

“Predictive value of absolute Eosinophil count for Bronchial Hyper reactivity in allergic rhinitis”

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ABSTRACT :

Background: Allergic rhinitis patients are at risk of development of asthma. These patients may also have peripheral eosinophilia and bronchial hyper reactivity. The present study was aimed to evaluate the correlation and predictive value of peripheral blood eosinophilia for bronchial hyper reactivity (BHR) in patients with allergic rhinitis but without asthma.

Methods: 41 Subjects with history of allergic rhinitis symptoms and peripheral eosinophilia but without asthma were tested for bronchial hyper reactivity with bronchial provocation test (BPT) with histamine. Absolute eosinophil count was estimated and correlated with degree of bronchial hyperreactivity .

Results: Bronchial hyperreactivity was observed in 24 patients out of 34 with peripheral eosinophilia . Positive predictive value was 70.59 %[95% CI: 52.52 % to 84.88 %] .

Conclusions: 71 % of allergic rhinitis patients with peripheral eosinophilia had bronchial hyperreactivity who are with significant risk of future development of asthma. Measures to retard the progression to asthma by environmental modification , pharmacotherapy including intranasal corticosteroids^[7,8,9] are recommended in these patients.

Key words: Eosinophilia , Bronchial hyper reactivity, Predictive value

INTRODUCTION:

Bronchial hyperreactivity (BHR), one of the hallmarks of bronchial asthma, is a risk factor for the development of asthma^[1,2]. Allergic rhinitis patients at risk of development of asthma. These patients will have bronchial hyperreactivity. This study was done to find out the correlation and predictive value of absolute eosinophil count for bronchial hyperreactivity . Data collected as part of the large, population-based European Community Respiratory Health Survey (ECRHS) have provided valuable information on the cross-sectional association between allergic rhinitis and BHR in young adults. In non-atopic asthma a relationship between the

peripheral blood eosinophil count and the FEV₁ has been observed and the eosinophil count shown to be useful in monitoring disease activity.^[4] In addition, a relationship between eosinophil count and methacholine PC₂₀ has been observed in subjects with allergen induced late phase asthmatic reactions.^[5]

MATERIALS AND METHODS:

41 allergic rhinitis patients without asthma were studied including 20 females and 21 males. 20 atopic patients (11 females and 9 males) had a mean age of 27 (range12-48) years. 21 non atopic patients (13males and 8 females) had a mean age-33 (range13-50 years.) All patients gave their informed consent before the study, which was approved by the local ethical committee. Consenting patients who had

allergic rhinitis without asthma were tested for peripheral blood eosinophilia. Inclusion criteria were consenting allergic rhinitis patients in the age group 12 to 50 years with baseline FEV₁ 80% or more. Exclusion criteria were airflow obstruction with FEV₁ less than 80%, pregnancy, lactating mothers, uncontrolled hypertension and cardiovascular diseases. Ethical committee approval was obtained and informed consent was taken from all patients.

HISTAMINE CHALLENGE TEST

The method of Cockcroft et al^[6] was employed. After baseline spirometry, aerosols of test solutions were generated by passing oxygen through the nebulisers at a flow rate of 6 litre per minute. The same nebulisers were used for given concentrations of histamine throughout, their outputs having previously been calibrated. Aerosols were inhaled by tidal breathing for two minutes. First phosphate buffered saline was inhaled, followed at five minute intervals by different concentrations of histamine solution from 0.5 mg per ml, 1 mg per ml, 1.5 mg per ml, 2 mg per ml, 2.5 mg per ml, 5mg per ml, 20mg per ml, 30 mg per ml, 50 mg per ml, 75 mg per ml through nebulizer. FEV₁ was measured at 30 and 90 seconds after each inhalation; the lower of the two values was used and the test was discontinued when the FEV₁ had fallen by more than 20% of the value obtained after inhalation of phosphate buffered saline. The concentration of histamine required to cause a 20% fall in the FEV₁ (PC₂₀) was obtained from the log dose response curve. The PC₂₀ for the histamine in these subjects were identified and categorized as patients with allergic rhinitis with bronchial hyperreactivity and patients with allergic rhinitis without bronchial hyperreactivity.

EOSINOPHIL COUNTS

Venous blood was taken just before histamine challenge

testing and put into a tube containing EDTA.

Absolute eosinophil counts were performed. The results were expressed as total eosinophils per litre. Counts were performed by one observer without knowledge of the patient's histamine PC₂₀.

