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Original Research Article

A study of pulmonary functions and Alpha-1 Antitrypsin in Chronic Obstructive Pulmonary Disease

Dr. Mittal Panchal[1*], Dr. Purva Hathila[2]

[1]Assistant professor, Department of Biochemistry, Parul Institute of Medical Sciences and Research, P.O. Limda, Ta. Waghodia, Dist. Vadodara-391760, Gujarat, India

[2]Assistant professor, Department of Physiology. Parul Institute of Medical Sciences and Research, P.O. Limda, Ta. Waghodia, Dist. Vadodara-391760, Gujarat, India

***Corresponding author**
Dr. Mittal Panchal
Email: drmittal2911@gmail.com

Abstract: Chronic obstructive pulmonary disease is a major cause of health care burden worldwide and the only leading cause of death that is increasing in prevalence. Reactive oxygen and nitrogen species, which are increased in smokers, may target and modify the alpha-1 antitrypsin. The aim of the present Study is to assess the pulmonary functions and Alpha-1 Antitrypsin in nonsmoker COPD and Smoker COPD patients and to find the correlation between them. 100 patients of COPD, 50 smokers (Group A) and 50 Non smokers (Group B) were included. Alpha-1 Antitrypsin was performed on ILAB-650 fully auto analyzer and Pulmonary function, FVC, FEV1, FEV1/FVC was assessed with computerized spirometry. Stastical analysis was done using GraphPad prizm 7.01 software. A1AT (group-A 149.6±21 and group-B 185.6±32.36), FVC% (group-A 70.3 ± 18.89 and group-B 88.24± 15.72), FEV1% (group-A 50.54± 16.19 and group-B 77.56 ± 13.99), FEV1/FVC % (group-A 71.64± 13.74 and group-B 71.64± 13.74) were significantly ($p<0.001$) lower in Smokers COPD patients, as compared to Non Smokers COPD Group.
Keywords: Alpha-1 antitrypsin, Chronic Obstructive Pulmonary Disease (COPD), Forced Expiratory Volume (FEV), Force Vital Capacity (FVC).

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is defined as a disease state characterized by airflow limitation that is not fully reversible and it includes emphysema, an anatomically defined condition characterized by destruction and enlargement of the lung alveoli; chronic bronchitis, a clinically defined condition with chronic cough and phlegm; and small airways disease, a condition in which small bronchioles are narrowed [1]. Chronic obstructive pulmonary disease is a major cause of health care burden worldwide and the only leading cause of death that is increasing in prevalence. The regional chronic obstructive pulmonary disease working group for 12 Asia Pacific countries and regions used a prevalence model for this disease and estimated an overall prevalence rate of 6.3 % with a range from 3.5 to 6.7 % [2]. Prevalence of COPD in India with a median of studies (up to 1995) was 5.0% and 2.7% in men and women, respectively and in 2006 was 5.0% and 3.2% in men and women respectively [3]. The major risk factors, contributing to COPD, Smoking – both active and passive - is responsible for Patho-physiology of COPD [4-6]. Cigarette smoke activates macrophages and epithelial cells to release chemotactic factors that recruit neutrophils and CD8 cells from the circulation. These cells release factors that activate fibroblasts, resulting in abnormal repair processes and bronchiolar fibrosis [7]. There are posttranslational modifications of alpha-1 antitrypsin in patients with chronic obstructive pulmonary disease, is that of oxidation, thought to be due to exposure to cigarette smoking components. Reactive oxygen and nitrogen species, which are increased in smokers, may target and modify the alpha-1 antitrypsin [8]. Normal level neutralizes the activity of neutrophil elastase, a protease that destroys elastin and other connective tissue components in the lung; however, a deficiency of alpha-1antitrypsin represents an imbalance in favour of neutrophil elastase and, therefore, increases the risk of emphysematous lung destruction [9, 10].

AIM AND OBJECTIVES

The aim of the present Study is to assess the pulmonary functions and Alpha-1 Antitrypsin in nonsmoker COPD and Smoker COPD patients and to find the correlation between them.

