ORIGINAL ARTICLE

Effect of Inhaled Corticosteroids and Oral Montelukast on Frequency of high Eosinophil count in poorly controlled Asthmatic patient

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ABSTRACT

Aim: To determine the frequency of high sputum eosinophil count (>3%) in poorly controlled asthmatic patients after 1 month inhaled corticosteroids and oral montelukast treatment.
Methodology: With the sample size of 254 asthmatic patients, a cross-sectional study was carried out from January-July 2017 at the department of Pulmonology, Jinnah Hospital, Lahore following the approval by Hospital's Ethical Committee. The patients received inhaled corticosteroids (ICS) (480µg/day) and oral montelukast (10mg twice daily) for continuous 1 month. All the patients had their sputum eosinophil count before and after treatment. The patients were labeled as having high eosinophil count (more than 3%). Data was entered and analyzed by Statistical Package for Social Sciences (SPSS software, version 20). Chi-square test was applied as p-value ≤ 0.05 was considered significant.
Results: In present study, both genders were included with age ranging from 18 to 55 years**.** Among 254 patients, mean duration of asthma was 30.49±6.18 days with 20 and 40 as minimum and maximum days. All patients had raised eosinophil count (>3%) before the treatment was given. Mean eosinophil count was 4.58±1.74% with 2% and 7% as minimum and maximum values. Among 254 patients, 169(66.5%) had high eosinophil count (>3%), while 85(33.5%) patients had low eosinophil count (<3%) after the treatment. Eosinophil count reduced significantly after 1 month treatment with inhaled corticosteroids and oral montelukast.
Conclusion: The sputum eosinophil count was significantly increased in all asthmatic subjects. Daily use of inhaled corticosteroids and oral montelukast for 1 month reduce eosinophil count.
Keywords: Asthma; Poorly controlled asthma; Sputum eosinophil count.

INTRODUCTION

The Global Initiative for Asthma (GINA) defines asthma as a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation[1].

It is estimated that asthma accounts for about 1 in every 250 deaths worldwide. Developing countries like Pakistan has around 80% of the mortality due to it. It is estimated that asthma will affect approximately 100 million people by 2025[2].

Global Initiative for Asthma classifies it as "Controlled" if symptoms (Wheeze, SOB and cough) and medication use is twice per week or less, or smooth night sleep, no activity limitation or airway obstruction reported by subject and "uncontrolled" when any three or more of these individual features occur within a week[1].

Asthma exacerbation, serious morbidity and mortality happen in approximately 20% of the patients due to its inadequate control[3,4]. One of the main features of asthma is the presence of airway inflammation, with involvement of several cellular populations and the release of many inflammatory mediators[5,6]. Eosinophils are considered as the main hallmark of airway inflammation in asthma[7]. Activated eosinophils and the severity of asthma are co-related strongly[8]. The recruitment of eosinophils into bronchial mucosa in which allergic inflammation occurs is a critical contributor to the late asthmatic reaction of congestion and mucus hypersecretion[5].

A combination of genetic and environmental factors like air pollution and allergens exposure with improper medications cause asthma. Pattern of symptoms with treatment response and spirometery findings lead to a diagnosis.[9] Asthma can only be prevented by avoiding triggers but cannot be cured permanently. Beta agonists (long acting) or anti-leukotriene medicines in combination with inhaled corticosteroids are used as its treatment option.[10] Treatment of rapidly worsening symptoms is usually with an inhaled short-acting beta- 2 agonist such as salbutamol and oral corticosteroids. In very severe cases, intravenous corticosteroids, magnesium sulfate, and hospitalization may be required[11].

The present study was carried out to determine the frequency of high sputum eosinophil count (>3%) in poorly controlled asthmatic patients after inhaled corticosteroids and oral montelukast treatment for continuous 1 month. Determination of sputum eosinophil count is therefore simple, safe, non-invasive and repeatable method of directly obtaining repeated samples of airway secretions and it correlates with the degree of underlying airway inflammation.

