Study of Pulmonary Function Test and Oxidative Stress Marker in Chronic Obstructive Pulmonary (COPD) Patients

Ranjana[1], Jyoti Batra[2,*], Yogesh Tripathi[3], Sudeep Kumar[4]

[1,2,4]Department of Biochemistry, [4]Department of Physiology, Santosh Medical College, Santosh University, Ghaziabad

***Corresponding Author:**
Email: jyotivinay89@gmail.com

ABSTRACT

Background: *Chronic Obstructive Pulmonary Disease (COPD) is a health problem with increasing severity, as exposure to risk factors such as cigarette smoke, pollution is inevitable. Oxidant antioxidant imbalance cause oxidative burden leading to lung tissue damage.*

Aims and Objective: *The aim of present study was to evaluate oxidative stress marker (MDA) and Lung function test COPD patients.*

Materials and Methods: *MDA level were estimated by thiobarbituric acid method.*

Result: *Serum mean level of MDA was significantly higher in COPD patients as compared to normal healthy individual. FEV1 andFEV1/FVC ratio significantly decreased in COPD patients as compared to control.*

Conclusion: *Increased MDA level indicate excess of oxidative stress in COPD patients. Dietary supplementation of antioxidantto COPD patients is strongly recommended.*

Keywords: *MDA, Oxidative Stress, COPD, FVC, FEV1*

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death globally. The prevalence of COPD is higher in countries where smoking is highly prevalent. In India, there is an increasing tendency to abuse tobacco and COPD is emerging to be a major public health problem[1]. American Thoracic Society defines Chronic Obstructive Pulmonary Disease as "A disease state characterized by the presence of air flow obstruction due to chronic bronchitis or emphysema; the airflow obstruction is generally progressive, may be accompanied by airway hyper-reactivity, and may be partially reversible[2].

COPD has been defined by global initiative of COPD (GOLD), as a state characterized by airflow limitation that is not fully reversible. There is considerable evidence that an increased oxidative burden occurs in the lungs of patients with COPD which plays a role in its pathogenesis. The lungs are continuously exposed to oxidants generated either endogenously or exogenously. Cigarette smoke, consisting of the gas phase and particulate phase (tar phase) is thought to contain 1017 oxidants molecules per puff[3].

Oxidant/antioxidant imbalance is thought to play a part in the pathogenesis of COPD. Oxidative stress leads to increase in concentration of free radicals which can cause damage to the biomolecules (protein, lipids, DNA) present in the cells. One of the targets of oxidantsis polyunsaturated fatty acids (PUFA) present in the cell membrane[4].

Among the main biological targets of oxidative stress, membrane lipids are the most commonly involved class of bio molecules. Lipid peroxidation forms a number of secondary products able to boost oxidative damage. In addition to their cytotoxic properties, lipid peroxides are increasingly recognized as being important in signal transduction for a number of events in the inflammatory response. Malondialdehyde (MDA) has been widely studied as a product of polyunsaturated fatty acid peroxidation. High MDA levels have been observed in several biological fluids from patients with different airways diseases including asthma COPD and bronchitis[5].

MATERIALS AND METHODS

The study was carried out in Department of Physiology& Department of Biochemistry, Santosh Medical College and Hospital, Ghaziabad from June 2012 to July 2013. This study was conducted on 30 healthy individuals and 30 COPD patients. These COPD Patients were diagnosed by physicians on the basis of detailed clinical history, relevant biochemical examinations and clinical condition including spirometry.

The control subjects were completely healthy non-smokers and showed no abnormality on Clinical examinations.

Exclusion Criteria:

Patients with hypertension, malignancy, overt cardiac failure recent surgery, severe endocrine, hepatic or renal diseases and lung disorders other than COPD were excluded from the present study.

Methods:

Physical Examination: Anthropometric data were verified, measured, or calculated: age (year), height (m), weight (kg), BMI (kg/m2). Height (90.01 m) was

measured with a height gauge (standing stadiometer type DETECTO†) with shoes removed, heels joined, and back straight. Weight (91 kg) was measured with a digital scale (OHAUS, Florhman Park, NJ, USA), and BMI (weight/height2) was calculated.

Serum Investigation: 3 ml of blood was collected from each patient. Serum was separated by centrifugation at 3000 rpm for 10 minutes at room temperature. Following parameters were carried out on the samples on the same day of collection.

