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Increased Immunoglobulin E is associated with low respiratory functional in asthma patients

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Key words: Asthma, spirometry, immunoglobulin E.

Abstract

Asthma is a disease that is associated with inflammation airway. The study objective was to determine whether the serum Immunoglobulin E (IgE) concentration was associated with marker indicative in respiratory functional in men with asthma. For this purpose, we measured fasting serum IgE levels in 44 middle-aged men with mild to moderate asthma and 30 none-asthma subject that matched for age and sex. In addition, all patients underwent a resting spirometry test for measuring FEV1, FVC and FEV1/FVC as markers indicative in respiratory functional. Pearson correlations were used to establish the relationship between IgE concentrations with spirometry markers in asthma patients. A p-value < 0.05 was considered to be statistically significant. The statistical findings showed that an IgE concentration in asthmatic patients was significantly higher than healthy individuals. Compared with healthy subjects, asthma patients had lower level of FEV1, FVC and FEV1/FVC. A negative association was observed between serum IgE and FEV1, FVC and FEV1/FVC.Based on this data, it was concluded that IgE may be a precise predictor of asthma diagnosis.

Key words: Asthma, Spirometry, Immunoglobulin E.

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Introduction

The worldwide prevalence of asthma continues to rise in children and adult people. Although, the specific mechanisms responsible for these observations are not obvious. Recent evidence has shown that asthma is a complex syndrome, broadly defined by inflammation of the airways associated with airways hyperresponsiveness (AHR) and mucus hypersecretion (Buses *et al.,* 2001). A number of studies have demonstrated that chronic asthma is associated with remodeling of the airways and associated vasculature (Davies *et al.,* 2003; Elias *et al.,* 1999). Immunoglobulin E (IgE) is one of the body's 5 classes (isotypes) of immunoglobulins (antibodies). It was reported that Circulating IgE levels are predominantly elevated in helminthic parasitic and allergic conditions (Winter *et al.,* 2000). There is considerable evidence that immunologic stimulus leading to degranulation of human mast cells is their activation when the immunoglobulin E (IgE) molecules on their surfaces bind a relevant antigen (Ishizaka *et al.,* 1984). IgE normally accounts for less than 0.001% of total serum immunoglobulin. The serum IgE concentration is age dependent and normally remains at levels less than 10 IU/ml in most infants during the first year of life (Anupama *et al.,* 2005). Some recent studies have shown an association between prevalence of asthma and total serum immunoglobulin E (IgE) levels independent of specific reactivity to common allergens and symptoms of allergy (Freidhoff *et al.,* 1993; Tollerud *et al.,* 1991). These authors noted a close interrelationship between asthma and total IgE, even in nonatopic subjects, and it has challenged the concept of intrinsic asthma (Burrows *et al.,* 1989). Considering to IgE role as a mediator of allergic response, quantitative measurement of IgE, when integrated with other clinical indicators, can provide useful information for the differential clinical diagnosis of atopic and non-atopic diseases. Therefore, IgE measuring may be useful as a diagnostic tool for detecting and diagnosis asthma and its severity. On the other hand, it is well known that respiratory functional decrease in asthma patients. In this area, review of research evidence shows that asthma patients have a lover level of FEV1, FVC and FEV1/FVC compared with normal subjects. But, the question is that whether there are an association between serum IgE and marker indicative of respiratory functional or each of them independently influenced airway functional, asthma prevalence or its severity. Therefore, the current study is designed to examine whether IgE is associated with spirometry markers as respiratory functional indicators in these population.

Material and methods

The study objective was to determine whether the serum IgE concentration was associated with asthma and explained the association between IgE with respiratory functional indicators in these patients. For this purpose, forty four males asthma patients (age, 41 +/- 5 yr, BMI, 31 +/- 3.11 kg/m^2) and none-asthma men with the matched age and BMI were included in the present study. Inclusion criteria for study group were determined as existing asthma for at least 3 years, being between the ages of 35-50 years. All subjects were non-smokers. All participants had not participated in regular exercise/diet programs for the preceding 6 months. Exclusion criteria for the study group were: history of alcohol use, having symptoms that may be indicative of ischemia in electrocardiography, cerebrovascular disease. All study participants gave informed consent for the study by signing a form approved by the Ethics Committee of the Islamic Azad University, Iran.