MATERIALS AND METHODS

Study was conducted on 100 patients of COPD attending Out Patient Department of the Pulmonary Medicine department at Sir Takhtsinhji General Hospital, Bhavnagar, Gujarat during period of November 2013 to March 2014. Out of 100 patients, 50 were smokers (Group A) and 50 were Non smokers (Group B). Ethical clearance was obtained from the institutional review board of Govt. Medical College, Bhavnagar. Informed consent was taken from all the subjects.

Inclusion criteria: Patient age > 40 years, both male and female with prior diagnosis of chronic obstructive pulmonary disease (COPD) by PFT (pulmonary function test). Exclusion criteria: Patient has alternative cause for their respiratory disorders e.g. asthma, lung cancer, sarcoidosis, tuberculosis, lung fibrosis, cancer or had cancer in the 5 years prior to study entry or had undergone lung surgery, patient having diabetes mellitus, renal failure, hypertension, cardiac disorders, liver disorders, hepatocellular carcinoma and bladder cancer, patient with habit of tobacco chewing along with smoking were excluded.

Venous blood was collected in plain vacutte from all the participants. Fresh serum was separated by centrifugation. Assay was performed on ILAB-650 fully auto analyzer (Instrumentation Laboratory, USA) at Biochemistry Laboratory accredited by National Accredited Board for Testing and Calibration Laboratory as per ISO 15189:2007 guideline. AAT was analyzed by serum anti-human alpha-1 antitrypsin which reacts specifically with the alpha1-antitrypsin of the sample to yield an insoluble aggregate which is measured by turbidimetry method [11] with commercially available ready to use reagent kits. The recorded parameters were compared in both the groups. PFT was performed using computerized Spirometer. Age, height and weight of the subjects were entered in the spirometer. The pulmonary function test was conducted by sitting the subject comfortably in a chair. Sterilization of the mouthpiece was done before use. The subjects were asked to perform maximum inspiration followed by maximal exhalation. Three tests were performed and the subjects were assisted to improve their efforts. The best of the three performances of FVC, FEV1, FEV1/FVC was taken. The spirometer gives two values: one is the expected value and the other is the actual value. The expected values are based on the height, age and weight of the subjects.

STATISTICAL ANALYSIS

Data were analyzed using GraphPad prizm 7.01 software. All the values were presented as Mean ± SD. In data analysis, comparison of this parameter between smokers (Group- A) and non-smoker (Group-B) COPD patients was carried out by applying unpaired t-test and their correlation was studied by applying Pearson Correlation test. Pearson's correlation coefficient test was used for correlation of serum A1AT level and predicted FEV1 %, FVC%, FEV1/FVC% in smoker and non smoker COPD patients. Interpretation was done according to p-value. P value < 0.05 was considered as statistically significant.

RESULTS AND OBSERVATIONS

The Mean Age of the subjects in Group-A and Group-B was 38.36±13.24 years and 43.72±13.58 years respectively. The number and percentage of male and female subjects in Group-A and Group-B were 45(90%), 5(10%) and 40(80%), 10(20%) respectively. Pulmonary Function Tests, namely FVC (%), FEV1 (%), FEV1/FVC % and were significantly ($p<0.001$) lower in Smokers COPD patients, as compared to Non Smokers COPD Group.

Table 1: Comparison of AAT Levels between Group A and Group B

Statistics	AAT(mg/dl)	
	Group A SMOKERS COPD	Group B NON-SMOKERS COPD
Mean	149.6	185.6
Standard Deviation (SD)	21.05	32.36
Std. Error of Mean (SEM)	2.977	4.577
Minimum	116	136
Maximum	229	309
Significance	95% CI: 25.13 to 46.79 *** p < 0.0001	

*** $p < 0.0001$: highly significant difference between two groups by applying unpaired t-test with confidence interval. Reference Interval (90-200 mg/dl)

Table 2: Comparison of PFT Parameters between Group A and Group B

Parameter	Group A SMOKERS COPD	Group B NON-SMOKERS COPD	P value
FEV1	50.54± 16.19	77.56 ± 13.99	< 0.0001
FVC	70.3 ± 18.89	88.24± 15.72	< 0.0001
FEV1/FVC%	71.64± 13.74	89.26± 11.82	< 0.0001

On analysis by using unpaired t – test the differences in PFT parameters between the two groups was statistically highly significant with 'p' value of <0.0001.

