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Original Research Article

A study of vitamin C, superoxide dismutase and FEV1/FVC ratio in chronic obstructive pulmonary disease

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a progressive lung disease characterized by incomplete reversible airflow limitation, which is associated with emphysema and chronic inflammation. Oxidative/antioxidant imbalance is one of the mechanisms of the current pathogenesis of COPD ECSOD is an antioxidant protein that scavenges superoxide free radicals from cigarette smoke and protects the lungs from free radical damage and chronic inflammation.
Methods: Vitamin C was estimated by acid phosphotungustate on spectrometer at 660nm (Ayekygw 1978) method. SOD was estimated by Marklund S and Marklund G (1974) modified by Nandi and Chatterjee. FEV1/FEV ratio was done by spirometry technique.
Results: The present study revealed that there was an increased oxidative stress in patients with COPD, when compared with controls and also decreased level of antioxidant activity in COPD patients, when compared with controls. In our studies significantly decreased sr. superoxide dismutase activity and FEV1/FVC ratio levels were found in subjects with COPD than healthy normal subjects.
Conclusions: A significant decline in lung function may be associated with altered antioxidant enzyme activity due to the strong correlation between SOD and lung functions with COPD severity.

Keywords: Chronic obstructive lung disease, FEV1/FVC ratio, Superoxide dismutase, Vitamin C

INTRODUCTION

COPD is a major, ever increasing global health problem due to increase in smoking rates, environmental and lifestyle changes and is projected to be the fourth leading cause of death worldwide by 2030.[1] A report submitted by National Commission on Macroeconomics and Health (NCMH), showed that the incidence of COPD in India may increase from 17.0 million (in the year 2006) to 22.2 million by 2016.[2]

COPD is a disease state defined by irreversible and progressive airflow limitation associated with an abnormal inflammatory response. Cigarette smoking (CS) is most important COPD etiological factor, and its diagnosis is confirmed by a decrease in the ratio of forced expiratory volume in the first second/forced vital capacity (FEV1%).[3]

Cigarette smoking can bring a large amount of oxygen free radical into lung and trigger oxidative stress, which directly damages the lung tissue in the pathological progression of COPD. To deal with the damage, a series of antioxidases are involved in the antioxidant system to resist the harm of oxygen free radicals.[4]

The prevalence of COPD is higher in countries where smoking is highly prevalent and COPD is the fourth

leading cause of death globally. In India, there is and increasing tendency to abuse tobacco and COPD is emerging to be a major public health.[5]

It currently affects around 10% of the population over 45 years of age but this rises to 50% in heavy smokers and it has been estimated that the cumulative life-time risk of developing COPD is now over 25%.[6] An important role is oxidative stress in the pathogenesis of COPD. Oxidative stress is caused by an imbalance between the production of oxidants and the presence of antioxidants (WHO global burden of disease study, Rahman et al, Repine et al).[5]

There is increasing evidence that increased oxidative stress in the lungs is a major driving mechanism of the disease through multiple and interacting molecular mechanisms. Oxidative stress arises as a result of endogenous anti-oxidant defences being impaired and/or overwhelmed by the presence of reactive oxygen species (ROS).[7] Oxidative stress may appears to drive may of the pathogenic mechanisms involved in COPD and its progression.

During acute exacerbations, oxidative stress is increased in COPD patients. Cigarette smoke, air pollution and biomass smoke are major exogenous sources of oxidative stress in the lungs, but oxidative stress persists even in ex-smokers, indicating that oxidative stress also arises endogenously. Alveolar macrophage numbers are enormously increased in the lungs of COPD patients and are more activated compared to control subjects, releasing increased amounts of ROS in the form of superoxide anions and hydrogen peroxide (H2O2).[8]

ECSOD is an antioxidant and anti-inflammatory protein found in high concentrations in both lung tissue and in the lung lining fluids. The release of free radicals and redox sensitive proteases that result in small airway inflammation, fibrosis and alveolar wall destruction, it assumed that COPD progression. ECSOD both scavenges free radicals and controls inflammation associated with COPD.[9]

The lung has a broad surface area that is exposed to environmental irritants, such as cigarette smoke, which causes free radical production. Each puff of cigarette smoke has been reported to contain up to 1014 free radical molecules as well as 4700 chemicals. Some of these chemicals are short term free radicals such as superoxide (O^-) and nitric oxide (NO) and others are long acting free radicals such as semiquinones.

