such as severe heart failure.

Our study demonstrates the presence of a previously unsuspected subclinical autonomic neuropathy in patients with COPD. The autonomic functions of patients were studied and compared according to grading of disease, arterial blood gases and age (young and elderly). The overall prevalence of definite and advanced cardiac autonomic dysfunction in the study population was 64% while 33% patients had a possible early autonomic dysfunction.

Among the variables determining the Parasympathetic functions (E:I ratio, 30:15 ratio and Valsalva ratio), the difference in E:I ratio among young and elderly was statistically significant ($p<0.05$) whereas other parameters i.e. 30:15 ratio and Valsalva ratio showed no significant difference ($p>0.05$). The parameters determining sympathetic function were similar among young and elderly age groups. Using the criteria set down by Ewing and Clarke [7] the young population contained 16 patients with possible early, 12 with definite and 21 with severe advanced dysfunction and 1 with normal autonomic functions. These findings were statistically insignificant ($p>0.05$) when compared to elderly population which had 2 normal patients and 17 patients with early, 12 with definite and 19 with advanced autonomic dysfunction.

Vinutha Shankar MS [11] et al in 2012 studied the parasympathetic functions among normal young and elderly subjects and concluded that the heart rate response to deep breathing, Valsalva manoeuvre and to standing which reflect integrity of parasympathetic function is reduced after the sixth decade even in normal healthy subjects.

In category A patients the autonomic functions were normal in 9% (n=1), possible early dysfunction in 45% (n=5), definite dysfunction in 0 and severe advanced dysfunction in 45% (n=5) patients. For category B patients normal autonomic function was found in 4% (n=1), possible early in 38% (n=9), definite dysfunction in 4% (n=1) and severe advanced dysfunction in 54% (n=13). Among the patients in category C normal autonomic functions were observed in none, possible early dysfunction in 43% (n= 3), definite dysfunction in 43% (n=3) and severe advanced dysfunction in 14% (n=1) subjects. For category D disease the values were 2% (n=1), 28% (n=16), 34% (n=20) and 36% (n=21) respectively for normal, possible early, definite and severe advanced dysfunction respectively. On statistical analysis by Chi-square test a p value was 0.061 and the data is statistically insignificant (Figure 2).

Thus from our study it can be concluded that the onset of autonomic dysfunction in COPD occurs at an earlier age and the prevalence is similar among the young and elderly population as seen in other chronic diseases like diabetes and hypertension . The findings are similar to previous study done by A. G. Stewart [14] et al which showed that the autonomic dysfunction among COPD has a poor correlation with age. Although a large population based study is needed to confirm the findings.

The prevalence and severity of autonomic dysfunction among the study population did not show any significant variation ($p<0.05$) with respect to the grades of severity of disease according to the GOLD 2014 guidelines. This suggests that the autonomic dysfunction does not correlate with the severity of airway narrowing as determined by FEV1 and the severity of symptoms. These findings are in cohesion with the previous studies done by Stewart et al [14] and Wei-Lung Chen [15] et al

Figure 3 portrays the prevalence of Blood gas anomalies in relation to various classes of COPD described in GOLD 2014. It was found that among 11 patients with Category A disease 81% (n=9) had normal ABG, 9% (n=1) had hypoxia without hypercapnea and 9% (n=1) had hypoxia with hypercapnea. In category B disease (n=14), 58% (n=14) had normal ABG, 17% (n=4) had hypoxia without hypercapnea and 25% (n=6) had hypoxia with hypercapnea. Total 7 patients belonged to Category C disease of which 57% (n=40) had normal ABG and 43% (n=3) had hypoxia without hypercapnea, no patient had hypoxia with hypercapnea. In Category D there were a total of 58 patients of which 24% had a normal ABG, 31% (n=18) had hypoxia without hypercapnea and 44% (n=26) had hypoxia with hypercapnea. The data obtained was analyzed by Chi-square test and was found to be statistically significant ($p<0.05$). On comparing the prevalence of autonomic dysfunction among patients with normal blood gas values with those having hypoxia with and without hypercapnea, we found that the severity of autonomic dysfunction bears no significant correlation to hypoxia.

