ORIGINAL ARTICLE

Is Malondialdehyde (MDA) used as a Oxidative Stress Marker in Chronic Obstructive Pulmonary Disease (COPD) & Cigarette Smokers

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Abstract

Background : The present study was aimed to study alterations in levels of oxidants and antioxidants in Chronic Obstructive Pulmonary disease (COPD) patients.**Methods:** 100 patients of diagnosed COPD & 100 cigarette smokers in age group of 40 to 65 years were included in the study and results were compared with controls. Glutathione peroxidase (GPX),glutathione reductase (GPX),superoxide dismutase(SOD),Vitamin C as an antioxidants & Malondialdehyde(MDA) as an oxidant were estimated. **Results:** Significant (<0.05) decreased levels of Glutathione peroxidase (GPX), glutathione reductase (GR),superoxide dismutase(SOD),Vitamin C were found in COPD and chronic smokers as compared to controls.MDA was significantly (<0.05) increased as compared to controls.**Conclusion**: COPD & Cigarette smokers generate increased amounts of Reactive oxygen species (ROS).ROS produce many of the pathophysiologic changes associated with COPD and may contribute further to its pathogenesis. The primary defence against Reactive oxygen species (ROS) is endogenous antioxidants, which are found to be altered in COPD & smokers. Antioxidants inhibit the changes produced by ROS & they get confused in the process. So antioxidants can be used as a marker for prevention of COPD due to Reactive oxygen species.

Key Words

COPD, Oxidative stress, MDA, ROS

Introduction

COPD has had many names in the past including: Chronic obstructive airways disease,(COAD),chronic obstructive lung disease(COLD),chronic airflow limitation(CAL) and Chronic airflow obstruction. COPD actually comprises two related diseases chronic bronchitis and emphysema, one rarely occurring without a degree of the other. Chronic obstructive pulmonary disease (COPD) is characterized by progressive, irreversible airflow limitation associated with airway inflammation.[1] It is speculated that oxidative stress has an important role in the pathogenesis of COPD. [2,3] Lungs are the most affected organs by oxidants. Oxidants cause damage to the extracellular matrix, to biological membranes, to the genetic structure of the cell and to ciliary function. Oxidants lead to a decrease in surfactants , cause mucus hypersecretion and increase the effects of cytokines and proteases. [4] Cigarette smoking, air pollution and increase of free radicals in

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respiratory epithelial cells by inflammation and infections are the leading causes of oxidative stress in COPD. [2,3] Free radicals cause an imbalance between oxidants and antioxidants. An imbalance in favor of oxidants may cause oxidative damage to the air space epithelial cells. Lipid peroxidation occurs at the cell membrane by the effect of free radicals. [3] Malondialdehyde (MDA), the end product of lipid peroxidation, is used as a marker of oxidative stress. [5] Smoking is the most important cause of COPD and may enhance oxidative stress not only through increasing oxidants but also by weakening the antioxidant defence mechanisms.

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. [6]

Cigarette smoking is the most important risk factor for COPD, it is estimated that 80% of COPD patients have significant exposure to tobacco smoke. The remaining 20% have a combination of exposure to environmental tobacco smoke, occupational dusts and chemicals, indoor air pollution from biomass fuel used for cooking in poorly ventilated buildings, outdoor air pollution ,airway infection familial and hereditary factors have been implicated in the development of COPD. [7]

American Thoracic Society defines "Chronic obstructive pulmonary disease state characterized by the presence of flow obstruction due to chronic bronchitis or emphysema: the airflow obstruction is generally progressive, may be accompanied by airway hyperactivity, and may be partially reversible.

A current hypothesis in the pathogenesis of COPD is that the increased oxidant burden both directly as a result of smoking and indirectly by the release of Reactive oxygen species. Leukocyte may not be adequately counter balanced by the lung antioxidant system, resulting in oxidative stress. An excess of oxidants may then lead to enhanced pro-inflammatory gene expression and oxidative tissue injury leading to COPD. [8]

Malondialdehyde (MDA) is a lipid peroxidation product is an indicator of oxidative stress has correlated inversely with pulmonary function. [9]

Antioxidants depletion or deficiency may contribute to oxidative stress. Antioxidants not only protect against the direct injurious effects of oxidants, but also alter the inflammatory events that play an important role in the pathogenesis of COPD. [10]

Erythrocyte antioxidants such as reduced glutathione functions as an efficient intra cellular scavenger of H2O2 and plays an important role in the prevention of peroxidative lung damage in patients with COPD. Vitamin C is a water soluble free radical scavenger, can directly scavenge O2 and OH radicals and helps to neutralize physiological oxidant burden created by exogenous and endogenous sources. [11]

Present study is undertaken to evaluated erythrocyte reduced glutathione, serum vitamin C, superoxide dismutase activity and Malondialdehyde in controls and in chronic obstructive pulmonary disease cases.

Materials and methods:

The present study was carried out in the department of Biochemistry, Lokmanya Tilak Municipal Medical College and Hospital, Sion, Mumbai. The diagnosed cases of COPD attending chest OPD/Indoor of Lokmanya Tilak Municipal Medical College and Hospital, Sion, Mumbai were selected for the study. Patient suffering from asthma , chronic bronchitis ,emphysema were served as the study of group.