RESULTS

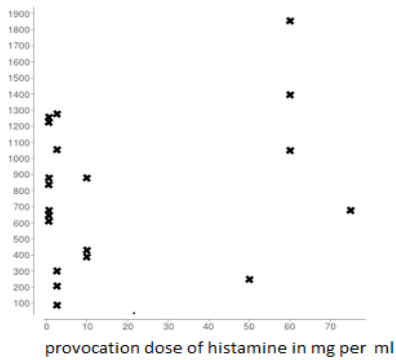
Individual eosinophil counts and histamine PC₂₀ values for atopic and non atopic were considered. There was a wide range of histamine PC₂₀ values, ranging from 0.5 mg to 75 mg/ml for atopic and non-atopic subjects. Absolute eosinophil count showed wide variation, with a mean value of 800 (range 90-1854 x 10⁶/L for the atopic subjects and 757 (range 280--2058) x 10⁶/L for the non atopic. The mean FEV₁ was 82% of predicted (range 65-100%) for the atopic subjects and 84% (range 71-111%) for the non-atopic subjects.

STATISTICAL ANALYSIS

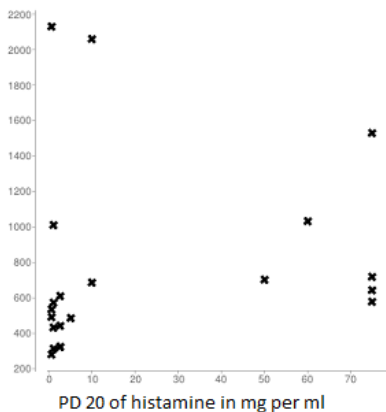
Out of 41 subjects 34 subjects had absolute eosinophil count above normal and out of this 24 subjects (71%) had bronchial hyperreactivity. Bronchial hyperreactivity was not observed in 10 subjects (29%) with peripheral blood eosinophilia. 71% of patients with peripheral blood eosinophilia had bronchial hyperreactivity. Positive predictive value peripheral blood eosinophilia in allergic rhinitis for BHR was 70.59 % [95% CI: 52.52 % to 84.88 %]. Pearson correlation coefficient (r) were calculated to assess relationships between variables. A p-value of <0.05 was considered significant. There was no significant inverse correlation between baseline eosinophil count and histamine PC₂₀ in atopic (Pearson correlation coefficient (r) 0.297, p = 0.203 and non atopic group (r) value 0.164, p = 0.478. There was no inverse correlation between baseline eosinophil count and baseline FEV₁ in the atopic (r value 0.254, p = 0.281) and non atopic group (r value was -0.278,

p =0.223). There was no significant correlation between baseline FEV₁, and histamine PC₂₀ for atopic (r value 0.366 and p= 0.1130 or non atopic (r value was -0.286 and p= -0.209 group and no correlation between duration and FEV₁ in atopic (r value -0.23330, p= 0.323) and non atopic (r value 0.352, p =0.118). Out of 30 patients who had bronchial hyperreactivity 50% had family history of allergic rhinitis and asthma. Among patients with bronchial hyperreactivity 57% were females.

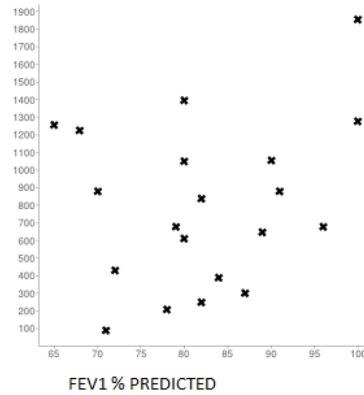
SCATTER PLOTS SHOWING THE CORRELATION BETWEEN DIFFERENT VARIABLES



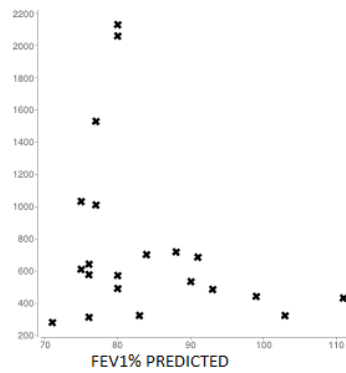
a) Relationship between provocation dose and absolute eosinophil count in atopic population



b) Relationship between absolute eosinophil count and PC₂₀ in non atopic population



C) Relationship between absolute eosinophil count and FEV₁ % in atopic population



d) Relationship between absolute eosinophil count and PC₂₀ in non atopic population.

From table 1 : with this observations and keeping the cut off value of normal upper limit of absolute eosinophil count as 440×10^6 per litre positive predictive value of the peripheral eosinophilia for bronchial hyperreactivity was 70.59 % [95% CI: 52.52 % to 84.88 %]. Sensitivity of the peripheral eosinophilia for bronchial hyperreactivity calculated was 80.00 % . [95% CI: 61.42 % to 92.24 %] . Positive likelihood ratio was 0.88 [95% CI: 0.68 to 1.14] .Disease prevalence was 73.17 % [95% CI: 57.05 % to 85.76 %] . positive predictive value of 70.59 % [95% CI: 52.52 % to 84.88 %]. Negative predictive value was 14.29 % . [95% CI: 2.37 % to 57.77 %]. Overall accuracy was 61%.

