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Research Article

EXERCISE AS A NONE-PHARMOLOGICEL INTERVENTION IN MAINTAIN IGE IN ASTHMA PATIENTS

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ABSTRACT
Immunoglobulin E (IgE) has a key role in asthma pathophysiology and contributes to both the early- and late-phase inflammatory cascade in the airways. The aim of this study was to evaluate the effects of acute exercise on serum IgE levels in males with mild to moderate asthma. Sixteen sedentary males with mild to moderate asthma and fourteen healthy people matched to age and body mass index were enrolled to the study. In each subject/patient, after control measurements of spirometry, a fasting venous blood sample was collected from all the subjects in order to measuring IgE and to compare with each other. Also, asthma patients were completed a cycling exercise test and blood samples were obtained immediately after stopping exercise. Differences between groups were calculated using the independent samples t-test. Pearson correlations were used to establish the relationship between IgE and spirometry markers. Serum leptin levels were significantly higher in asthma patients in comparison to healthy subjects. Significant correlations were found between IgE and FEV1 and FEV1/FVC in asthma patients. Additionally, cycling exercise test resulted in significant decrease in serum IgE in patients. Based on this data, it was concluded that serum IgE is a precise predictor of asthma diagnosis and exercise training even for a session can decrease this inflammation marker in these patients.

***Key Words**: IgE, Cycling Exercise, Asthma, Spirometry*

INTRODUCTION
Chronic inflammation of the respiratory pathways in patients with asthma is often associated with high levels of immunoglobulin E (IgE) and bronchial eosinophils (Feleszko *et al.,* 2006; Bryce *et al.,* 2006)**.** World Health Organization defines asthma as a chronic inflammatory disease of the respiratory pathways and some cells, especially mastocytes; eosinophil and T lymphocytes play an important role in the spread of it (Mayr *et al.,* 2003). IgE is produced by B cells in response to allergens and has a short half-life (MacGlashan *et al.,* 1999). Recent evidence suggests that asthma has an allergic source (Holt *et al.,* 1999; Kay et al., 2001) and IgE has a key role in the initiation of both allergic and non allergic asthma (Powe *et al.,* 2003; Ying *et al.,* 2001), although its role in the pathogenesis of asthma is not yet fully identified. Human studies over have shown a close association between asthma the excessive response of respiratory routes and levels of IgE serum (Gergen *et al.,* 2009). Scientific studies also indicate increased IgE in asthmatic patients (Burrows *et al.,* 1989). Some studies also suggest that patients with atopic and asthma have relatively higher serum IgE levels than healthy individuals (Heidenfelder *et al.,* 2010; Thomas *et al.,* 2003). These studies point out that increased IgE levels are often associated with bronchus excessive response and reduced FEV1 (forced expiratory volume within a second) as a determinant of asthma intensity in these patients (Sears *et al.,* 1991). According to GINA guidelines it is not usually possible to control severe asthma with the existing curative methods (Bateman *et al.,* 2008). Hence, researchers have recently shifted their focus on the role of non-medical factors as therapeutic agents in reducing inflammation and intensity of asthma or other respiratory disease in these patients. In this regard, some studies have pointed up the positive effects of exercise and physical therapy alongside other drug treatments in reducing the intensity of asthma and reducing levels of other inflammatory markers such as of leptin, resistin and interleukin (Jamurtas *et al.,* 2006; Nassis *et al.,* 2005; Jung *et al.,* 2007). However, Serum IgE response to exercise has been paid less attention and the few findings in this area are often contradictory and heterogeneous. The results of a relevant study showed that 20 minutes of activity on the

treadmill did not lead to a change in IgE levels (Eliakim et al, 1997). On the other hand, the findings of a recent study showed that levels of IgE significantly reduce in response to an exercise session (Aldred *et al.,* 2010). This study was performed in order to determine the effect of an acute exercise on Serum IgE levels in patients with mild to moderate asthma.

MATERIALS AND METHODS

The primary aim of the present semi-experimental study was to compare levels of Serum IgE level between asthma patients and healthy adult males (age: 40 ± 5 year, BMI: 31 ± 2.3 kg/m^2) and to determine the effect of a short exercise session on its levels in the patients. For this purpose, sixteen male adults with mild to moderate asthma in the city of Saveh volunteered to participate in this research. Also, sixteen healthy adult male with a range of ages and similar physical conditions like asthma participated in the study to compare baseline IgE levels with asthmatic patients.

Prior to the exercise written consent was obtained from all patients. Subjects had no cardiovascular diseases, gastrointestinal diseases, kidney and liver disorders or diabetes. In addition, if any of the participants had been participating in regular exercise or diet program during the past 6 months, they were barred from participating in the study. Use of tobacco or alcohol or having orthopedic deformities was among the exclusion criteria of the study. Asthma intensity was measured by a specialist physician through measuring spirometry indicators (using pyrometer Model Minispire, made in Italy). Patients were asked to avoid for at least 3 hours prior to spirometry testing consuming tea or coffee and other foods foodstuff dilating respiratory tracts. Date on age, height and weight were recorded at the site of spirometry testing.