Wei-Lung Chen[15] et al compared 30 COPD patients with age matched controls and studied normalized high-frequency power (nHFP) and the low-/high-frequency power ratio (LFP/HFP), which were used as indices of vagal activity and sympathovagal balance, respectively. They found that there was a negative correlation between nHFP and PaO_2 and a positive correlation between LFP/HFP and PaO_2 in COPD patients. No correlation existed between forced expiratory volume in 1.0 s/forced vital capacity (FEV1/FVC), % predicted of FEV1 (%FEV1) and nHFP or LFP/HFP in COPD patients.

Scalvini [16] et al evaluated ANS of 11 stable COPD patients by analysis of variability in cardiac frequency at rest and during both vagal (controlled breathing) and sympathetic (tilting) stimuli breathing with and without oxygen supplementation and compared them with 13 controls. They concluded that in stable patients with chronic obstructive pulmonary disease with chronic respiratory insufficiency, hypoxemia is associated with derangements in the autonomic nervous system which may be partially reversed by oxygen administration.

Chhabra [17] et al studied the autonomic functions of 56 COPD patients and compared them with age matched controls; they concluded that the prevalence of early and definite autonomic dysfunction was more common among the COPD patients than the controls. Also while autonomic dysfunction was more prevalent in patients with hypoxemia, it was also found to occur in those without hypoxemia. The responses to tests of autonomic function had weak relationships with FEV1% predicted and PaO_2.

The findings of our study are in concordance with Chhabra et although the results of the study do not correlate well with those done by Stewart et al[14] and Wei-Lung Chen[15] et al. This could be possible due to different parameters used for assessment of autonomic dysfunctions by Wei-Lung Chen et al.

Table 1
(Population distribution according to age)

Group	N	Mean Age	Std. Deviation	Min. Age	Max. Age
Young Group (<60 yrs)	50	52.00	5.551	40	59
Elderly Group (> 60 yrs)	50	70.34	6.426	60	85

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Table 2
(Comparison of spirometry, ABG and autonomic parameters among young and elderly COPD patients)

Parameters	Young		Elderly		P-Value	Interpretation
	Mean	SD	Mean	SD		
pO_2	79.29	11.75	70.16	12.46	0.000	Significant
pCO_2	41.31	5.68	41.73	10.79	0.807	Not Significant
pH	7.41	0.03	7.41	0.05	0.450	Not Significant
SpO_2	95.39	3.70	93.24	8.96	0.120	Not Significant
FVC(% pred)	61.44	16.57	63.08	12.07	0.573	Not Significant
FEV1(% pred)	44.78	15.89	43.78	12.04	0.724	Not Significant
FEV1/FVC	58.33	7.84	57.69	7.62	0.684	Not Significant
E: I Ratio	1.11	0.07	1.23	0.40	0.039	Significant
30:15 Ratio	1.09	0.20	1.12	0.20	0.494	Not Significant
Valsalva Ratio	1.57	0.44	3.09	5.74	0.065	Not Significant
Sustained Handgrip	11.52	7.08	6.76	6.60	0.001	Significant

Figure 1
(Classification of patients according to GOLD 2014 guidelines and comparison among young and elderly)

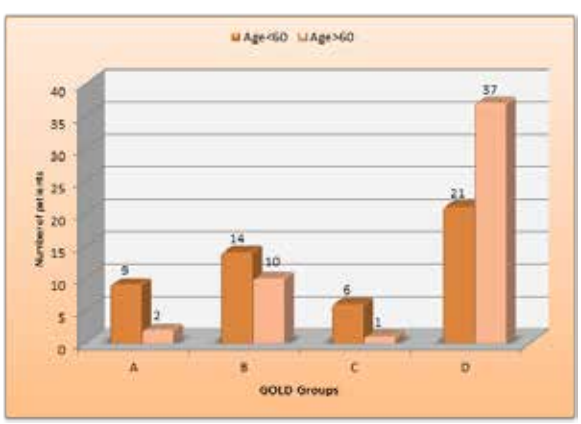


Figure 2
(Prevalence of Cardiac Autonomic Dysfunction among different risk categories of COPD patients)

