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Original Research Article

MOLECULAR MARKERS OF INFLAMMATION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE – A CROSS SECTIONAL STUDY

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ABSTRACT

Background: Chronic Obstructive Pulmonary Disease (COPD), occurs due to obstruction in the airways or alveolar destruction. Apart from genetic disposition, chronic exposure to cigarette smoke, aerotoxins and biomass fumes are considered to be etiological agents. Forced Expiratory Volume at 1st second (FEV_1), one of the parameters evaluated using spirometry is the most commonly used one for diagnosing, categorizing and monitor the treatment in COPD patients. Since the reliability is poor and also due to the fact that COPD is also a systemic inflammatory disease, as evident from numerous extra pulmonary effects of COPD, inflammatory biomarkers are being researched upon as an additional tool to FEV_1.

Materials and Methods: In our study, we recruited 40 COPD patients and estimated their baseline values of C-Reactive Protein (CRP) and fibrinogen. Diagnosis of COPD was confirmed from their health records. 40 normal subjects were recruited and same test was done in them.

Results: In this study, the mean CRP values in COPD group was significantly higher than that of normal group (5.73 ± 2.621 vs 3.85 ± 1.833). Similarly, mean serum fibrinogen levels in COPD group was 375.25 mg / dl which was significantly higher than mean levels in control group (304.1 mg / dl).

Conclusion: From our study, we concluded that, inflammatory biomarkers namely, CRP and Fibrinogen are significantly elevated in COPD patients, stressing the fact that it is more than a pulmonary disease and future studies can prove the effectiveness of these biomarkers in assessing the severity of the disease, monitor the progress, predict the complications and assess the effectiveness of anti inflammatory drugs as treatment.

Keywords: Chronic Obstructive Pulmonary Disease, C-Reactive Protein, fibrinogen, inflammatory biomarkers.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a very common respiratory ailment marked by persistent symptoms and signs of the respiratory system. The leading causative agent is tobacco smoking, with exposure to toxic and other chemical agents playing a crucial role in development of this disease both in smokers and passive smokers. Host factors like genetics, hyperresponsiveness of airways and congenital diseases of the lungs also add to the woes. Destruction of alveoli and changes in airways lead to airway obstruction. Although it has been considered primarily as pulmonary disease, recent studies suggest it is a systemic inflammatory disorder since it is associated with a host of co-morbidities like ischemic heart disease, osteoporosis, metabolic syndrome and heart failure.[1]

Assessment of disease status, progression and treatment responsiveness has been traditionally done using the pulmonary function test. The most used parameter has been the Forced Expiratory Volume at 1st second (FEV1). Due to poor correlation with symptoms and disease progression, latest studies suggest using biomarkers for prognosis and therapeutic guidance in COPD patients. A few of

these biomarkers are interleukin - 6 (IL-6) and IL-8, plasma fibrinogen, serum amyloid protein (SAA), surfactant protein - D, C- Reactive protein (CRP), total bilirubin, club cell secretory protein 16 and Matrix Metalloproteinases MMP-8 and MMP-9.[2] Of these, fibrinogen, IL-6, CRP and total bilirubin have shown promise in predicting mortality in COPD patients.[3]

In our study, we planned to study two inflammatory molecular biomarkers namely, serum fibrinogen levels and C-Reactive Protein (CRP) level in COPD patients. Estimation of the biomarker levels can guide in administration, tapering and withdrawal of corticosteroids in COPD patients and help in better outcome from treatment.

MATERIALS AND METHODS

After obtaining Institutional Ethical approval, this cross-sectional study was done in the outpatient department of Thoracic Medicine in a tertiary care centre. 40 COPD patients were recruited for the study. COPD diagnosis was confirmed from their medical records. Patients who were recently hospitalised, those who had blood transfusion in recent past, those who used anti-inflammatory drugs in past 2 months, those with a history of cancer, connective tissue disorder and inflammatory bowel diseases and those with recent fever were excluded from the studies. After obtaining written and informed consent from patients, peripheral venous blood sample was collected following standard laboratory procedures. CRP levels and Serum fibrinogen levels were estimated using ELISA method. The same test was done in venous blood samples of normal subjects recruited as controls.