Measurements

The measurements for weight, height were first performed, than fasting blood samples were taken for the determination of serum IgE. Weight and height were measured in the morning, in fasting condition, standing, wearing light clothing and no shoes. Body mass index (BMI) was calculated as weight (kg) divided by squared height (m). All participants refrained from any severe physical

activity 48 h before measurements. Serum IgE was determined by ELISA method (Monobind Inc, CA 92630, USA). The Intra- assay coefficient of variation and sensitivity of the method were 5.87% and 1/0 IU/mL, respectively. Spirometry test were also reformed for measuring forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and ratio of forced expiratory volume in 1 s to forced vital capacity (FEV1/FVC). Patients were asked to avoid having tea or coffee as well as other airways dilator food for at least 3 hours prior to spirometry test.

Statistical analyses

All values are represented as mean ± SD. Statistical analysis was performed with the SPSS software version 15.0. An Independent sample T-test was used to compare the serum levels of IgE and the other variables between asthma and normal subjects. Pearson correlations were used to establish the relationship between IgE concentration with FEV1, FVC, and FEV1/FVC in asthma subjects. A p-value less than 0.05 were considered statistically significant.

Results

No baseline differences were found between groups for any body composition parameters such as BMI (31 +/- 3.11 versus 30.6 +/- 2.65 kg/m2, P = 0.006), body weight (94 +/- 7 versus 95 +/- 7 kg, P = 0.223) and body fat percentage (31 +/- 2.63 versus 30.2 +/- 3.01 %, P = 0.211). Serum IgE (356 +/- 71 versus 98 +/- 21 IU/ml, P = 0.007), FEV1 (76 +/- 6 versus 96 +/- 7, P = 0.011), FVC (89 +/- 8 versus 97 +/- 7, P = 0.021), FEV1/FVC (70 +/- 5 versus 81 +/- 11, P = 0.033) and PEF (80 +/- 6 versus 98 +/- 10, P = 0.033) in asthma patients were significantly higher than those without asthma.

The findings of Pearson correlation method showed that serum IgE concentration was negatively related to FEV1 (p = 0.021, r = 0.58, Fig 1). On the other hand, we observed that high serum IgE was associated with decrease in FEV1. This finding demonstrated increased serum IgE lead to increase in asthma severity.

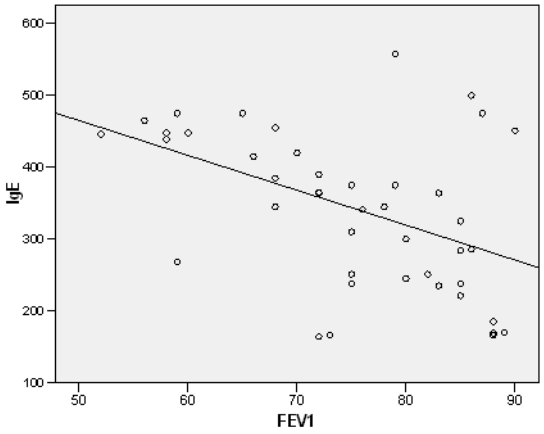

Fig 1. The correlation pattern between IgE and FEV1 in asthma patients.

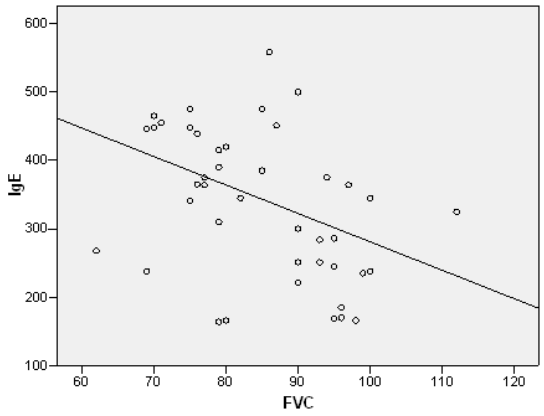

Fig 2. The correlation pattern between IgE and FVC in asthma patients.

In addition, a negative correlation were observed between serum IgE with FVC (p = 0.019, r = 0.59, Fig 2), PEF (p = 0.038, r = 0.55) and FEV1/FVC (p = 0.028, r = 0.56). On the other hand, negative relationship between IGE and FEV1/FVC, we can say IgE measuring may be a predictor of asthma diagnosis.

Discussion

An initial finding of this study is that serum IgE in asthma patients was significantly higher than healthy subject that matched for age and sex. These results were supported by other authors. Consistent with these findings, a recent study showed that Serum IgE was significantly increased in obese children when compared with normal subjects

