ORIGINAL RESEARCH PAPER
VOLUME-6 | ISSUE-7 | JULY-2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

SERUM PARAOXONASE 1 (PON 1) ARYLESTERASE & LACTONASE ACTIVITY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Medical Science

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ABSTRACT

Chronic obstructive pulmonary disease subjects (COPD) is a disease characterized by persistent airflow limitations and is progressive in nature. Major factor related to prevalence of COPD is tobacco smoking. Indoor, outdoor and air pollutions are other factors.
Objective: The objective of present study is to investigate the role of paraoxonase 1 (PON 1) Arylesterase and Lactonase activities in COPD subjects. Design: The study group consists of 40, COPD and 40 healthy subjects as a control group. PON 1 arylesterase (PON 1 ARE) activity was measured by using phenylacetate as substrate. PON 1 Lactonase activity was estimated by using Dihydrocoumarine (DHC) as substrate. Results: PON 1 ARE and lactonase activities were found significantly lower in COPD subjects as compare to healthy controls ($p<0.05$). Conclusion: Significantly decreased PON 1 activities (ARE and lactonase) in COPD subjects than in controls showed increased oxidative stress in COPD subjects. Serum paraoxonase 1 (PON 1) arylesterase & lactonase activity in chronic obstructive pulmonary disease (COPD)

KEYWORDS:

Paraoxonase 1, oxidative stress, COPD

Introduction:
COPD is a disease characterized by persistent airflow limitations and is progressive in nature. Major factor related to prevalence of COPD is tobacco smoking. Indoor, outdoor and air pollutions are other factors. The Global Burden of Disease Study which ranked it as sixth leading cause of death in 1990 and is expected to be third and fourth leading cause of death worldwide in 2020 and 2030 respectively.[1] In both developing and developed countries, COPD is a great burden on health due to its frequency, severity and economic impact.[2]

In COPD there is imbalance between oxidant and antioxidant which leads to oxidative stress.[3] Increase in oxidant may cause oxidative damage to air space epithelial cells.[4]

The paraoxonase gene family includes three members: PON 1, PON 2 and PON 3 in mammals. These are located on chromosome 7q21.3-22.1 in humans.[5] Paraoxonase 1 (PON 1) is a Ca2+ dependent, 354 amino acids containing enzyme with molecular weight about 45 kDa.[6] PON 1 is a HDL associated glycoprotein which protects LDL and HDL from lipid peroxidation.[7] PON 1 has both esterase and lactonase activities.[8]

The aim of this study was to estimate the potential role of PON 1 activity in the pathophysiology of COPD.

Materials and methods:
This COPD subject- control study was done on 40 diagnosed COPD subjects of COPD subjects and 40 age and sex matched healthy controls from SRTR Government Medical College, Ambajogai, Maharashtra, India (Table.1). The study was approved by local ethical committee of same medical college. The written informed consent was taken from all participants.

The inclusion criteria included the diagnosed COPD subjects of COPD subjects with age between 40 to 75 years. The subject exclusion criteria included recent surgery, active infection, chronic inflammatory diseases, significant hepatic, or renal dysfunction, malignancy and or any other chronic illnesses.

Blood for investigations was collected within 24 hour of admission to the hospital by venipuncture of 40 COPD subjects and 40 controls. Serum was separated by centrifugation and stored frozen at - 80^{0}C until analysis.

Serum PON 1 arylesterase (PON 1 ARE) activity was estimated as the rate of hydrolysis of phenyl acetate as substrate by modified Eckerson et al method. The rate of phenol liberation from hydrolysis of phenylacetate was measured spectrophotometrically at 270 nm. The activity was expressed as kU/L, based on molar extinction coefficient of phenol (1310 M-1 cm-1) at 270 nm, pH= 8 at 25^{0}C after correction for non-enzymatic hydrolysis.[9]

Serum lactonase activity was measured as described by Billecke S et al by using Dihydrocoumarine (DHC) as substrate. Rate of hydrolysis was measured was measured at 270 nm. The activity was expressed as U/L, based on molar extinction coefficient (1295 M-1cm-1) at 270 nm, pH= 8 at 25^{0}C after correction for non-enzymatic hydrolysis.[10]

Statistical analysis
Results were presented in terms of mean ± standard deviation (SD). Normality of distribution was tested by Shapiro - Wilk test. Student's unpaired t-test used for statistical analysis between COPD subjects and controls. Numerical variables were in Gaussian distribution. $P< 0.05$ was considered as significant. All analysis were carried out with the statistical software SPSS version 21.

Results:
Table 1: Demography of study population.

Parameters	COPD subjects	Controls
Male (n)	27	27*
Female (n)	13	13*
Age in years (Mean ± SD)	59.200 ± 7.609	58.250 ± 9.211*
BMI in Kg/m^2 (Mean ± SD)	25.625 ± 2.656	25.306 ± 1.421*

*NS= Non-significant.

Table 2. Student unpaired t test.

Parameters	COPD subjects (mean ± SD)	Controls (mean ± SD)
Arylesterase activity (KU/L)	65.9722 ±17.688	123.0901±30.868**
Lactonase activity (U/L)	14.553 ± 1.224	16.329 ± 1.017**

**$p < 0.05$

Discussion:
The aim of this study was to estimate serum PON 1 activity of COPD subjects and healthy controls.

Continuous formation of reactive oxygen species (ROS) takes place in the body during normal metabolism. Body's antioxidant defense mechanism takes care of it. The ROS concentration exceeds beyond such level so that antioxidant defenses cannot detoxify it. This

condition is called oxidative stress. ROS causes tissue damage and also affect lipids and lipoproteins. Under oxidative stress lipoproteins as well as lipids undergoes lipid peroxidation.[11]

In COPD there is imbalance between oxidant and antioxidant which leads to oxidative stress which may cause oxidative damage to air space epithelial cells.[4] HDL prevents oxidation of lipoproteins and this antioxidant effect of HDL is due to associated PON 1 as it prevent lipid peroxidation and also remove lipid peroxidation products.[12]

Oxidative stress can activate many signal transduction pathways, epidermal growth factor receptors, alteration of chromatin remodeling, NF-kappa ß, activator protein-1 and formation of lipid peroxidation products. Oxidized LDL inactivate PON 1 by interacting with the free sulfhydryl group of PON 1 enzyme.[13] In this manner oxidative stress plays a very important role in pathogenesis of COPD.[14]

HDL associated paraoxonase (PON 1) protects LDL and HDL from lipid peroxidations by different mechanisms and acts as an antioxidant enzyme against lipoprotein oxidation.[15,16,17]

The serum levels of PON 1 ARE and lactonase activities were significantly lower in COPD subjects ($p<0.05$) as shown in Table 2. This lower expression of PON 1 in COPD subjects than control may be the reason for high oxidative stress in COPD subjects than controls.

Conclusions:

Therefore, PON 1 activities (ARE & lactonase) may be considered as an additional parameter in diagnosis and management of COPD but larger studies are required to serve this purpose.

Acknowledgements:

Present study was not funded by any organization.

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