Table1. Relationship of bronchial hyperresponsiveness (BHR) and absolute eosinophil count (AEC)

		Bronchial hyperreactivity	
		Yes	No
Absolute eosinophil count	Greater than 440×10^6 per litre	24	10
Absolute eosinophil count	Less than 440×10^6 per litre	6	1

DISCUSSION

The present study shows the relationship between peripheral blood eosinophilia and bronchial hyperreactivity in allergic rhinitis and also reveals a strong association between allergic rhinitis and lower airway dysfunction. The results from the present analysis extend these cross-sectional findings by showing that allergic rhinitis precedes the development of bronchial hyperreactivity.

Allergic rhinitis is a frequent inflammatory chronic disease induced by an IgE-mediated reaction after allergen exposure in the nasal mucosa. It is now clear from a large number of cross-sectional studies that allergic rhinitis is strongly associated with asthma and BHR⁽¹³⁾. These studies have demonstrated that dysfunction of the upper and lower airways frequently occur together and appear to share common risk factors, such as atopy. Many patients with allergic rhinitis and no clinical evidence of asthma showed increased response to methacholine or histamine^(12, 14)

An association between the peripheral blood eosinophil count and the level of bronchial responsiveness after methacholine has been shown in subjects who developed an allergen induced late phase reaction, and the eosinophil count increased

24 hours after challenge in these subjects^[10]. Present study findings are consistent with the initial observations in this study done by Durham et al.^[10] Roquet A, HalldCn G, Ihre E, Hed J, Zetterstrom et al showed that eosinophil activity markers in peripheral blood have high predictive value for bronchial hyperreactivity in patients with suspected mild asthma.^[15]

In the study by Roquet A et al^[15]; with one eosinophil activity marker, either serum ECP or EG2, bronchial hyperreactivity could be predicted in 70% of the patients. If combined any two of the activity markers (this study adds to the available evidence, effects on patient care and health policy, or the percentage of eosinophils), the predictive value increased to 100%. They concluded that the blood eosinophil concentration, as well as, to some extent, serum ECP, has a high specificity for BHR in patients with recently developed clinical symptoms of asthma^[15]. However, the intracellular expression of ECP did not correlate with the PD₂₀ value, and no significant difference between the groups was found. In the present study also there was no correlation between absolute eosinophil count and the histamine PC₂₀ in patients with bronchial hyperreactivity among atopic and non atopic population (for atopic r value 0.366 and p= 0.1130 or non atopic r value was -0.286 and p= -0.209).

Treatment with either inhaled sodium cromoglycate produces a small reduction in bronchial hyperreactivity as demonstrated by Rocchiccioli K et al.^[11]

Remission of bronchial hyperreactivity occurred more frequently in subjects treated with intranasal corticosteroids. Clinical studies^[7,8,9] done by Aubier M et al^[7], Corren J et al^[9], Watson WT et al^[10] demonstrated that intranasal steroids are effective in improving bronchial hyperreactivity in patients with nasal inflammation, and that this effect was principally due to improvement in nasal function. Strengths of the study is this study addresses the common question of how often a patient with allergic rhinitis will develop bronchial hyperreactivity and asthma; and finds out the effect of family history in bronchial hyperreactivity, yet another clinical question often raised. This study adds to the available evidence to the predictive value of absolute eosinophil count for prediction of bronchial hyperreactivity with a common laboratory test with absolute eosinophil above the cut off value of 440×10^6 per litre. The predictive value by this study is as that of Roquet A et al^[15]; in which they could predict same with one eosinophil activity marker, either serum ECP or EG2 with positive predictive value of 70%. Present study is having effects on patient care since peripheral eosinophilia in allergic rhinitis patients needs environmental modification and pharmacotherapy of allergic rhinitis including intranasal corticosteroids for future prevention of manifestations of asthma since 71% of patients are at risk of bronchial hyperreactivity. Eventhough the sample size was 41, the study could predict the equal incidence of the bronchial hyperreactivity done with different sample sizes in different countries.

Controversies raised by this study are the non correlation between different parameters like PC₂₀

absolute eosinophil count, FEV₁, duration which was also raised by previous studies. Future research directions for underlying mechanisms of absence of bronchial hyperreactivity in periferal eosinophila which was seen in 24% of patints are also raised by the study observations.

CONCLUSION

Present study reveals the significance of peripheral blood eosinophilia for predicting bronchial hyperreactivity in allergic rhinitis without asthma. Patients with allergic rhinitis with peripheral blood eosinophilia who are with significant risk for future development of asthma needs measures to retard the progression to asthma by environmental modification and pharmacotherapy for allergic rhinitis including intranasal corticosteroids^[7,8,9,10].

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