RESULTS

The biochemical parameters were compared between the cases and control group using independent 't' test. Mean CRP levels in cases group and control group are compared in table 1. It was statistically significant at 'p' value < 0.005.

Table 1: Comparison of mean levels of C-Reactive Protein between COPD patients and control group

Group	Number of participants	Mean ± Standard Deviation	'p' value
Cases	40	5.73 ± 2.621	0.000
Controls	40	3.85 ± 1.833	

The comparison of serum fibrinogen levels is given in the figure 1. The difference in the levels was statistically significant with a 'p' value of 0.003 ('p' < 0.05).

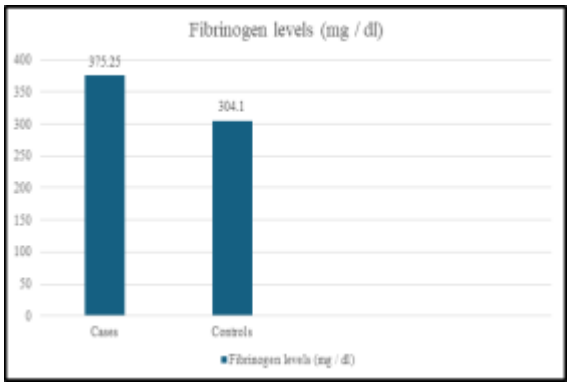

Figure 1: Comparison of mean levels of serum fibrinogen between COPD patients and Normal controls

DISCUSSION

Our study aimed at evaluating the baseline values of inflammatory markers namely CRP and fibrinogen in COPD patients. CRP is considered as one of the important inflammatory markers in various studies. In our study, the level of CRP in COPD patients was significantly higher than the normal subjects. The normal value of CRP, as per the lab standards is < 6 mg / L, the mean value of CRP in COPD group was on the higher side of normal range. This is in accordance with the study done by Gan.W.Q et al,[4] where it was proven that levels of CRP and other inflammatory markers including fibrinogen was significantly elevated in COPD patients than the controls. Another study by Suzana et al., also correlated positively with our findings.[5] Another study by Ferrari et al., followed the levels of CRP and Interleukin – 6 (IL-6) over 3 years. In that study, 21 % of patients presented with an increase of CRP levels by > 3 mg/L after 3 years. The mean levels of the COPD group though did not change.[6] From the above studies we can conclude that, baseline CRP levels are elevated in COPD patients and can be used as a tool along with other inflammatory markers during follow up and prediction of severity and mortality.

In our study, serum fibrinogen levels were found to be significantly higher in COPD group than the control group. The levels though were within normal limits, was found on the higher side of the range. This is in accordance with various cross-sectional studies which had shown higher blood fibrinogen levels in COPD patients.[7,8,9] A study by Mannino and colleagues showed that plasma fibrinogen levels were associated with severity in moderate and severe disease.[9]

Our studies have shown that, baseline CRP and fibrinogen levels are elevated in COPD patients as COPD is now considered a systemic inflammatory state. A possible reason for the mean values to be in the normal range may be due to the sample size. Higher sample size would give a better picture. Moreover, we haven't correlated the levels with the severity of the disease.

Future perspectives

This study can be extended with higher sample size. Correlation of the levels with the Forced Expiratory Volume at 1st second (FEV1) can be done, thereby correlating with severity of the diseases. A follow up study can also be done to determine whether the levels rise with increasing severity and whether the levels decrease with appropriate treatment.

CONCLUSION

To summarize, CRP and serum fibrinogen levels are proving to be useful biomarker in predicting the severity in COPD, in identifying which patients will have exacerbation, monitoring progression and response to treatment by anti-inflammatory drugs. Since FEV1 value alone is not a reliable indicator of the disease, it can be combined with these commonly done inflammatory biomarkers along with few other biomarkers and be a valuable tool in management of COPD.

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