METHODS

It was a cross-sectional study conducted in Department of Pulmonology, Jinnah Hospital, Lahore, Pakistan, from January 2017 to July 2017 following the approval by

Hospital's Ethical Committee. The sample size of 254 was estimated by 95% confidence level with 6% margin of error and considering 61% of eosinophil count in uncontrolled asthmatic patients.[12] Patients were enrolled by non-probability consecutive sampling. Diagnosed asthmatic patients since 5 years including both genders with age range (18-55 years) presenting with poorly controlled asthma were enrolled. Exclusion criteria involved patients who were unable to give informed consent with the history of smoking, biomass exposure (e.g. burning woods/cow dung) and pregnancy. Written informed consent was taken from the patient at the time of enrollment. Diagnosed asthmatic patients with the help of history, investigations (chest x-rays) and lung function tests like spirometery were given fluticasone (480µg/day) and oral montelukast (10mg twice daily) for continuous 1 month. Sputum eosinophil count was checked for all patients. The patients were labeled as having high eosinophil count if it came out to be more than 3%.

Statistical analysis: Data was entered and analyzed by SPSS Vr 20. Quantitative data like age (in years) and eosinophil count were presented as Mean±S.D. The qualitative data like gender, number of patients with high eosinophil count (>3%) were offered as frequency and percentages. Modifiable factors like age, gender and duration of asthma were controlled by stratification of data. Chi-square test was applied as p-value ≤ 0.05 was considered significant

RESULTS

In this study, 254 asthmatic patients were included. Demographic parameters like gender, age and duration of asthma were noted at the time of enrollment. Males and females were in ratio of 119:135. Parameter like age was categorized as 18-30, 31-45 and above 45 years. Number of Patients enrolled (87, 99 & 68) were below 30, 45 and above 45 years of age respectively. Asthma was categorized depending on duration in days. Group of patients having duration of asthma (20-26 days) were 81. Group of patients having duration of asthma (27-34 days) were 91. Group of patients having duration of asthma above 35 days were 82.

At the time of enrollment all asthmatic patients had raised eosinophil count (>3%). Results showed among 254 patients, 169(66.5%) had high eosinophil count (>3%), while 85(33.5%) patients had low eosinophil count (<3%) after treatment. Mean eosinophil count was 4.58±1.74 with 2 and 7 as minimum and maximum values. No significant difference between High Sputum Eosinophil Count and Gender (p<0.627) present. Insignificant difference between High Sputum Eosinophil Count and Age (p<0.832). Insignificant difference between High Sputum Eosinophil Count and duration of asthma (p<0.589).

Table 1: Stratification of high sputum eosinophil count with gender

Gender	High Sputum Eosinophil Count		Total
	Yes	No	
Male	81(68.1%)	38(31.9%)	119(100%)
Female	88(62.2%)	47(34.8%)	135(100%)
Total	169(66.5%)	85(33.5%)	254(100%)

P value 0.627, Chi-Square test

Table 2: Stratification of high sputum eosinophil count with age

Age group	High Sputum Eosinophil Count		Total
	Yes	No	
18-30	60(69%)	27(31%)	87(100%)
31-45	65(65.7%)	34(34.3%)	99(100%)
>45	44(64.7%)	24(35.3%)	68(100%)
Total	169(66.5%)	85(33.5%)	254(100%)

