

C- Reactive Protein in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Abstract

Original Research Article

Background: Patients with chronic obstructive pulmonary disease (COPD) have raised serum levels of C- reactive protein (CRP). This may be related directly to COPD and its associated systemic inflammation or secondary to other factors such as concomitant smoking status. The aim of this study was to evaluate infection and inflammation are potential causes of raised CRP levels in COPD and also evaluate relationship between increased counts of inflammatory cells in circulation and serum CRP levels. **Results:** Patients with COPD acute exacerbation were characterized by a systemic inflammatory process indicated by an increased leucocyte count (15.2 ± 6.4) vs (8.6 ± 3.1) $\times 10^3$ cells/ μ l, raised levels of CRP (32.1 ± 26.0) vs (3.42 ± 2.70) μ g/ml. After treatment of disease exacerbations, systemic levels of CRP (on the day of discharge) was significantly reduced (5.42 ± 3.20) compared with day of admission and with the control group (3.42 ± 2.70). **Conclusion:** CRP levels are raised in COPD patients with acute exacerbation and also in stable patients at the time of discharge without clinically relevant any other chronic inflammatory diseases. CRP may be a systemic marker of the inflammatory process that occurs in patients with COPD.

Keywords: COPD (chronic obstructive pulmonary diseases), C-RP (C-Reactive protein), FEV1 (Force expiratory volume in one second), FVC (force vital capacity), TLC (total leukocyte count).

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a complex chronic inflammatory disease of the lungs involving several types of inflammatory cells and a variety of inflammatory mediators. The relationship between these cell types, cytokines, and the sequence of events that concludes with progressive airflow limitation and destruction of lung parenchyma remains largely unknown [1].

C-reactive protein is a homo pentameric acute-phase inflammatory protein, a highly conserved plasma protein that was initially discovered in 1930 by Tillet and Francis while investigating the sera of patients suffering from the acute stage of Pneumococcus infection and was named for its reaction with the capsular (C)-polysaccharide of Pneumococcus [2].

The prognostic role of baseline C-reactive protein in chronic obstructive pulmonary disease is controversial.

The prevalence of chronic obstructive pulmonary disease is ~10% in adults older than 40

years. According to World Health Organization (WHO) estimates, 65 million people have moderate to severe COPD and more than 3 million people died of COPD in 2005, corresponding to 5% of all deaths globally. The estimates show that COPD will become the third leading cause of death worldwide in 2030[3].

Patients with COPD are prone to exacerbations that cause a decline in health status. Exacerbations are diagnosed usually on clinical grounds when there is deterioration in specific symptoms or a reduction in lung function. However, in patients with COPD, spirometric changes associated with exacerbations may be small [4].

COPD is defined as an inflammatory disease and the airway inflammation influences all parts of the respiratory tree from the bronchi down to the alveoli and pulmonary vessels. The inflammatory process in the larger airways (bronchitis) is mainly causing production of phlegm and contributes only to a minor extent to the airway obstruction. Small airway inflammation (bronchiolitis) causes airway obstruction and starts early in smokers. As the disease progresses, tissue

destruction in the most peripheral airway and in the alveoli (emphysema) takes place, which contribute greatly to the development of respiratory failure. Pulmonary vessels are also involved in the inflammatory process at an early stage and recent findings indicate that vascular involvement is most likely of great importance for the development of the disease [5].

The airflow limitation in COPD is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, and it is increasingly recognized that in addition to an inflammatory process in the lung itself, systemic inflammation plays an important role in COPD [6].

This is orchestrated by multiple inflammatory cells and mediators in the airways and the lung tissues, is induced by inhalation of noxious gases and particulate matter. This persistent inflammatory response in the lung is also associated with a significant systemic inflammatory response yielding adverse clinical outcomes, so-called systemic effects of COPD [7].

The aim of the present study was to assess CRP as a cost-effective auxiliary marker other than spirometry in determining severity of COPD and better control of disease prognosis in patients with exacerbations.

MATERIAL AND METHODS

Study population

Patients with stable COPD: The study group consisted of 55 patients consecutively admitted to a pulmonary ward. COPD was defined as forced expiratory volume in one second (FEV1) < 80% predicted for age and height, with airflow obstruction evidenced by a ratio of FEV1 to forced vital capacity (FVC) of < 70%. Patients with concomitant confounding diseases such as diabetes mellitus, lung carcinoma, thyroid and cardiovascular disease and those with bronchiectasis were excluded from the study.

Patients with an exacerbation of COPD

This group consisted of 60 subjects consecutively admitted to hospital suffering from an acute exacerbation of COPD. The presence of an acute disease exacerbation was determined by an independent chest physician and was defined as a recent increase in dyspnea, cough, and sputum production of sufficient severity to warrant admission to hospital. The patients were treated with a standard protocol of medication, starting immediately after admission to hospital (day 0).

Exclusion criteria

For this analysis included a previous diagnosed of acute myocardial infarction, angina, congestive heart failure, cancer, hepatic cirrhosis, chronic renal failure, rheumatoid arthritis or any other systemic inflammatory disease.

Measurement of inflammatory parameters

Blood samples obtained at hospital arrival from March 2017 to June 2018 (in the emergency room, Katihar Medical college, Katihar) were used to simultaneously measure CRP levels by commercially available turbidimetric methods. The turbidimetric method assesses agglutination of latex particles coated with antibody against CRP by quantifying the absorbed light (detection limit >0.4mg/dL).

CRP was measured quantitatively and interpreted in the ranges of < 6 mg/L (normal and low risk) and \geq 6 mg/L (high risk). Data were analyzed using descriptive statistics (e.g. percentage and mean). $P < 0.05$ was considered statistically significant.