An enhances inflammatory cells to the lung by cigarette smoking. Neutrophils and macrophages these inflammatory cells, can produce large amounts of reactive oxygen species (ROS), mainly through the NADPH oxidase system. More tissue damages which leads to chronic inflammation by ROS released by inflammatory cells recruited to sites of injury, ROS release by neutrophils and macrophages not only damages surrounding tissues, it can also directly damage/inactivate antioxidant enzymes. Proteolysis of the antioxidant, ECSOD, rendering it inactive by ROS. Thus, chronic free radical production can inhibit the activity of the very enzymes released to protect the body from free radical damage.[10]

Oxidative stress occurs when the formation of oxidants is not successfully offset by various antioxidants in the body. Oxidants come from outside the body such as cigarette smoke or air pollution and that comes from the inflammatory process. Oxidative stress will cause lipid peroxidation, which causes damage to the lungs due to decreased lung function. So, all these system was affected on strength of COPD patients. Various antioxidants are needed to counterbalance the oxidants. Vitamin C is a water- soluble antioxidant that is abundant in the lung epithelial lining fluid. Its ability as an electron donor, enabling vitamin C to scavenge and quench free radicals.[11] The FEV1/FVC is a ratio that reflects the amount of air you can forcefully exhale from your lungs. It's measured by spirometry, a test used to evaluate lung function.[12] The main aim of this study was to know the alterations in serum vitamin C, SOD activity andFEV1/FVC ratio in COPD patients.

METHODS

This case-control study enrolled 50 patients with COPD who are non-smokers or ex-smokers and 50 healthy controls picked from the JIIU'S IIMSR medical college and Noor Hospital, warudi, District Jalna, Maharashtra. Department outpatient clinics during the period of January 2020 to September 2022. The sample size was according to the time and criteria, and computerized simple randomization was done. All participants were divided into two groups based on clinical features according to global initiative for chronic obstructive lung disease criteria. Patients with COPD were clinically stable, with no evidence of respiratory infection or an acute exacerbation for at least. The groups contained 50 blood samples in each control group and COPD group, for this study age group 38-65 years was included.

Estimation of ascorbic acid was done manually by colorimetric method using acid phosphotungustate on spectrophotometer at 660. Estimation of ec SOD was done manually by modified kinetic method (Nandi and Chaterjee, 1988). It is based on colorimetric measurement of inhibition of autoxidation of pyrogallol at pH 8.5. All the readings were taken on spectrophotometer at 420 nm. Statistical analysis was done using graph pad and SPSS version 17 software.

FEV1/FVC ratio was done by spirometry technique. The diagnosis of COPD requires spirometric demonstration of persistent airflow limitation, as defined by post bronchodilator FEV1/FVC <70%, in patients with

appropriate symptoms and history of exposure to noxious stimuli.

Inclusion criteria

Only COPD patients included in this study.

Exclusion criteria

Patients with acute exacerbation, at the time of the study, of COPD, any obvious abnormal lung parenchymal lesions, lung cancer, congestive heart failure, current smokers, patient taken drugs, e.g., anti-inflammatory, steroids, analgesics, insulin, antineoplastic, and antipsychotic drugs in the previous 2 weeks before the study were excluded.

Both participants were exposed to the general and local study of history, chest X-ray, spirometry has been calculated by a spirometery (ZAN 300, Germany), sputum cellular analysis.

Statistical analysis

Statistical analysis was performed using the Statistical Program for Social Science (SPSS) for Windows version 20.All values are expressed as the means±SE. One-way or two-way ANOVA followed by the Tukey test or the Student's t-test for unpaired results was used to evaluate differences between two groups, respectively. Differences were considered to be significant for values of P±0.05.

RESULTS

A total number of 100 subjects were included in this study. Among them 50 were controls who were normal healthy individuals and 50 were chronic obstructive pulmonary disease (COPD) cases. Of the 50 controls, their mean age 44.30±4.51 years. Among 50 chronic obstructive pulmonary diseases cases, 45.64±5.21 there was no statistically significant difference (P>0.05) in sex and age between the two groups by an independent-samples t-test and chi-squared ($\chi 2$) test, respectively. No significant difference as serum vitamin C was found between COPD subjects and healthy control. Furthermore, FEV1/FVC (%) and FEV1 (%) were significantly lower in COPD groups compared with control (P<0.01), suggesting that smoking was closely related to the occurrence of COPD.

Table 1: Comparisons of serum ceruloplasmin, serum bilirubin and BMI in COPD and control group.