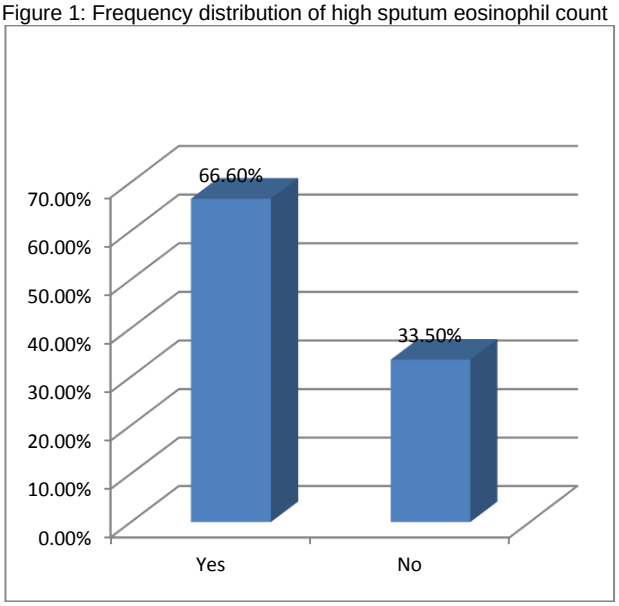
P value 0.832, Chi-Square test ; p value > 0.05 = insignificant

Table-3: Stratification of High sputum eosinophil count with asthma

Duration of Asthma	High Sputum Eosinophil Count		Total
	Yes	No	
20-26	55(67.9%)	26(32.1%)	81(100%)
27-34	63(69.2%)	28(30.8%)	91(100%)
35-40	51(62.2%)	31(37.8%)	82(100%)
Total	169(66.5%)	85(33.5%)	254(100%)

P value 0.589, Chi-Square test ; p value > 0.05 = insignificant

Figure 1: Frequency distribution of high sputum eosinophil count



DISCUSSION

Through this study, an attempt was made to study the level of sputum eosinophils in poorly controlled asthmatic patients after treatment with high dose inhaled fluticasone and cysteinyl leukotriene antagonist for continuous 01 month. This study suggested that there is a significant association between asthma and sputum eosinophilia.

Enrolled patients were given a combination of high dose inhaled corticosteroids and oral montelukast. The patients received ICS (480µg/day) and oral montelukast (10mg twice daily) for continuous 1 month. They recieved treatment as per GINA (Global Initiative for Asthma) guidelines. Our work was in lines with previous researchers who prescribed ICH with montelukast to their patients in their studies[13].

Preventing asthma exacerbation is one of the important goals in management of asthma. Inflammation has been assumed to be an important factor in underlying asthma exacerbation. Exacerbations of asthma are characterized by increasing airway obstruction. In this study it has been shown that the sputum eosinophils is significantly increased in exacerbation of asthma. We summed-up asthma as inflammatory disease as previous studies did[14].

According to Jatakanon *et al* (2000), loss of asthma control was predicted by eosinophil count changes in sputum[15]. Higher eosinophil percentages in induced sputum from asthmatic subjects are associated with lower FEV_1 and high sensitivity to methacholine[16]. As Yeung *et al* (2006) documented that the degree of symptoms were more sensitive tool in assessing the onset of an exacerbation as it precedes the deterioration in peak flow rate. Similarly, in this present study the asthma was assessed based on symptoms as well as the spirometry as it was done in previous research work[17].

As Miranda *et a*l (2004) showed that eosinophilic airway inflammation was associated with increased symptoms and near fatal events[18]. A study by Anees *et al* (2002) showed that asthmatics with high sputum eosinophil count had poor lung functions. They had greater bronchial hyper-responsiveness as well[19].

The current study had a number of limitations like financial constrains and less resources. No bronchoscopy was done. Only single cell line i.e sputum eosinophil count was evaluated in present study. The current project evaluated the effects of ICS and cysteinyl leukotriene antagonist on sputum eosinophil count and clinical improvement in symptomatic poorly controlled asthmatic patients. Determination of sputum eosinophil count is therefore simple, safe, non-invasive and repeatable method of directly obtaining repeated samples of airway secretions and it correlates with the degree of underlying airway inflammation.

CONCLUSION

Measurement of sputum eosinophils is simple and an inexpensive tool in monitoring asthma. This makes it a practical tool of potentially widespread applicability. Daily use of inhaled corticosteroids and oral montelukast for 1 month reduce eosinophil count.