The study was conducted on the serum, whole blood and plasma of 100 individuals between age group of 40 to 65years who were distributed in three groups. Study group includes COPD and Non-COPD chronic smoker patients. Control group comprised of 100 persons aged 40 to 65 years who are not suffering from COPD. Patients suffering from those diseases, terminally ill patient, active chest infection age group below 40 years & above 65 years were also excluded.

A fasting blood sample were obtained from cases & control group and sent to the laboratory. GPX by PA glia method, GSH by Beutler E method, GR by Goldberg DN method, Superoxide dismutase by S. Marklund & Vitamin C by 2,6 dichlorphenol indophenols colorimetric method, Malondialdehyde (MDA) by modified method of

Table No. 1 Oxidative Stress & Antioxidant Markers

S.No.	Parameter	Control (n=100)	Non-COPD smokers (n=100)	COPD patients (n=100)	Sig./Non-sig. (P<0.05)
1	MDA	1.03 ± 0.06	4.97±1.8	4.61±0.71	Significant
2	GSH	219.51±19.77	112.23±32.5	132.15±28.60	Significant
3	GPx	2.59±0.74	1.41±0.29	1.33±0.23	Significant
4	GR	1.63±0.35	0.38±0.19	0.34±0.12	Significant
5	SOD	2.13±0.45	1.23±0.49	1.35±0.56	Significant
6	Vitamin C	96.35±7.34	34.46±10.65	32.33±9.28	Significant

Sadasiwdu et al were estimated.

Statistical Analysis:

All results are expressed in mean ± S.D. The biochemical parameters in serum samples were estimated and results were subjected to statistical analysis. Anova test was applied and statistically significance was established.

The levels of serum MDA in COPD patients (4.61±0.71) & non-COPD smokers (4.97±1.8) were significantly (P<0.05) higher as compared with controls (1.03 ± 0.06). The levels of erythrocyte GSH in COPD patients (132.15±28.60) & non-COPD smokers (112.23±32.5) were significantly (P<0.05) lower as compared with controls (219.51±19.77). The levels of erythrocyte GPX in COPD patients (1.33±0.23) & non-COPD smokers (1.41±0.29) were significantly (P<0.05) lower as compared with controls (2.59±0.74).

The levels of erythrocyte GR in COPD patients (0.34±0.12) & non-COPD smokers (0.38±0.19) were significantly (P<0.05) lower as compared with controls (1.63±0.35). The levels of serum SOD in COPD patients (1.35±0.56) & non-COPD smokers (1.23±0.49) were significantly (P<0.05) lower as compared with controls (2.13±0.45). The levels of serum Vitamin C in COPD patients (32.33±9.28) & non-COPD smokers (34.46±10.65) were significantly (P<0.05) lower as compared with controls (96.35±7.34).

Discussion

Several studied have been conducted in COPD patients to know the alteration in markers of oxidative stress and antioxidants such as MDA, GSH, GPx, GR, Vitamin C & SOD & their role in development of COPD.

"Statistically significant elevation in the levels of MDA & low levels of antioxidants (SOD, GSH, GPx, Vitamin C) in COPD patients as compared to control subjects. These results match with Rahman *et al* , Holger J *et al* , Leo MA *et al* , Adcock *et al*, M.K. DAGA *et al*. This shows that decreased antioxidant capacity in smokers as well as COPD patients indicating the presence of systematic oxidative stress. This leads to negative association of lipid peroxidation & positive association of antioxidants with lung function, suggesting increased lipid peroxidation is associated with pulmonary airway narrowing in general population. [12-16]

"As compared to control subject's GSH was significantly increased in COPD patients (p<0.001). Our results were in accordance with Macro Vander Toorn et al who examined whether cigarette smoke irreversibly modifies glutathione in airway epithelial cells. They observed that cigarette smoke does not oxidize GSH to GSSG but reacts to non-reducible glutathione aldehyde derivatives, thereby depleting the total available reduced glutathione pool. [17]

" The present study revealed significant decrease in the levels of Vitamin C in study subjects than those of healthy controls (p<0.001). Our results were corroborated with Romieu et al observed that an increase in vitamin C intake is associated with increase in FEV1 & FVC suggests that vitamin C may protect lungs from damage. [18]

" Voskresenska N *et al* studied in 2015 that persistently heightened systemic inflammation followed by oxidative stress seems to support COPD exacerbation. [19]

"In the present study, the COPD patients were screened for serum MDA, as a measure of lipid peroxide index and found increased levels when compared with controls

($p<0.001$). Similar results were found in Saeed Z H et al study , that blood concentrations of SOD and MDA are consistently higher in COPD patients when compared to non-smoker healthy controls. [20]

Conclusion

Oxidative stress is a major driving mechanism in the pathogenesis of COPD. There is increased oxidative stress in the lungs of COPD patients due to exogenous oxidants in cigarette smoke and air pollution and due to endogenous generation of reactive oxygen species by inflammatory and structural cells in the lung. [21] Thus, Oxidative stress parameters can be used as a marker for diagnosis of COPD and further prognosis and treatment.

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Conflicts of Interest
There are no conflicts of interest.

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