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Original Article

Comparative study of malondialdehyde and superoxide dismutase in diagnosed COPD patients

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ABSTRACT

Background: Chronic Obstructive Pulmonary Disease (COPD) represents a major health problem, and its prevalence and fatality rates are increasing worldwide. Oxidative stress and oxidative damage play a vital role in the pathogenesis of COPD.

Aims: To investigate the oxidative stress in COPD patients and healthy controls.

Methods: In this case-control study, a total of 102 subjects (51 diagnosed COPD patients and 51 healthy controls) aged between 20-60 years was enrolled. The plasma Malondialdehyde (MDA) levels and Superoxide dismutase (SOD) activity were estimated in all the subjects. A P value <0.05 was considered as statistically significant for all data analyzed.

Results: The mean age of controls and cases were found 42.14±7.73 and 52.92±13.72 years, respectively. The mean weight of COPD patients was lower than healthy controls (P<0.001). Similarly, the body mass index (BMI) in COPD patients was lower than healthy controls (P<0.001). The plasma levels of MDA (micromol/l) was significantly higher in COPD patients than healthy controls (P <0.001). The SOD activity (U/mg protein) was significantly lower in COPD patients than healthy controls (P<0.001). A significant negative correlation was found between MDA levels and SOD activity among COPD patients (r= -0.76, P<0.001).

Conclusion: The study showed that the level of MDA has significantly increased and SOD activity has significantly decreased in COPD patients as compared to healthy controls. In addition, a significant negative correlation was found between MDA levels and SOD activity among COPD patients. These results supported that oxidative stress in COPD patients plays an important role in the pathogenesis and progression of the disease.

Keywords: MDA, SOD, COPD, Oxidative stress, Antioxidants.

INTRODUCTION

COPD is among the most common lung disease and has rising incidence worldwide (1). As defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD), it is a preventable and treatable disease characterized by

persistent airflow limitation which is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to injurious particles or gases (2). COPD represents a major health problem, and its prevalence and fatality rates are increasing worldwide (3). It is always associated with hypoxemia, hypercapnia, pulmonary arterial hypertension which increases the chance of occurrence of cardiopulmonary complications (4). Currently, COPD is the fourth leading cause of death in the world but is estimated to be the third leading cause of death by 2020 (5). The most common risk factor that leads to COPD is tobacco smoking and approximately 50% of the smokers develop COPD. Other studies have reported that 15-20% of smokers develop COPD (6). There is overpowering evidence that oxidative stress and oxidative damage play a vital role in the pathogenesis of COPD. Cigarette smoking is the most important source of environmentally derived reactive oxygen species (ROS) in COPD (7). ROS induces lipid peroxidation and yield products such as MDA, which in turn stimulates pulmonary inflammation (8). Lipid peroxidation products (MDA) are one of the key indicators of oxidative stress (9). However, there are also protective mechanisms that diminish the deleterious effects of these oxidants; known as antioxidants i.e., SOD (10).

In this study, it is aimed to investigate the oxidative stress in COPD patients. The status of oxidative stress and anti-oxidants in COPD patients may help for the assessment of disease progression and its severity. This study may also help in better treatment and management of the disease.

MATERIALS AND METHODS

Subject Selection

In this case-control study, a total of 102 subjects (51 diagnosed COPD patients and 51 healthy controls) aged between 20-60 years was enrolled from outpatient Department of TB & Chest Clinic of IIMS&R, Integral University, Lucknow (India). The study was conducted out from January 2017 to June 2017. The study was ethically approved by the ethical committee of the institution. This study adhered to the principles of the Declaration of Helsinki and its later amendments or comparable ethical standards (11). Written informed consent was taken from each subject recruited for the study.

Inclusion for COPD patients was done by clinical and spirometric investigations. COPD is characterized with lung function levels of $FEV_1/FVC < 70\%$ and presence of post-bronchodilator $FEV_1 < 80\%$ of the predicted value (3, 12, 13).

Subjects with diabetes, ischemic heart disease, angina, Myocardial Infarction (MI), electrocardiogram abnormalities, those with other concurrent sicknesses like the chronic liver disease, hypothyroidism or those on drugs like antihypertensive, antioxidants and diuretics were excluded for both (COPD patients and healthy control) groups. Healthy controls with a history of smoking and exposure to biomass fuels were also excluded. Detailed medical history was taken from each subject.

Laboratory investigations

About 3ml of venous blood was collected in EDTA vial from each subject for estimation of MDA levels and SOD activity. The plasma MDA levels were estimated by Thiobarbituric acid reactive substance (TBARS) method and expressed as micromol/l (14). The SOD activity was estimated by Nitroblue Tetrazolium (NBT) method and expressed as U/mg protein (15).

