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PULMONARY FUNCTIONS IN PATIENTS OF BRONCHIAL ASTHMA AND ITS ASSOCIATION WITH INFLAMMATORY MARKER (hs-CRP)

Physiology

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ABSTRACT

Asthma is a chronic inflammatory airway disorder characterised by variable degrees of airway inflammation which is possibly accompanied by systemic inflammation. Thus, hs-CRP may play a role in its pathogenesis. The study was carried out to measure and correlate pulmonary functions and hs-CRP in patients of bronchial asthma. Spirometry was done using Exercise Physiology System, Ganshorn Medizin Electronics System, Germany and hs-CRP levels were determined using ELISA kit supplied by DRG International Inc., USA. The mean value of FEV1 was 1.63 ± 0.07 lts, PEF was 3.89 ± 0.20 l/s, MEF was 1.31 ± 0.09 l/s and hs-CRP was 4.84 ± 0.27 mg/L. A statistically significant negative correlation was found between

- FEV^1 (Lts) and hs-CRP ($r= -0.5649$, $p<0.0001$)
- PEF (l/s) and hs-CRP ($r= -0.5685$, $p<0.0001$)
- MEF (l/s) and hs-CRP ($r= -0.3122$, $p=0.0085$)

This negative correlation between pulmonary functions and serum hs-CRP levels suggests that increased levels of inflammation are related to poor pulmonary function and increase in airflow limitation in patients of Bronchial Asthma.

KEYWORDS

Bronchial Asthma, Pulmonary Functions, Hs-crp

INTRODUCTION

Asthma is a chronic disorder characterized by reversible episodes of airway obstruction which are recurrent and might resolve spontaneously or with treatment [1].According to GINA burden report around 300 million people are suffering from asthma worldwide [2].

Airway inflammation in asthma is associated with recruitment of inflammatory cells and both central and peripheral airways are affected. Cytokines such as IL-1, IL-6 and nuclear factor kβ have a role in airway inflammation and they regulate hs-CRP [3,4]. It has also been postulated that airway inflammation is accompanied by systemic inflammation in asthma and thus hs-CRP may play a role in the pathogenesis of asthma [5]. The association between asthma and CRP is not clear and could also reflect the role of obesity in CRP production[6,7] as the incidence of asthma in young adults is significantly more in subjects with a higher body mass index (BMI)[5,8,9]

There have been reports of an association between increased levels of hs-CRP and respiratory symptoms of asthma like wheeze, attack of breathlessness and nocturnal cough [10]. So it is reasonable to consider that there could be an association between severity of inflammation in asthma and levels of hs-CRP.

AIMS AND OBJECTIVES

This present study was conceived with the objective to measure Pulmonary Functions and Inflammatory marker (hs-CRP) in patients of Bronchial Asthma and to establish a correlation, if any, between them, in the Delhi population representing India who may have their own genetic makeup and environmental exposure.

MATERIALS AND METHODS

An observational cross sectional study was carried out in the Department of Physiology in association with Departments of Biochemistry and Medicine, Lady Hardinge Medical College & Associated Hospitals, New Delhi. The study was approved by the Institutional Ethics Committee for Human Research. 70 physician diagnosed cases of bronchial asthma (as per GINA 2011 guidelines)[2] were recruited consecutively from the medical clinic and ward according to the inclusion/exclusion criteria and a written informed consent was obtained. Cases of Bronchial asthma of either gender, 18-45 years of age and confirmed by the Physician/Chest Physician were included in the study. Patients who have taken any oral or inhalational Bronchodilators in the past 8-12 hours, patients with severe acute exacerbations, hepatic, renal, cardiovascular diseases, diabetes mellitus, cancer, systemic inflammatory disorders, neuromuscular disease, skeletal disorders, smokers and those with Body Mass Index (BMI) ≥25 kg/m2 were excluded from the study.

The subjects were called to the Department of Physiology in morning hours between 9 am to 11 am after an overnight fast of at least 8 hours. They were allowed to adapt to the experimental conditions and the nature of the tests was explained to them .Age and anthropometric measurements were taken and Body mass index was computed [11]

Pulmonary Functions were measured by using Exercise Physiology System, Ganshorn Mediegin Electronics System, Germany. Guidelines of ATS/ERS were followed for the entire procedure [12]. A minimum of 3 acceptable IVC/FVC maneuvers were performed. Acceptability of maneuver and reproducibility of IVC, FEV1, level of effort and cooperation by the subject, equipment function or malfunction were evaluated during spirometric measurements to ascertain validity of the results. The reversibility in PFT was tested after inhalation of a short-acting bronchodilator(400 µg of salbutamol) through a spacer device. The criteria for reversibility included 12% as well as 200 ml of increase in FEV1 after 20 minutes of inhalation of salbutamol.

Blood samples for the assays were collected from the study participants under all aseptic precautions. The serum levels of hs-CRP

were determined using the hs-CRP ELISA kit supplied by DRG International Inc., USA on the principle of a solid phase enzyme-linked immunosorbent assay. The minimum detectable concentration of the CRP ELISA assay as measured by 2SD from the mean of a zero standard was estimated to be 0.1 mg/L.

The data was submitted for statistical evaluation using Graph Pad Prism version 6 software. Correlations were assessed using the Spearman's correlation coefficient.

