Research Article

Study of serum malonyldialdehyde (marker of lipid peroxidation) and paraoxonase-1 in chronic obstructive pulmonary disease patients with alterations in their lipid profile in Muzaffarnagar region

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a term for a group of diseases that affects lung. **Objective:** Objective of our study was to evaluate paraoxonase-1 (PON1) activity, malonyldialdehyde (MDA) and lipid profile in COPD patients and healthy control. **Materials and Methods:** Serum MDA and PON1 level were measured by Kei Satoh and arylesterase method, where lipid profile was determined by biochemistry fully autoanalyzer (CPC TurboChem 100). **Results:** The mean level of (marker of oxidative stress malonyldialdehyde) MDA was profoundly higher in cases ($P < 0.0001$) as compared to control group. The antioxidant enzyme PON1 were lower ($P < 0.0001$) in cases than control. The mean levels of total cholesterol, triglyceride, low-density lipoprotein (LDL), very LDL were significantly higher in cases as compared to control group. The mean level of high-density lipoprotein was lower in COPD patients as compared to control group. **Conclusion:** Our results concluded that the reduction in PON1 activity could reflect oxidative changes of enzyme free cysteine residues.

KEY WORDS: Malonyldialdehyde; Paraoxonase-1; Chronic Obstructive Pulmonary Disease; Lipid Profile; Oxidative Stress

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a complex respiratory disease characterized by progressive decline in lung function, chronic airway inflammation and impairment in quality of life.[1] COPD develops slowly and worsens over time. The airways and the air sacs in the lungs lose their elasticity and become inflamed. This causes them to produce more mucus and clogged, preventing the normal flow of air in and out of the lungs. It is speculated that oxidative stress has an important role in the pathogenesis of COPD.[2] Oxidants cause damage to the extracellular matrix, to biological membranes, to the genetic structure of the cell, and to ciliary function. Lipid peroxidation occurs at the cell membrane by the effect of free radicals.[3] Malonyldialdehyde (MDA), the end product of lipid peroxidation, is used as a marker of oxidative stress.[4] Smoking is the most important cause of COPD and may enhance oxidative stress not only through increasing oxidants but also by weakening the antioxidant defense mechanisms.

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Paraoxonase-1 (PON1) is a lipophilic antioxidant which is found in the liver and serum as bounded to high-density lipoprotein (HDL), and PON1 activity may play a protective role against oxidative stress in the lung.[5] The antioxidant role of PON1 is due to its protective effect on low-density

lipoproteins (LDLs) against oxidation. The serum PON1 is found in plasma together with HDL and involved in the prevention of plasma lipoprotein oxidation.[6] As lipids undergoing peroxidation are metabolized by this enzyme, the accumulation of lipid peroxides is prevented in both HDL and LDL. Thus, PON1 accounts from protective effect of HDL against LDL oxidation.[7] Abundant epidemiological evidence establishes the multifactorial character of this disease and indicates that underlying mechanistic link between impaired lung function[8] and inflammatory aspects of the COPD.[9]

MATERIALS AND METHODS

This study was carried out in the Department of Biochemistry in collaboration with the Department of Medicine at Muzaffarnagar Medical College and Hospital, Muzaffarnagar, UP, India. A total 100 subjects was selected for this study.

Inclusion Criteria

Cases

50 clinically and radiologically diagnosed COPD patients of age group 40-60 years having history of smoking.

Controls

50 normal healthy subjects of age group 40-60 years without any major illness belonging to the same socioeconomic status.

Exclusion Criteria

Patients with sexually transmitted diseases, patients with diabetes mellitus, patients with cardiac diseases, patients with renal diseases, patients with hepatic diseases, patients with prolonged illness, patients with pneumonia, asthma, or other chronic respiratory diseases were excluded from the study.

Collection of Blood Sample

The individual was requested for overnight fast. Blood samples were drawn with a disposable syringe and collected in a clean, disposable plastic tube from anterior cubital vein. The serum was separated and lipid parameters done in the freshly collected sample. Rest of the serum were kept at −20°C in small fractions for further investigation.