Statistical analysis

Data analysis was performed using IBM SPSS software version 20.0 (Armonk, NY, USA). All the data were compared between the two groups by using ANOVA or unpaired t-test. Values were represented as mean ± SD (Standard Deviation). Pearson correlation coefficient was calculated among COPD patients. A P value <0.05 was considered as statistically significant for all data analyzed.

RESULTS

The mean age of controls and cases was found 42.14±7.73 and 52.92±13.72 years, respectively. The mean weight of COPD patients was lower than healthy controls (P<0.001). Similarly, the body mass index (BMI) in COPD patients was lower than healthy controls (P<0.001) shown in Table 1.

Table 1: Anthropometric characteristics of case and control group

Parameters	Case	Control	P value
Age (years)	52.92 ± 13.72	42.14 ± 7.73	<0.001*
Weight (kg)	54.51 ± 7.45	59.78 ± 8.58	<0.001*
Height (cm)	160.14 ± 11.27	164.80 ± 5.93	<0.01*
BMI (kg/m^2)	20.71 ± 2.26	21.84 ± 2.75	<0.05*

Values are expressed as Mean ± Standard Deviation

**Significant considered as P<0.05.*

BMI: Body mass index

The plasma levels of MDA (micromol/l) was significantly higher in COPD patients than healthy controls (P <0.001). The SOD activity (U/mg protein) was significantly lower in COPD patients than healthy controls (P<0.001) shown in Table 2 & Figure 1.

Table 2: Mean level of MDA and SOD in case and control group

Parameters	Case	Control	P value
MDA (micromol/l)	2.49±0.74	1.11±0.61	<0.0001*
SOD (U/mg protein)	0.81±0.26	3.12±1.02	<0.0001*

Values are expressed as Mean ± Standard Deviation

**Significant considered as P<0.05.*

MDA: Malondialdehyde, SOD: Superoxide dismutase

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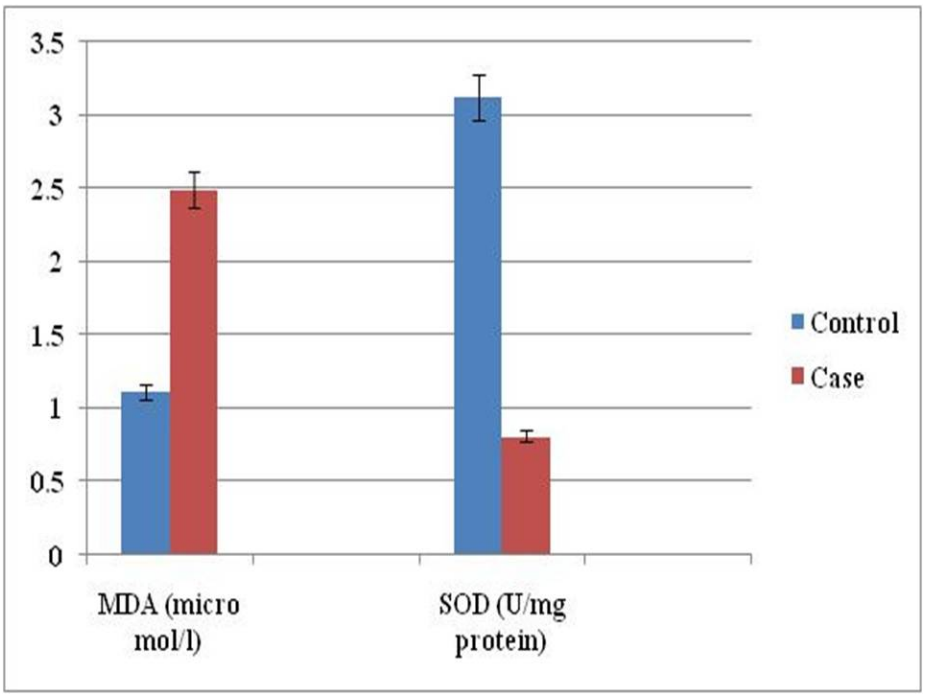

Figure 1: Comparison of mean level of SOD (U/mg protein) and MDA (micromol/l) in case and control group

A significant negative correlation was found between MDA levels and SOD activity among COPD patients (r= -0.76, P<0.001) shown in Table 3 & Figure 2.