(Chawes *et al.,* 2010). Review of research findings show that IgE is a key mediator of the inflammatory reactions that are central to the pathogenesis of allergic diseases such as asthma and rhinitis (Nowak *et al.,* 2006). Recent evidence also supports Immunoglobulin E as a key mediator of allergic reactions and plays a central role in allergic responses to allergens in patients with asthma and rhinitis (Platts-Mills, 2001; Sutton *et al.,* 1993). Although the molecular mechanisms for this are less understood. There is evidence that in industrialized populations in which the frequency of helminthes parasitic infection is low, the adverse actions of IgE are manifested as a high frequency of type I hypersensitivity (Leung, 1997; Leung, 1998). While allergy (hypersensitivity) was unusual at the turn of the century, allergies now affect up to 20% of adults. It is generally accepted that despite low serum concentrations, IgE is immunologically highly active due to the large number of high-affinity IgE receptors on mast cells and basophiles (Bousquet *et al.,* 2003). A number of previous studies have demonstrated that immunoglobulin E and mast cells are believed to play important roles in allergic inflammation (Mayr *et al.,* 2003). However, the specific mechanisms responsible for these observations are not obvious. In contrast to other immunoglobulin that binds to immunoglobulin Fc receptors only when antigen has been bound by an antibody, IgE will bind to FceR in the absence of antibody. Immunoglobulin E binding to mast cells ‘‘sensitizes” the mast cells to degranulate when multivalent antigens cross-link FceR-bound IgE. Despite its low levels in the blood, IgE is immunologically highly active due to the large number of high-affinity IgE receptors on mast cells and basophiles (Bousquet *et al.,* 2003). Additionally, IgE up-regulates receptors on several cell types, including basophiles and mast cells (Macglashan *et al.,* 1999). It has been suggested that IgE binding to the receptors on these cells results in the formation of cross links between the allergen and the IgE molecule and initiates the inflammatory cascade through release of a variety of mediators, including histamine, leukotrienes (LT), and platelet-activating factor (Arshad *et al.,* 2001).

Other findings of this study are that respiratory functional in asthma patients was significant higher than those without asthma. Some previous studies have shown that impaired lung function as measured by FVC or FEV1 is a powerful predictor of nonfatal ischemic heart disease and of mortality due to cardiovascular disease (Sin *et al.,* 2005; Schroeder *et al.,* 2003). The association between low FEV1 and cardiovascular mortality also exists in lifetime nonsmokers (Sin *et al.,* 2005). Most patients with reduced FEV1 have asthma, chronic obstructive pulmonary disease (Mannino *et al.,* 2003). In these conditions, cytokines are over expressed in lung tissue, potentially resulting in systemic low-grade inflammation (Mannino *et al.,* 2003; Barnes *et al.,* 2003; Sin *et al.,* 2003; Sin *et al.,* 2005). This led to the suggestion that inflammation is an important pathway between lung disease and vascular disease (Sin *et al.,* 2005). The major finding of this investigation was a negative association between IgE and marker indicative of respiratory function. In the other word, the finding or study showed that increased IgE is associated with low level of FEV1, FVC and FEV/FVC. It has been demonstrated that IgE-mediated activation of mast cells enhances pulmonary responsiveness to cholinergic stimulation (Martin *et al.,* 1993). It is also important to present evidence for a role of IgE-dependent mast cell activation as a trigger for allergic airway inflammation. Literature suggests that high levels of serum IgE develop in response to increased asthma intensity and the degree of inflammation and blockage of the respiratory pathways in patients with asthma are directly proportional with IgE Serum levels (Anupama *et al.,* 2005). Another study also found that Serum IgE levels have a significant and inverse correlation with FEV1 in patients with asthma (Sears *et al.,* 1991). IgE is responsible for the release or secretion of certain inflammatory mediators such as histamine or Prostaglandins in asthmatic patients. In a recent

study, when asthma intensity was compared with IgE Serum levels, the findings showed that the increase in IgE levels also increases the intensity of asthma (Anupama *et al.,* 2005). In this context, the findings of a recent study showed that higher levels of IgE indicate increased inflammation in the respiratory pathways (Chowdary *et al.,* 2003).

On the whole, the findings of this study are indicative of increased serum levels of IgE and also lower spirometric indices in asthmatic patients than in their healthy counterparts. Although increased levels of IgE and reduced respiratory functions parameters have also repeatedly been reported in some previous studies, as well as confirming the previous findings the findings of this study also support a significant inverse relationship between IgE and respiratory functions parameters (Freidhoff *et al.,* 1993). These findings suggest that measurement of IgE levels is considered a proper predictive criterion for a diagnosis of asthma and its intensity. Because exposure to allergens can precipitate inflammation of respiratory pathways and is associated with increased intensity of asthma, identification of allergic factors and IgE-dependent diseases or disorders in asthmatic patients is of particular importance. It is also emphasized that despite the study findings and the findings of some previous studies, many questions about the interaction between asthma and reduced respiratory function with changes in IgE levels remain unanswered and require further studies in the future. Further studies are needed to clarify possible mechanisms by which IgE or other allergic agents influenced respiratory function.

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