Increased respiratory functional by aerobic training is independent of serum IgE in asthmatic patients

Eizadi Mojtaba*, Shahgholiabasi Rose, Iranshahi Farzaneh, Daraei Shokrabad Firouz

Department of Physical Education and Sport Science, Parand Branch, Islamic Azad University, Iran

*Corresponding author: izadimojtaba2006@yahoo.com

Received: 10 January 2011, Revised: 31 January 2011, Accepted: 3 February 2011

Abstract

Chronic airway inflammation is often associated with increased Circulating levels of Immunoglobulin E (IgE). The aims of present study were 1) to evaluate the effect of aerobic exercise training on serum IgE in asthma patients, 2) to determine relationship between serum IgE and respiratory functional before and after exercise program in these patients. For this purpose, 32 adult males with asthma participated in this study and divided to exercise and control groups by randomly. Fasting serum IgE and some markers indicative of respiratory functional (FEV1, FVC, and FEV1/FVC) were measured before and after an aerobic exercise program (60 min, 3 days/week for 3 months) in two groups. Statistical analysis was performed with the SPSS software version 15.0 using an independent paired t-test. Pearson correlation method used to determine the relationship between serums IgE with spirometry markers in differ condition. At baseline, a significant negative correlation was found between serum IgE with each of spirometric markers (P<0.05). Compared to pre-training, respiratory
functional increased significantly (p<0.05) after exercise program but serum IgE was not changed. There were no correlations between serum IgE concentrations and spirometric markers after exercise program in exercise group (p≥0.05). All variables remained without change in control group (p≥0.05). Considering to these findings, our study supports of IgE as effective factor in asthma and we can say IgE levels is a strong predictor of allergy in asthmatic patients. But despite this close association, increased respiratory functional by exercise training is independent of serum IgE in these patients.

Key words: Immunoglobulin E, Respiratory functional, Asthma, Aerobic exercise.

Introduction
Accumulating evidence indicates that impaired cardiovascular and respiratory functions are associated with increased mortality and morbidity (Blair et al., 1996; Schunemann et al., 2000). Among respiratory diseases, Asthma is a complex syndrome, broadly defined by inflammation of the airways associated with airways hyperresponsiveness (AHR) and mucus hypersecretion (Busse et al., 2001). Recent evidence has shown that adiposity is associated with chronic low-grade systemic inflammation (Takahashi et al., 2003). This inflammatory state is related to adipokines proteins mainly produced by adipocytes which may be pro-inflammatory or anti-inflammatory (Sood et al., 2008). For example, it was observed that high serum concentrations of leptin may be an independent risk factor for asthma in premenopausal women (Shore et al., 2006).

On the other hand, the chronic airway inflammation present in asthma is a predominantly helper T-cell type 2 (Th2) response characterized by high levels of total and allergen-specific IgE, bronchial eosinophilia, CD41 T cell infiltrate in the airways (Feleszko et al., 2006; Georas et al., 2005). 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., 1994). IgE is produced by B cells in response to allergens and has a
short half-life (MacGlashan et al., 1999). Human studies over have shown a close association between asthma the excessive response of respiratory routes and levels of IgE serum (Gergen et al., 2006). Scientific studies also indicate increased IgE in asthmatic patients (Burrows et al., 1989). Some recent studies found a high positive association between increased IgE and asthma intensity (Rotsides et al., 2009). Also serum total IgE level is a strong predictor of allergy in asthmatic children (Satwani et al., 2009).

Because allergen exposure can prompt airway inflammation, trigger asthma exacerbations, and possibly lead to negative health outcomes for patients with asthma, identifying allergies and immunoglobulin E (IgE)-mediated disease in patients with persistent asthma is crucial.