1. The level of serum Malondialdehyde (MDA) was determined by Kei Satoh method.[6]

Lung function Measurements: Pulmonary functional tests were evaluated with the use of body plethysmography (Jaeger, Germany). All pulmonary function testing was performed according to the European Respiratory Society standards with the patients in a sitting position by the same technician in order to ensure consistency of the technique. Three technically acceptable measurements were performed in each patient, and the highest value was included in the analyses.

Statistical analysis:

Results were statistically analysed by 'GraphPad QuickCals t-test calculator'. Student's t-test was used to assess the significance of difference between the groups. All results are presented as mean ± S.D. A '*p*' value of less than 0.05 was considered significant.

RESULTS

Table 1: Showing Demographic Data, Pulmonary Function and Malondialdehyde levels in COPD and normal Healthy Individuals

Variables	Control	Cases	p-Value
No. of Participants	30	30	
Age (Years)	40.03±4.33	44.90±3.93	p<0.05 **S**
Height (m)	65.85±3.82	68.23±5.41	p<0.05 **S**
Weight (Kg)	164.9±5.65	170.90±6.78	p<0.05 **S**
FEV1(L)	2.46±0.45	2.15±0.45	p=0.009**S**
FVC (L)	3.11±0.52	3.70±0.77	p=0.009 **S**
FEV1/FVC %	80.06±12.21	60.08±16.42	p<0.0001 **S**
MDA (nmol/ml)	1.78±0.52	2.40±0.20	p<0.0001 **S**

S = statistically significant

Table 1 shows biochemical characteristics of the Cases and Control subjects. The mean level of FEV1 significantly decrease in COPD patients as compared to control(p =0.009). The mean level of FVC was increased significantly in COPD as compared to Healthy Individual.

DISCUSSION

Oxidative stress plays an important role in the pathogenesis of chronic bronchitis. Our results indicate that there is an increase in oxidative stress marker and decrease in antioxidant levels in COPD Patients. Lung cells, in particular alveolar epithelial type II cells, are susceptible to the injurious effects of oxidants. Lungs are continuously exposed to oxidants, either generated endogenously during metabolic reactions or exogenously, such as air pollutant or cigarette smoke. Cigarette smoke contains many oxidants and free radicals, both in the gas and the tar phase and cause sequestration of neutrophils into the pulmonary microcirculation and accumulation of macrophages in respiratory bronchioles[7]. All these factors tend to decrease lung function so we did pulmonary function test in COPD patients. In present study, we observed lung function parameters namely FEV1% predicted and FEV1/FVC % ratio were significantly decreased in COPD (P<0.0001). Our results are in accordance with Pierachille S et al[8] and Daphne CR et al[8].

We also evaluate MDA, as a marker of lipid peroxidation in COPD patients. We found significantly increased level of MDA in COPD patients as compared to healthy individuals(p <0.0001). Our results are in accordance with Pawar et al[10], Raut et al[11], Menon et al[12], Nagraj et al[13], Yessica D et al[14], Kirkil et al[15]. Lipid peroxidation, resulting from the reaction of free radicals with polyunsaturated fatty acid side chains in membrane lipoproteins, is a further reaction that can results in cell damage, and is a self-perpetuating process that continues as chain reactions. ROS causes lipid peroxidation as well as protein oxidation, which may cause direct lung injury or may induce a variety of cellular responses through the generation of secondary metabolic reactive species.

Oxidative stress has been implicated in the pathogenesis of tobacco smoke induced chronic obstructive pulmonary disease. Reactive oxygen species present in the tobacco smoke may cause damage to human alveolar epithelial cells by lipid peroxidation of cell membranes. Increased MDA concentration in patients with COPD is due to increased production of reactive oxygen species and hence more lipoxidation products.[16] Increased MDA level in emphysema patients indicates more oxidative stress compared to chronic bronchitis patients. This may be due to patients with emphysema having more severe lung function impairment, lower body mass index, poor quality of life and more serious systemic dysfunction.[17]

CONCLUSION

Present study demonstrates that there is increased oxidative stress in patients with COPD when compared to controls. This study demonstrates the role

of oxidative stress and antioxidant imbalance in pathogenesis of COPD. On evaluating oxidative stress in lung disease patients by measuring lipid peroxidation and antioxidant status can lead to better understanding of free radical mediated damage in chronic bronchitis patients**.** An inequity between oxidative stress and antioxidant capacity has been proposed to play an important role in the development and progression of chronic bronchitis and it is related to the severity of disease. Further studies are needed to analyse the pathophysiological mechanisms involved in lung injury related to oxidant/antioxidant imbalance.