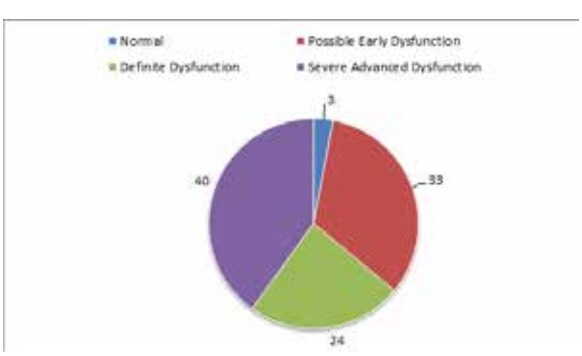
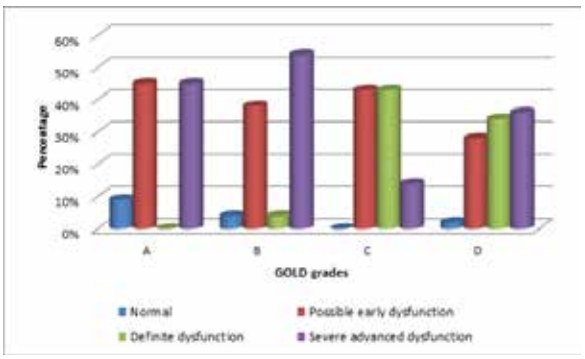


Figure 3
(Comparison of ABG among various Groups of COPD according to GOLD 2014)



Summary and conclusions

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by persistent respiratory airflow obstruction, usually progressive, associating chronic inflammatory response of the airways and lungs, due to the action of noxious particles or gases. The study was conducted to compare and analyze the spirometry, arterial blood gases and autonomic functions of young and elderly patients suffering from COPD.

The study showed that the severity of disease as determined by spirometry was more among elderly population as compared to young patients. The risk of development of comorbidities and acute exacerbations also was more among the elderly. Although the development of hypoxia with and without hypercapnea increased with the increasing severity of disease, it showed no correlation with the age of patients.

The study also demonstrated a high prevalence (97%) of early and definite cardiac autonomic neuropathy among patients suffering from COPD. The autonomic dysfunction developed independent of the age of the patients suggesting that COPD is responsible for earlier onset of cardiac autonomic neuropathy.

In accordance with the previous studies, the study demonstrated that the autonomic dysfunction does not depend upon the degree of airway limitation (FEV1). The prevalence of autonomic dysfunction did not show any significant correlation with the presence of hypoxia as well.

Our study demonstrates the presence of a previously unsuspected subclinical autonomic neuropathy in patients with COPD. The cardiac autonomic neuropathy in COPD can be an important factor for early development of cardiovascular morbidity and mortality in COPD. Thus we would suggest various interventions for management like patient education, high-salt diet (10–20 g/d), high-fluid intake (2 L/d), elevation of head end of bed, maintaining postural stimuli, physical counter-manoeuvres and correction of anaemia. However, further studies with a bigger population and more number of parameters must be taken into consideration.

CONCLUSION

The study demonstrates that the patients with COPD develop increased severity of disease and risk of development of comorbidities with age. The patients with chronic obstructive pulmonary disease may suffer from an abnormal cardiac autonomic nervous system, as assessed by reduced variability in cardiac frequency and abnormal responses to

vagal and sympathetic stimuli. The development of autonomic dysfunction occurs independent of age and usually has an earlier age of onset. This may be responsible for increased cardiovascular morbidity and mortality in these patients. Thus it is suggested that patients with COPD be adequately educated regarding the various symptoms of autonomic dysfunction and adequate treatment being used when needed.

Acknowledgement:
We thankfully acknowledge to Regional Geriatric Centre, NPHCE, Jodhpur for sponsoring this research project.

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