Table 3: Correlation between AAT and pulmonary functions in control and COPD group

Correlation	Group A SMOKERS COPD		Group B NON-SMOKERS COPD	
	r	P	R	p
AAT-FEV1	0.1587	0.2709	0.2313	0.1061
AAT-FVC	1.93	0.1794	0.203	0.1573
AAT-FEV1/FVC%	-0.02889	0.8421	0.00865	0.9525

DISCUSSION

The reported prevalence of COPD is higher among men than women [12-14]. In India, prevalence rates, varying between about 2 -22% in men and between 1.2-19% in women, have been shown in different reports [15]. Loganathan R *et al*, reported a lower prevalence of COPD in females, as compared to males [16].

COPD can be attributed to greater prevalence of smoking among men, as well as cumulative effects of smoking, and other exposures with advancing age. Tobacco use kills more than five million people a year and accounts for 10% of adult deaths worldwide. In COPD, there appears interplay of Inflammation, remodeling, bronchospasm, mucus hypersecretion, loss of elastic recoil and increased airway resistance, resulting in progressive reduction in the expiratory airflow. Smoking recognized as a most important causative factor for COPD [17].

In alpha-1 antitrypsin, amino acid methionine is present at position 358 and it is susceptible to convert in methionine sulfoxide by oxidants from cigarette smoke, rendering it much less potent inhibitor of neutrophil elastase [18].

AAT level was lower in COPD patients with smoking as compared to COPD patients without smoking. The present study shows the significant difference in serum AAT level between the two groups (p<0.0001). This study supports the data of previous studies F. Ogushi *et al*. [19], Oliver Senn, Erich W Russi, Christian Schindler *et al*. [20] and Deore Deepmala *et al.* [21].

Pierachille S *et al*, reported a marked reduction in FEV1 and FEV1 % in COPD patients, when compared with the Healthy Controls [22]. The Study conducted by Daphne CR *et al* in 2008, reported FEV1 % decline in the COPD Group [23]. Lung functions namely FEV1, FVC, FEV1/FVC% and showed significant reduction in Smoker COPD group, as compared to non-smokers. The pulmonary function tests of both groups showed obstructive pattern which was worse in the 1st group. In the 1st group the mean FEV1: 50.54± 16.19, mean FVC: 70.3 ± 18.89 and mean FEV1/FVC: 71.64± 13.74 while in the 2nd group the mean FEV1: 77.56 ± 13.99, mean FVC: 88.24± 15.72, and mean FEV1/FVC: 89.26± 11.82 with highly significant difference between both groups (Table 2). AAT in group-1 and group-2 (149.6±21.05 and 185.6±32.36 mg/dl respectively) showed significant changes (P<0.001). Our Study results also demonstrate significant Positive correlations of AAT with FEV1 % PREDICTED (r=0.1587, P sig at<0.001 level), AAT with FVC(r=1.93, P sig at <0.001 level) and negative correlation of AAT with FEV1/FVC % (r=-0.02889, P sig at <0.001 level) in group-1 while in group-2 Positive correlations of AAT with FEV1 % PREDICTED (r=0.2313, P sig at<0.001 level), AAT with FVC(r=0.203, P sig at <0.001 level) and negative correlation of AAT with FEV1/FVC % (r=0.00865, P sig at <0.001 level) (table 3).

CONCLUSION

A1AT is decreased in Smoker COPD patients, as compared to non smokers COPD patients, and it causes deterioration in the lung functions. And there is positive correlation of pulmonary functions with serum A1AT. Therefore smoking cessation and correction of A1AT level may be beneficial in COPD patients for better management of the disease.

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