OBSERVATION AND RESULTS

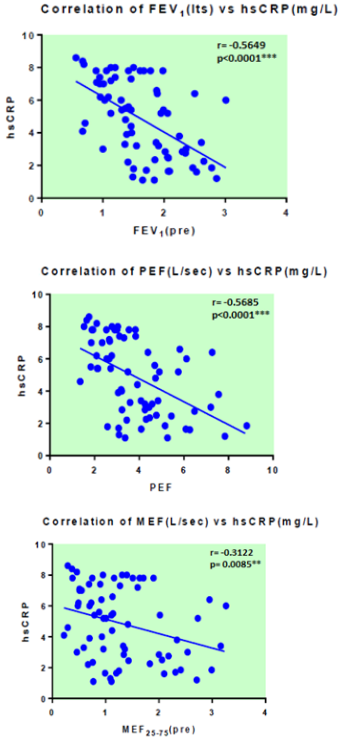
Table 1: Distribution of Sex and mean values of Age, Height, Weight and BMI of participants in the study group (n=70)

Parameters	Mean ± S.E.M
AGE(yrs)	33.63 ± 1.10
M:F RATIO	43:27
Height(cms)	161.30 ± 1.05
Weight(kg)	57.41 ± 1.40
BMI(kg/m^2)	22.01 ± 0.47

Table 2: Shows the mean observed values of spirometry parameters and hs- CRP in the study group (n=70)

Parameters	Mean ± S.E.M.
IVC(lts)	2.66 ± 0.08
FVC(lts)	2.40 ± 0.08
FEV_1(Pre in lts)	1.63 ± 0.07
FEV_1(Post in lts)	2.09 ± 0.08
ΔFEV_1(% Change)	30 ± 1.82
FEV_1/IVC %	60.96 ± 1.57
PEF(l/s)	3.89 ± 0.20
MEF(l/s)	1.31 ± 0.09
Hs-CRP(mg/L)	4.84 ± 0.27

Fig. 1: Shows the correlation of FEV1 (lts), PEF (lts/sec), MEF (lts/sec) with hs-CRP(mg/L) in patients of Bronchial Asthma (n=70)



DISCUSSION & CONCLUSION

We evaluated the correlation between serum levels of hs-CRP in our study group were correlated with pulmonary functions and observed a significant negative / inverse correlation between FEV1 and hs-CRP, PEF and hs-CRP & MEF and hs-CRP (Fig.1).

Our study also confirms that hs-CRP is related to age which has been shown to be a confounding factor of elevated hs-CRP levels. We tried to minimise this by taking patients between 18-45 years of age but nevertheless found a positive correlation between age and hs-CRP.(p=0.0410*,r=0.2449)

We also found that females had a statistically significant higher hs-CRP(p=0.0010***) than males whereas the difference in age and BMI was not statistically significant. The gender difference in CRP seems to be controversial as our finding is in contrast to a study by Tracy et al which included subjects aged 65 years and above of either gender.[13] In our study, meticulous steps were taken in order to minimize the effects of various confounding factors which could influence hs-CRP in patients of Bronchial Asthma, all our subjects were non-smokers because smoking is an independent confounding factor of elevated levels of hs-CRP as suggested by Ridker et al[14] .This could probably be explained by the fact that cigarette smoke induces IL-6 in lung tissues[15]. Moreover, our subjects were free of any past / current history of co-morbid conditions which could have a possible influence on serum levels of hs-CRP.

We also took subjects with a BMI<25 kg/m^2 in order to remove the confounding effect of low grade systemic inflammation in obese people as suggested by earlier studies[16,17] which is probably due to adipocyte derived IL-6[7].When we correlated the BMI within our study group with hs-CRP, the results were not statistically significant thus confirming that increase in hs-CRP with BMI probably occurs at higher BMI values.

There have been studies demonstrating a discordant relationship between hs-CRP and pulmonary functions in Bronchial Asthma with varying observations. A few studies have also failed to elucidate any association or correlation between hs-CRP and pulmonary functions. In two different studies [18,19] the mean hs-CRP levels were not found to be correlating with indices of pulmonary function (FEV_1, FVC and MEF) although the mean serum hs-CRP levels were significantly higher in patients with acute asthma compared with controls. Kilic et al[20] although found a significant positive correlation between the levels of hs-CRP and the severity of asthma (p = 0.04, r = 0.38), no significant correlation among hs-CRP and forced expiratory volume (FEV_1), FEV_1%, Peak Expiratory Flow (PEF) and PEF% values was found. Similar results were reported by Qian et al[21] and Wu et al[22] where levels of serum hs-CRP gradually increased with severity of Asthma.

In a population-based study, Kony et al [5], found out a high frequency of airway hyperresponsiveness and low FEV_1 with increased levels of serum hs-CRP and concluded that systemic inflammation may be associated with respiratory impairment.

Takemura et al [23]demonstrated that in patients with steroid-naive asthma, levels of serum hs-CRP were higher compared with healthy volunteers and also correlated negatively with pulmonary functions (FEV_1% pred, FEV_1/FVC% and $FEF_{25-75\%}$ pred)

In cross-sectional analysis, FEV_1 as a % of predicted values was negatively associated with serum CRP concentration (p=0.002) and changes in CRP levels during follow-up were associated with annual FEV_1 decline.[24]

Our study documents that there is a negative correlation of pulmonary functions including FEV_1, PEF and MEF with inflammatory marker hs-CRP suggesting that increased levels of inflammation(hs-CRP) are related to a decrease in pulmonary function and increase in airflow limitation(FEV_1,PEF,MEF) in patients of Bronchial Asthma. This is in accordance with few previous studies but also includes flow rates (MEF & PEF) along with FEV_1.Our findings indicate an association of systemic inflammation as detected by hs-CRP with airway obstruction and thus hs-CRP may be considered a surrogate marker of airway inflammation and might also be used as a risk factor marker for Bronchial Asthma.

LIMITATIONS

The results from the study may be viewed with caution because of a small sample size (n=70) and further research is warranted in a larger sample size and a wider array of inflammatory markers.

CONFLICT OF INTEREST

The authors declare no conflict of interest

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