Methods

1. Assay of lipid peroxidation (MDA) by Satoh (1978)[10]
2. Assay of PON by arylesterase method using phenyl acetate as a substrate (1979)[11]
3. Lipid profile was measured by enzymatic kit method (CPC TurboChem 100).

Statistical Analysis

Results were statistically analyzed by GraphPad Quick Cals *t*-test calculator'. All results are presented as mean ± standard deviation $P < 0.05$ was considered as statistically significant.

RESULTS

Table 1 shows biochemical characteristics of cases and controls. The mean levels of total cholesterol, triglyceride (TG), very LDL (VLDL), LDL, and MDA were significantly increased ($P < 0.0001$) in COPD patients as compared to control. The mean HDL and PON1 levels were significantly decreased in COPD patients as compared to control.

DISCUSSION

In this study, we observed significantly increased levels MDA, TC, TG, LDL, and VLDL and significantly decreased levels of HDL and PON1 in COPD patients as compared to healthy individual. Smoking-induced radical chain reaction leading to lipid peroxidation of membrane phospholipids, altering cellular physiology. The lipid peroxides yield variety of by products including aldehydes reactive oxygen species and reactive nitrogen species cause alteration of proteins, chemical fragmentation or increase susceptibility to proteolytic attack, free radicals react with nucleic acid by addition to bases or abstractions of hydrogen atoms from the sugar moiety.[11]

PON1 is a calcium-dependent esterase closely associated with HDL containing apo A-I that has been reported to confer antioxidant properties on HDL by decreasing the accumulation of lipid peroxidation products. PON1 activity is under genetic and environmental regulation and appears to vary widely among individuals and populations.[12] In this study, PON1 levels were significantly decreased and MDA significantly increased in COPD patients as compared to healthy controls. Raut et al.,[13] Nadeem et al.,[14] Rumora et al.,[15] and Isik et al.[16] obtained the same results. Reduction of PON1 activity and increase in oxidative stress observed

Table 1: Biochemical parameters in COPD patients and normal healthy control

Variables	COPD	Control	*P*-value
Total cholesterol (mg/dl)	220.24±42.62	160.12±13.26	<0.0001
TGs (mg/dl)	201.10±46.78	144.10±14.52	<0.0001
HDL (mg/dl)	37.26±4.66	41.00±3.98	<0.0001
LDL (mg/dl)	141.96±44.62	89.96±15.48	<0.0001
VLDL (mg/dl)	40.62±9.47	28.82±2.90	<0.0001
PON1 (U/l)	35.40±4.41	103.60±17.86	<0.0001
MDA (nmol/ml)	5.59±1.20	2.26±0.76	<0.0001

TG: Triglyceride, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, PON1: Paraoxonase-1, MDA: Malonyldialdehyde

in COPD patients could be partly caused by oxidative environment. Lower concentrations of reduced thiol groups in COPD patients suggest that a decrease in PON1 activity could reflect oxidative changes of enzyme free cysteine residues. Furthermore, decreased PON1 arylesterase activity might indicate a down-regulation of PON1 concentration.[17]

Smoking can cause major changes in serum lipid profile simultaneously smoking is a major risk factor in COPD. Smoking affects the lipid profile such a way that the plasma LDL, cholesterol, and TGs concentration are higher and HDL cholesterol is lower in smoker than in nonsmokers.[17] Nicotine causes the release of adrenaline from the adrenal cortex leading to increased serum concentration of free fatty acids which stimulates hepatic synthesis and secretion of cholesterol as well as hepatic secretion of VLDL and hence increased TG.[18] Mitra et al.[19] and Begum et al.[20] obtained the same results.

Strength and Limitations

As the PON1 is closely associated with HDL which has profound effect on cardiovascular disease, therefore, it can be used as a marker for cardiovascular disease. Considering the prevalence of the COPD patients this work has to be done with the larger sample size for to confirm the results.

CONCLUSION

This study concludes that there is increase in MDA, total cholesterol, TG and LDL-cholesterol and decrease in the level of PON1 activity and HDL-cholesterol as compared to control. This study demonstrates that there occurs role of lipid peroxidation in the pathogenesis of COPD. Thus evaluation of oxidative stress in lung disease patients can lead to understanding of free radical mediated damage in COPD patients.

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