Parameters	Patients, N=50	Controls, N=50	P- values
Mean sr. vitamin C	0.3608±0.0443	0.3718±0.0577	0.2878 Not sig. p>0.05
Mean sr. SOD	2.186±0.517	3.097±0.206	0.0001 High sig. p<0.01
Mean FEV1/FEVc ratio	71.60±3.97	80.52±2.87	0.0001 High sig. p<0.01

DISCUSSION

Various factors, including sex, age, resident district, type of residence, household income, educational level, occupation, and smoking history, affect the prevalence of COPD. Subjects living in suburban/rural areas and general residence types, and low income, low educational level, and agriculture or fisheries employment had a more prevalence of COPD. However, these factors may be related to male gender, old age, and a heavy smoking history, which are already well-known risk factors for COPD.[13]

ROS are produced by the Consecutive decline of oxygen. The addition of one electron to oxygen produces super oxide anion (O2-), the addition of a second electron results in hydrogen peroxide (H2O2) and a third yields the formation of hydroxyl radical (OH). These intermediates are called ROS and react readily with molecules such as proteins, lipids and DNA.[14] Antioxidant deficiency contributes to develop and aggravate various chronic diseases, including COPD which is sensitive to oxidative stress.[15]

In previous study, found significantly decreased level of vitamin C in COPD patients as compared to control. There results are in accordance with the studies performed by Nagraj et al, Raghunath et al, Sargeant et al and Mukadder et al. Vitamin C functions as an important free radical scavenger. The mechanism involved in the reduction of vitamin C level in COPD is due to rapid oxidation of ascorbic acid by free radicals. Vitamin C prevents other compounds from oxidation by their functions as an antioxidant by donating its electrons, in this process vitamin C itself is oxidized. The species formed after the loss of one electron is a free radical i.e., ascorbyl radical. As compared to other free radicals ascorbyl radical is relatively stable with half life of 10-5 seconds and is fairly unreactive which explains the antioxidant nature of vitamin C and its preference. Reduction of a reactive free radical with formation of a less reactive compound is sometimes called free radical scavenging or quenching.[16]

Low level of vitamin C was associated with hypertension and impaired endothelial function, because vitamin C improves endothelial dysfunction, and protects against heart and blood vessel system. Kirkil et al reported that

the plasma levels of SOD decreased in the COPD group.[17]

The family of superoxide dismutases (SODs) is the only enzymatic system able to degrade a superoxide anion. Impairment of the mitochondrial SOD (SOD2) activity was related to asthma pathophysiology and extracellular SOD (SOD3) was shown to protect lungs against oxidant mediated injury. In more advanced studies shows that, it is of interest to investigate whether single nucleotide polymorphisms (SNPs) in these SOD genes contribute to the development of BHR bronchial hyper responsiveness and/or COPD.

Tobacco smoke and environmental air pollution are the significant factors directly and particularly exposed noxious free radicals to the lungs are most common of all human tissues,. Therefore, the redox balance regulation can be an important factor for the development of BHR, excess decline in lung function and development of COPD.[18]

There is an evidence that oxidative stress reaches the circulation by a fall in the plasma antioxidant capacity SOD associated to smoking. In addition, a similar fall in plasma antioxidant occurs in exacerbations of COPD (MacNee W, 1999, Mac Nee, 2005).[16]

The significant correlation found between the antioxidant enzymes and FEV1 suggests that decrease in antioxidant enzyme activities might be the result of greater airway obstruction in COPD patients. This present analysis was the antioxidant enzyme activities in COPD comorbidities.

This study may have useful clinical implications in view of increased understanding of COPD risk parameters.[19]

This study has some limitations. This study was a retrospective study which used already completed survey data. We could not assess occupational or environmental exposure. The nutritional status was also assessed using self-reported questionnaires, with assistance from an interviewer. Measurement of vitamin C using blood sampling may be more helpful to confirm the nutritional status. The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

Increased oxidative stress in the lungs of COPD patients is a major driving mechanism for chronic inflammation, disease progression and exacerbations, whereas systemic oxidative stress is linked to the worsening of comorbidities. Targeting oxidative stress with antioxidants is therefore a logical approach in a common disease where there are no effective disease modifying therapies. Oxidative stress not only produces direct injurious effects in the lungs, but also activates the molecular mechanisms that initiate lung inflammation and may have a role in many of the processes thought to be involved in the complex pathological events that result in COPD. COPD is one of the most important lung illnesses caused by smoking cigarettes. Therefore, oxidative stress is present in COPD both in the lung and systemic circulations.

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