REFERENCES

1. Premanand R, Santhos PH, Mohan A. Study of thiobarbituric reactive substances and total reduced glutathione as indices of oxidative stress in chronic smokers with and without chronic obstructive pulmonary disease. J Chest Dis Allied Sci, 2007; 49: 9-12
2. Mephie SJ, Papadakis MA, Lawrence MT. Current medical diagnosis and treatment. 47th edition, McGraw Hill Medical Publisher, New Delhi, 2008; pp216 -221.
3. Dalle-Done, I. Rossi, R. Colombo, Giustarini, D., & Milzani, A. Biomarkers of oxidative damage in human disease. Clin. Chem 2006;52, 601-623
4. Bast A, Haenen GR, Doelman CS. Oxidants and antioxidants. Am. J. Med. 1991;91:2-13S.
5. Altuntaş E., Turgut T, Ilhan N, Deveci F, Muz HM, Celik I. The levels of oxidant and antioxidant in patients with COPD. Tuberk Toraks. 2003;51(4):373-9.
6. Keisatoh: Serum lipid peroxide in cerebro vascular disorders determined by a new colorimetric method. Clin. Chim. Acta.1978; 90, 37-43.
7. Paul K, Rahman I. Oxidative stress in asthma and COPD: Antioxidant as atherapeutic strategy. Pharmacology and Therapeutics. 2006;1(2):476-494.
8. Pierachilli J, Alessandra S, Carlucci P, Fumagalli F, Gennaro AD, Mondoni M, et al. Lipid peroxidation and 5 lipooxygenase activity in COPD. Am. J. Respir. Crit. Care. Med. 2005;171:838-843.
9. Daphne CR, Jame RJ, Nell H , Mae MS, Elvism I. Diagnostic value of post bronchodilator pulmonary function testing to distinguish between stable moderate to severe COPD and asthma. Intr. J. COPD. 2008;3(4):693-699.
10. Pawar R.S., Abhang S.A., Borale P., Lokhande R. Study of Correlation of Pulmonary Function Test with the Markers of Oxidative Stress and Non-enzymatic Antioxidants in Chronic Obstructive Pulmonary Disease (COPD) Patients. British J Medicine & Medical Research 2014;4(28):4710-4722.
11. Raut A.M., Suryakar A.N., Mhaisekar D. study of oxidative stress in relation with antioxidant status in chronic Bronchitis. IJBR 2012;3(7):331-333.
12. Menon B, Pandita S. Evaluation of oxidant-antioxidant status in different stages of COPD: Determination of serum paraoxonase1 and MDA levels. Eur. J. Res. 2012;23(1):66-71.
13. Nagaraj, Chandrakanth K H, Anand P., Sreenivasa M. Oxidative stress and antioxidant status in chronic obstructive pulmonary disease patients. IJPBS 2011;1(4):447-456.
14. Yessica D, Torres R, Maria L, Guillen G, Ivonne M ,Corichi O, Hicks JJ. Correlation of plasma protein carbonyl and C-reactive protein with GOLD stage progression in COPD patients. The Open Respir. Medi. J. 2009;3:61-66.
15. Kirkil G, Muz MH, Seckin D, Sahin K, Kucuk O. Antioxidant effect of zinc picolinate in patients with chronic obstructive pulmonary disease. Respir Med 2008;102:840-844.
16. Daga MK, Chhabra R, Sharma B, Mishra TK. Effects of exogenous vitamin E supplementation on the levels of oxidants and antioxidants in chronic obstructive pulmonary disease. J Biosci 2003;28(1):7-11.
17. Papaioannou AI, Mazioti A, Kiropoulos T, Tsilioni I, Koutsokera A, Tanou K et al. Systemic and airway inflammation and the presence of emphysema in patients with COPD. Respir Med, 104: 275-282, (2010).