Generally, scientific resources suggest a close relationship between increased asthma intensity and respiratory pathways inflammation, and there are various pharmacological agents in reducing the severity of asthma and preventing and controlling markers effective in airway inflammation available to these patients. But it seems that excessive use of these drugs is associated with irreversible complications. As some sources suggest that branchodilating inhaled corticosteroids reducing airway resistance in asthma and other respiratory diseases and pose the risk of osteoporosis in these patients (Denise et al., 2006; Jan et al., 2000). Hence identification of non-pharmacological strategies to improve or control the disease is the focus of health professionals and health sciences. Some previous studies indicate the role of exercise in reducing inflammatory mediators such as inflammatory cytokine in these patients, although there are still conflicting findings in this field. Also the research findings on IgE response to various exercise training are different; as some report the positive role of physical activity on IgE levels (Aldred et al., 2010; Moreira et al., 2008) and some others report no effect of exercise on it (Eliakim et al., 1997; Vieira et al., 2007). Hence, this study aims to determine the serum IgE response to a relatively long-term aerobic exercise program in patients with asthma and the relationship between its levels and respiratory indicators in response to exercise in these patients.
Materials and Methods

Subjects
The aim of this study was to evaluate the effects of three months aerobic training on serum IgE levels and also to determine IgE in relation to markers indicative of respiratory functional before or after exercise training in adults asthma patients. Thirty two males (Age; 38 ± 6 year, height; 176.5 ± 6 cm, BMI; 27.4 ± 4.6 kg/m2) with moderate asthma divided to exercise (exercise training) and control (no training) groups by randomly. Written consent was obtained from each subject after the experimental procedures and possible risks and benefits were clearly explained. Asthma intensity was measured by a specialist physician through measuring spirometry indicators (using pyrometer Model Minispire, made in Italy).

Inclusion and exclusion criteria
Inclusion criteria to study for asthma group were as existing asthma for at least 3 years. All subjects were non-smokers and had not participated in regular exercise/diet programs for the preceding 6 months. Subjects with a history or clinical evidence of impaired fasting glucose or diabetes, orthopedic abnormalities, recent myocardial infarction, congestive heart failure, active liver or kidney disease were excluded. All patients underwent anthropometrical measurements, a resting spirometry testing and fasting blood sampling for measuring serum IgE.

The measurements for weight, height and other anthropometrical indexes were taken pre and post-exercise training in the physiology laboratory. Body weight and height were measured with a standard physician’s scale and a stadiometer, respectively when subjects were in a fasting state when the participant had thin clothes on and was wearing no shoes. Body mass index (BMI) was calculated using weight divided by squared height. Systolic and diastolic blood pressure was measured using the left arm after the subject had been sitting comfortably for 5 min, using an oscillometric device (Alpikado, Japan).
**Blood sampling and exercise program**

Fasting blood samples and spirometry was performed before and after an aerobic exercise program (48 h after last exercise session) in two groups. Blood sampling were collected in order to measuring serum IgE and spirometry test was performed measuring FEV1, FVC, FEV1/EVC and other markers of respiratory functional asthmatic groups. The subjects were advised to avoid any physical activity or exercise 48 hours before the exercise test. Subjects were asked to refrain from tea, coffee, chocolates and caffeinated soft-drinks on the day of recording Spirometry. The intra-assay and inter-assay coefficient of variation of ghrelin (Monobind Inc, CA 92630, USA) were 4.03% and 4.64% respectively.

Patients in experimental group trained under supervision (60 min, 3 days/week for 3 months) at intensity of 60-80% of HRmax. Adherence to the exercise prescription was documented through the use of Polar heart rate monitors, and subjects received feedback if training intensities were either too high or low in comparison with desirable intensities. After a warm-up, subjects trained for approximately 30 - 45 min and 5–10 min of cool down activity. Aerobic exercises in each session included walking on a treadmill and stationary cycling. Initially, subjects exercised at low intensity and the intensity of exercise was gradually increased to 80% of peak heart rate in next sessions. Attendance was taken at each exercise session to monitor compliance with the program. Subjects were contacted if an exercise session was missed. In this 12-week period, participants in the control group were barred from participating in any exercise training.

**Statistical analysis**

Experimental data are presented as means ± SD and were analyzed with the SPSS software version 15.0. For the descriptive statistics after having checked the normality of the variables using the Kolmogorov-Smirnov test. Baseline characteristics were compared by using independent t-tests. Student’s paired ‘t’ test was applied to compare the pre and post training values. Pearson correlation coefficients were used
to determine the associations between serum ghrelin with spirometry markers. An alpha-error below 5% was considered as statistically significant.