RESULT

COPD patients were male and female subjects aged 40–70 yrs., with a baseline post-bronchodilator Forced Expiratory Volume in 1 sec. (FEV1) < 80% of the reference value, an FEV1/Forced Vital Capacity (FVC) ratio \leq 0.7 and a current or former smoking history of \geq 10 pack-yrs. Controls were healthy male and female subjects aged 40–70 yrs. with normal spirometry.

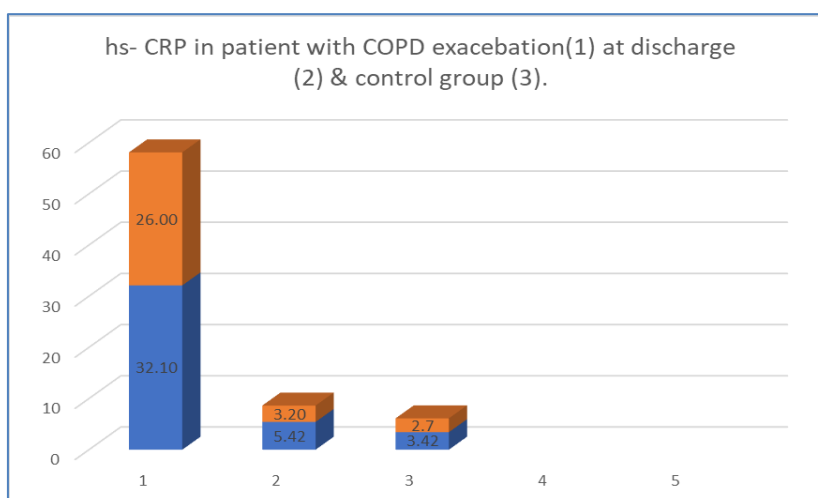
Table-1: Showing comparison of various parameters in patients of COPD at the time of admission and at the time of discharge from the hospital.

	At Admission (Mean \pm S.D.)	At discharge (Mean \pm S.D.)	p-value
FEV1(L)	0.8 \pm 0.2	1.4 \pm 0.2	< 0.001
FEV1 % predicted	32.1 \pm 7.2	58.4 \pm 7.0	< 0.001
SpO2 (%)	92.7 \pm 4.3	97.3 \pm 1.4	< 0.001
CRP (mg/L)	32.1 \pm 26.0	5.42 \pm 3.20	< 0.001
TLC(/mm3)	15200 \pm 6400	8600 \pm 3100	< 0.001

Patients with COPD presented with exacerbation were characterized by a systemic inflammatory process indicated by an increased leucocyte count (15.2 ± 6.4) vs (8.6 ± 3.1) $\times 10^3$ cells/ μ l), raised levels of CRP in COPD exacerbation (32.1 ± 26.0) vs normal control group (3.42 ± 2.70) μ g/ml). After treatment of disease exacerbations, systemic levels of CRP (on the day of discharge) was

significantly reduced (5.42 ± 3.20) compared with day of admission and with the control group (3.42 ± 2.70).

Graphical representation of c-reactive protein level in various groups of like 1) Patients with COPD exacerbation 2) Patients of COPD at the time of discharge and 3) Normal healthy control, plotted using of Microsoft excel.



DISCUSSION

Persistent, low-level, systemic inflammation is thought to play a significant pathogenic role in many Non-Communicable Diseases, including COPD. Elevated circulating levels of white blood cells (WBC) and C-reactive protein have been reported in patients with COPD[8].

The main finding of the present study is that CRP levels are raised in COPD. Our results also demonstrate higher CRP levels were related to low FEV1% predicted and SpO2. The airflow limitation in COPD is associated with abnormal inflammatory response of the lung to noxious particles or gases. Although in modernized sites of our country modern heating systems are used, in rural areas biomass heating and cooking is still traditionally important and is widely used. Cigarette smoking, on the other hand, is still the most commonly encountered risk factor. It is probable that such as in the case of smoking, biomass exposure also disturbs the cellular oxidant-antioxidant balance and initiates inflammatory process in the lungs of COPD patients [9].

There is a large number of cytokines, chemo-attractants and other mediators that are of importance for the interplay of inflammatory mechanisms in COPD. Neutrophilic granulocytes are key players in the inflammatory reaction and the most important chemo-attractants for these cells seem to be IL-8 (CXCL8) and leukotriene B4 (LTB4)[10].

In the lung, CRP has protective functions in innate immune responses against bacteria and apoptotic cells. CRP enters the lung from plasma and is primarily produced by hepatocytes in response to IL-6 stimulation. Activated epithelial cells and increased numbers of alveolar macrophages and other inflammatory cells in COPD may release IL-6 into the circulation. This stimulates an acute-phase response and increases the level of plasma CRP[11].

The reasons for the inverse association between systemic inflammation and reduced pulmonary function are unclear but several mechanisms maybe involved. First, reduced lung function may be responsible for systemic inflammation. Like hepatocytes, inflammatory lung or pulmonary epithelial cells, have been shown to express CRP and IL-6. An alternative mechanism—reverse causation— cannot be excluded. High levels of cytokines and acute phase reactants in peripheral circulation may be a cause rather than a consequence of poor lung function [12].

CONCLUSION

We have confirmed that CRP levels are significantly raised in patients with COPD exacerbation and also in stable patients at the time of discharge when compared with stable control group. Therefore, this proves that infection and inflammation are potential causes of raised CRP levels in COPD and also evaluate relationship between increased counts of inflammatory cells in circulation and serum CRP levels.

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