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REFERENCES

1. Kroegel C. Global Initiative for Asthma (GINA) guidelines: 15 years of application. J Clin Immunol.2009;**5**(3):239-249.
2. Masoli M., Fabian D., Holt S., Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee report. Allergy; 2004; **2**(59): 469– 78.
3. Global Initiative for Asthma, National Heart, Lung and Blood Institute, 2002. Pocket Guide for Asthma Management and Prevention: A Pocket Guide for Physicians and Nurses. National Institutes of Health, National Heart, Lung, and Blood Institute.
4. Robinson D.S., Campbell D.A., Durham S.R., Pfeffer J., Barnes P.J and Chung K.F. Systematic assessment of difficult-to-treat asthma. ERJ. 2003;**22**(3):478-483.
5. Marcus P. Dosing inhaled steroids in asthma: is once-a-day administration effective?. Chest.2003;**124**(4):1196-1198.
6. Wardhana S.E and Datau E.A. Typhoid fever as a triggering factor in acute and intractable bronchial asthma attack. Acta Med Indones. 2013;**45**:312-320.
7. Brightling C.E. Eosinophils, bronchitis and asthma: pathogenesis of cough and airflow obstruction. Pulm Pharmacol Ther. 2011;**24**(3), pp.324-327.
8. Humbert M and Kay A.B. Chronic inflammation in asthma. Eur Clin Respir J.2003; **8**:126-137.
9. Lemanske R.F and Busse W.W. Asthma: clinical expression and molecular mechanisms. J Allergy Clin Immunol. 2010; **125**(2):95- 102.
10. Scott J.P and Peters G.M. Antileukotriene agents for the treatment of lung disease. Am J Respir Crit Care Med. 2013;**188**(5):538-44.
11. Garcia G., Taillé C., Laveneziana P., Bourdin A., Chanez P and Humbert M. Anti-interleukin-5 therapy in severe asthma. Eur Respir Rev.2013;**22**(129):251-257.
12. Harish M and Suryanarayana V. A Prospective Study of Sputum Eosinophils in Acute Exacerbation of Asthma. Int J Med Sci. 2014; **10**(2):145-149.
13. Rojas R.A., Paluga I., Goldfrad C.H., Duggan M.T. and Barnes N. Initiation of maintenance therapy with salmeterol/fluticasone propionate combination therapy in moderate asthma: a comparison with fluticasone propionate. J Asthma. 2007; **44**(6):437-441.
14. BarrattS. Mepolizumab in corticosteroid-resistant eosinophilic asthma. Thorax. 2009;**64**(6):552-552.
15. Haldar P., Brightling C.E., Hargadon B., Gupta S., Monteiro W., Sousa A. et al. Mepolizumab and exacerbations of refractory eosinophilic asthma. N Engl J Med. 2009;**360**(10):973-984.
16. Cowan D.C., Cowan J.O., Palmay R., Williamson A and Taylor D.R. Effects of steroid therapy on inflammatory cell subtypes in asthma. Thorax.2010;**65**(5):384-390.
17. Dougherty R.H. and Fahy J.V. Acute exacerbations of asthma: epidemiology, biology and the exacerbation-prone phenotype. Am J Clin Exp Immunol. 2009; **39**(2):193-202.
18. Moore W.C., Meyers D.A., Wenzel S.E., Teague W.G., Li H., Li X et al. Identification of asthma phenotypes using cluster analysis in the Severe Asthma Research Program. Am J Respir Crit Care Med. 2010;**181**(4):315-323.
19. Vandenplas O., Dressel H., Wilken D., Jamart J., Heederik D., Maestrelli P et al. Management of occupational asthma: cessation or reduction of exposure? A systematic review of available evidence. Eur Respir J. 2011;**38**(4):804-811.