Then a blood sample was taken from the subjects after overnight fasting for 12 hours to compare Serum IgE levels among asthmatic patients and healthy subjects. In the next stage the asthmatic group performed the YMCA standard bike test on laboratory Ergometer (Tunturi, made in Finland) for 15 minutes consisting of three 5-minute parts to determine the response of serum IgE to a short exercise session. Each of the patients started the test with two minutes of no-load (no resistance) pedaling for warming up. They then performed the main step of the test in 3-minute consecutive stages of exercise with no rest intervals. The intensity or workload increased from each three-minute stage to the next step in accordance with protocol instructions. The patients were advised to avoid any physical activity for two days before the test. The second blood sample was taken immediately after the cessation of exercise testing in patients with asthma to determine the effect of an exercise session on Serum IgE. IgE was measured by ELISA method (Monobind Inc, CA 92630, USA). The Intra- assay and inter-assay coefficient of variation and sensitivity of the method of serum IgE were 4.03(%), 4.64 (%) and 1.0 IU / ml. respectively

Statistical analysis: The raw data were analyzed using SPSS version 15. Independent t test was used to compare baseline levels of IgE in asthmatic and non-asthmatic groups. To determine correlation levels with spirometry indexes, Pearson correlation test was used. Paired T-test was used to determine the significance of changes associated with IgE in asthmatic group due to the exercise test. P value of less than 5 percent was considered significant.

RESULTS

All values are represented as mean ± SD. There were no significant differences in anthropometric indices between patients with asthma and healthy individuals ($p \geq 0.05$). Serum IgE levels in asthmatic patients was significantly higher than in healthy individuals (345 ± 51 versus 148 ± 31 IU/mL, $p = 0.01$). The findings also showed that patients with asthma have lower levels FEV1/FVC (67 ± 6 versus 77 ± 6) and FEV1 (73 ± 5 versus 85 ± 7) and FVC (84 ± 6 versus 94 ± 7) than healthy individuals ($p < 0.05$). A significant negative correlation between serum IgE was detected with FEV1/FVC ($P = 0.019$, $R = 0.46$). Also, the Pearson correlation test showed that the Serum IgE concentration has a significant and inverse correlation with FEV1 ($P = 0.011$, $R = 0.59$). In other words, in the asthmatic patients studied, the increase in Serum IgE is associated with reduction in FEV1, which suggests a direct correlation between

blood IgE concentration and the intensity of asthma in people. The main finding of this study was the significant reduction in Serum IgE concentration in asthmatic patients in response to exercise (345 ± 51 to 256 ± 38 IU/mL). In other words, exercise led to a 24% reduction of Serum IgE concentration ($p = 0.000$).

DISCUSSION

IgE has been known for more than 30 years as a key mediator of allergic reactions and has a central role in allergic responses to allergens in patients with asthma (Platts-Mills *et al.,* 2001). Our study showed that levels of serum IgE in patients with asthma were much higher than those in their healthy counterparts. Also a significant inverse relationship was observed between Serum IgE levels with FEV1/FVC ratio as an indicator of asthma diagnosis and with FEV1 as the index of asthma intensity in studied patients. These findings suggest that in patients with asthma, increased Serum IgE level in these patients is associated with increased intensity of asthma. The main finding of this study is the significant reduction in serum IgE in response to a session of exercise in patients with mild to moderate chronic asthma. Despite low concentrations in serum, IgE has a high immunological activity due to its large number of receptors on mast cells and basophiles (Bousquet *et al.,* 2003). IgE binding to receptors on these cells leads to formation of a transverse connection between allergens and IgE molecules and in turn the onset of inflammatory reactions through the release of numerous inflammatory mediators including histamine and leukotrienes (Arshad *et al.,* 2001).

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). 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. These inflammatory mediators cause narrowing of the respiratory tracts due to overproduction of mucus, spasm of smooth muscles of respiratory routes and tumor or edema of the respiratory pathways (Lebowitz *et al.,* 1984). 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).

The role exercise in pathophysiology of asthma and the control the disease has been a focus for considerable attention. Improved ventilatory capacity and abatement of symptoms associated with asthma are among the benefits of exercise for asthmatic patients (Ram *et al.,* 2005). Exercise brings about improvement of physical fitness, reduced shortness of breath, reduced exercise-induced bronchospasm and reduced consumption of inhaled steroids in patients with asthma (Ram *et al.,* 2005; Fanelli *et al.,* 2007), Though the physiological effects of exercise on this response is not yet fully known. Confirming the findings of the present study, the study of Aldred *et al* (2010) showed that one exercise session leads to a significant reduction of Serum IgE in allergic patients. Also, in a recent study, long-term exercise program was associated with significant reduction of Serum IgE in patients with asthma (Moreira *et al.,* 2008). It is also possible that physical activity may affect the levels of serum IgE indirectly, through changing or reducing other inflammatory factors such as cytokines. Despite the observed decrease in Serum IgE in response to exercise in the present study, it is not clear whether the response to an exercise session is temporary and transient or not. Hence, it appears that its delayed reaction can provide more appropriate information in this area once measured in the hours after the cessation of activity.

Conclusion

Asthma is associated with inflammation of the respiratory pathways and IgE is a key factor in the inflammatory response which plays an important role in the pathogenesis of this disease. Our study showed that patients with asthma have higher Serum IgE levels than healthy individuals and increased levels of IgE have been associated with increased intensity of asthma and exercise, even for a single

session leads to reduction of the serum levels of this immunoglobulin. Considering that baseline IgE levels are correlated inversely with the intensity of asthma (FEV1) in this study and other studies, it appears that the reduction of IgE serum in response to long-term exercise is associated with improvement or abatement of the intensity of this disease in patients with asthma. To achieve this, the need to more studies in this area is noted.

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