Results

Descriptive characteristics of the participants are presented in Table 1. At baseline there were no differences in the age, body weight, BMI, Height between the two groups (p≥0.05). Also, serum IgE level in the exercise and control subjects were almost the same (p≥0.05). There was no marked difference in spirometric markers between the two groups at baseline (p≥0.05). At baseline, significant negative correlation was found between serum IgE with FVC (p = 0.033, r = -0.53, Fig 1), FEV1 (p = 0.007, r = -0.66, Fig 2) and FEV1/FVC (p = 0.024, r = -0.58, Fig 3). Exercise training resulted in significant increase in maximal FEV1 (p = 0.021), FVC (p = 0.28), FEV1/FVC (p = 0.36) and MVV (p = 0.19) (Fig 4), while Serum IgE levels were not affected by aerobic exercise program in studied patients (p = 0.212). We found no evidence that changes in alcohol intake were associated with changes in cardiorespiratory function. After aerobic exercise program, we did not observe significant correlation between serum IgE with each of spirometric markers (P<0.05). All variables remained without change in control group.

Table 1. Mean and standard deviation of anthropometrical, spirometric biochemical variables of study groups in baseline and after intervention

<table>
<thead>
<tr>
<th>variables</th>
<th>Exercise group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>post-exercise</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>96.3 ± 5.4</td>
<td>93.8 ± 6.4</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>174.6 ± 6.3</td>
<td>174.6 ± 6.3</td>
</tr>
<tr>
<td>Age (year)</td>
<td>37.8 ± 5.6</td>
<td>37.8 ± 5.6</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>31.57 ± 4.16</td>
<td>30.75 ± 4.23</td>
</tr>
<tr>
<td>FVC (%)</td>
<td>84.3 ± 6.13</td>
<td>93.7 ± 7.3</td>
</tr>
<tr>
<td>FEV1 (%)</td>
<td>75.3 ± 5.6</td>
<td>84.3 ± 7.6</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>68.3 ± 4.11</td>
<td>75.3 ± 6.8</td>
</tr>
<tr>
<td>MVV (%)</td>
<td>116 ± 13.2</td>
<td>127 ± 21.3</td>
</tr>
<tr>
<td>IgE (IU/ml)</td>
<td>358 ± 46</td>
<td>371 ± 63</td>
</tr>
</tbody>
</table>

FEV1, forced expiratory volume in 1 s; FEV1/FVC: forced expiratory volume in 1 s / forced vital capacity
BMI, body mass index; MVV: Maximal voluntary ventilation, FVC: forced vital capacity.
**Fig 1.** The relationship between IgE and FVC at baseline.

**Fig 2.** The relationship between IgE and FEV1 at baseline.

**Fig. 3.** The relationship between IgE and FEV1/FVC at baseline.
Discussion
Physical activity is known to improve physical fitness and to reduce morbidity and mortality from numerous chronic conditions (U.S. Department of Health and Human Services, 1996). In the present study, although respiratory functional markers were significantly increased after aerobic physical training in these patients, no significant differences were found in serum IgE by aerobic exercise training in experimental group with compared to baseline.

IgE and mast cells are part of the IgE-associated immune response. Accordance with the definition by the National Heart and Lung Institute and World Health Organization, asthma is a chronic inflammatory disorder of the airways in which many cells play a role, in particular mast cells, eosinophils and T-lymphocytes (Mayr et al., 2003). The
role of IgE and IgE-dependent mast cell activation in asthma is underlined by the close
correlation of increased serum IgE levels and the prevalence of asthma (Burrows et al.,
1998). The inability to measure IgE-based sensitivity to all allergens has limited our
understanding of what portion of asthma is related to IgE (Gergen et al., 2006). Initial
finding of this study showed that Serum IgE levels were significantly higher in asthma
patients in comparison to in those without asthma. We also found higher respiratory
functional in asthma patients than healthy subjects.