Table 3: Correlation between variables in COPD cases

	MDA (micromol/l)	SOD (U/mg protein)	Age (years)	Weight (kg)	Height (cm)	BMI (kg/m^2)
MDA (micromol/l)	1	-0.759**	0.003	-0.118	-0.177	-0.125
SOD (U/mg protein)	-	1	-0.095	0.184	0.283	0.227
Age (years)	-	-	1	-0.354*	-0.124	-0.350*
Weight (kg)	-	-	-	1	0.539**	0.829**
Height (cm)	-	-	-	-	1	0.365**
BMI (kg/m^2)	-	-	-	-	-	1

**Correlation is significant at the 0.05 level (2-tailed).*

***Correlation is significant at the 0.01 level (2-tailed).*

MDA: Malondialdehyde, SOD: Superoxide dismutase

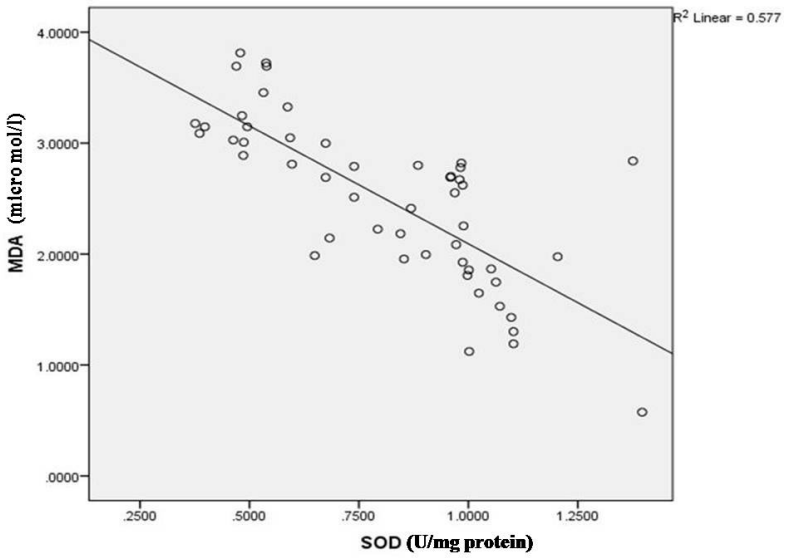

Figure 2: Correlation between SOD (U/mg protein) and MDA (micromol/l) among cases

DISCUSSION

Results suggested significant evidence that ROS are generated in COPD patients, which may play a vital role in the pathogenesis of the disease. Increased oxidative stress may play an important role in enhancing the inflammatory response and it is now recognized as the main pathogenic factor for progression and increasing severity of COPD. A significant amount of oxidative stress is caused by the household use of solid biomass fuels (16).

Subjects with COPD have higher MDA levels which are probably due to the ROS induced lipid peroxidation of the biological membranes interfering with the lungs normal physiology. Lipid peroxidation was obviously increased in patients with COPD especially at the severe stage of this disease (17).

Various enzymatic and non-enzymatic antioxidant defense mechanisms protect the tissue against the harmful effects of the oxidants. The explanation for reduced SOD activity is a possible direct inactivation of the enzyme by hydrogen peroxide or by the superoxide anion itself (6) or the increased production of free radicals in the patients with COPD or smokers leads to increased consumption of SOD leading to decrease in SOD levels (18, 19). Weight loss in COPD has been associated with increased circulating levels tumor necrotic factor-α (TNF-α). Low BMI may be attributed to skeletal muscle atrophy and weight loss (6).

We observed an increase in MDA levels and decrease in SOD levels in COPD patients and there was a significant negative correlation between MDA levels and SOD activity, which corroborates with the results of other studies in the same field of research. Similar findings were reported by Waseem et al have reported that there is a negative correlation between MDA and SOD (20). Montano et al have reported an inverse correlation between MDA and SOD (21). Arja et al have reported that COPD patients had higher levels of MDA and lower levels of antioxidants (SOD) when compared with control. SOD activities are negatively correlated with MDA (22).

Bajpai et al stated that SOD activity was significantly decreased in chronic bronchitis patients than in controls and serum mean level of MDA; a biomarker of lipid peroxidation was significantly increased in chronic bronchitis

patients when compared to controls (24). The results indicated that there was an increase in oxidative stress and a decrease in antioxidant level. Ahmad et al & Nadeem et al also reported an increase in the level of MDA and decrease in the level of SOD (17, 24).

CONCLUSION

The study showed that the level of MDA has significantly increased in COPD patients as compared to healthy subjects. However, the level of enzymatic antioxidant i.e. SOD has significantly decreased in COPD patients as compared to healthy controls. A significant negative correlation was found between MDA levels and SOD activity among COPD patients. These results supported that oxidative stress in COPD patients plays an important role in the pathogenesis and progression of the disease.

DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST

Funding: This study was not funded by any funding agency or company.

Conflict of Interest: Author A. Khan, S. Khan, M. M. Khan, R. Alam, & V. K. Srivastava declare that they have no conflict of interest.

Ethical Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent: Written informed consent was obtained from all individual participants included in the study.

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