A large body of evidence suggests 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). An
increased immunoglobulin E (IgE) production is the strongest predisposing factor for the
development of asthma (Skiepko et al., 2009). It has been established that IgE is a key
component of asthma pathophysiology and contributes to both the early- and late-phase
inflammatory cascade in the airways (Skiepko et al., 2009).

From a biological perspective, despite low serum concentrations, IgE is immunologically
highly active due to the large number of high-affinity IgE receptors on mast cells and
basophils (Bousquet et al., 2003). In addition, IgE up-regulates receptors on several cell
types, including basophils and mast cells (MacGlashan et al., 1999; MacGlashan et al.,
1997). IgE binding to its 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). Data from a recent observational study
indicate that plasma reactive oxidants, eosinophils, and neutrophils (absolute counts
and percent of total white blood cell counts), total IgE, and allergen-specific IgE levels
were elevated in asthmatics after adjusting for age, gender, and ethnicity (Heidenfelder
et al., 2010). A growing body of literature suggests that the majority of asthma has an
allergic basis (Holt et al., 1999; Kay, 2001) and that IgE is central to the initiation of both allergic and nonallergic asthma (Powe et al., 2003; Ying et al., 2001).

Physical activity rehabilitation as a none-pharmological treatment is widely used in patients with cardio-vascular and respiratory diseases. Exploration of the relation between physical activity and respiratory functions will aid in understanding the mechanisms of how physical activity improves patients’ quality of life and in finding a better way to evaluate effects of rehabilitation. But most studies on the effects of physical activity on respiratory function are cross sectional ones on special populations such as athletes or patients with chronic obstructive pulmonary disease (Malkia et al., 1998; Tiep, 1997).

The main findings of this study showed that aerobic exercise for three months, would not affect serum IgE levels in patients with mild to moderate asthma. However, although some studies have pointed to beneficial effects of exercise on levels of IgE (Aldred et al., 2010; Moreira et al., 2008), the absence of significant changes in IgE levels in response to exercise has also been reported in some previous studies on asthmatic patients or other populations (Eliakim et al., 1997) which support the findings of this study. Also, in another study, although 4 weeks of aerobic exercise improved exercise capacity and respiratory symptoms in asthmatic mice, IgE levels did not change in response to this exercise program (Vieira et al., 2007).

In the present study, serum IgE remaining unchanged was observed while the exercise program significantly increased the determining markers of respiratory function such as FEV1, FVC, MVV and FEV1/FVC. The three-month aerobic exercise program was associated with a significant improvement of respiratory function in these patients. While no changes in respiratory function was observed in levels of these markers in the control group after three months detraining. However, most of studies suggest a close correlation between IgE levels and respiratory function markers in patients with asthma or other respiratory diseases (Anupama et al., 2005). The initial findings of this study also confirm significant negative relationship between baseline levels of IgE with FEV1,
FVC and FEV1/FVC in the subjects. But despite the close relationship between baseline levels of these variables, no significant relationship between IgE and the said spirometric indices after exercise program. Hence, given the close relationship between baseline levels of respiratory performance indicators (asthma severity) and blood IgE in these patients on the one hand, and improved respiratory function in the absence of change of IgE in response to exercise on the other hand, it appears that the improvement of respiratory function in response to aerobic exercise is independent of IgE levels. It is possible that the due to changes in other biochemical mediators such as inflammatory or non inflammatory cytokine exercise program has improved the spirometric indices in these patients which requires further studies in this field. On the other hand, even in the absence of changes in inflammatory or inflammatory mediators and other biochemical variables, improved respiratory function patients in this study can be attributed to increased volume and strength of respiratory muscles in response to exercise these patients.

**Acknowledgment:** Hereby, the authors wish to acknowledge the Research Deputy of Islamic Azad University and all participants in this study.

**References**


**Arshad SH, Holgate S. 2001.** The role of IgE in allergen-induced inflammation and the potential for intervention with a humanized monoclonal anti-IgE antibody. Clin Exp Allergy 31, 1344–51.


