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LACK MEANINGFUL EFFECT OF CHRONIC TRAINING ON ALLERGIC AGENT IN DIABETIC PATIENTS

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ABSTRACT
Obesity is regarded as a potential risk factor for allergy and atopy but no direct evidence is currently available about allergic agent in diabetes. In this study, we aimed to investigate the effect of aerobic training on serum IgE as a allergic agent in type II diabetes. For this purpose, twenty four individuals with type 2 diabetes were selected for participate in this study by accessible simples and divided to experimental or control groups matched for age 44 ± 6 year, sex (men) and body weight 92 ± 6 kg. Subjects in experimental group were completed a three month aerobic training (3 time-weekly) at 55-75 (%) of maximal heart rate. pre and post training of anthropometrical and fast serum IgE were measured in two groups. All analyses in the statistical evaluation were carried out with SPSS-15.0 software. Aerobic training resulted in a significant decrease in body weight, body mass index and body fat percentage ($p < 0.05$). There were no statistically significant differences in serum IgE between pre and post training values ($p = 0.000$). In conclusion, we conclude that there is no meaningful effect of aerobic training with regard to serum IgE in type II diabetes patients.

KEYWORDS: Allergy, Diabetes, Exercise training.

INTRODUCTION
Imonoglobin E (IgE) is a key factor in the inflammatory reactions that have an important role in the pathogenesis of allergic diseases such as asthma (Nowak *et al*., 2006). This stimulus is produced by B cells in response to the allergens and has a relatively short half-life (MacGlashan *et al*., 1998). Despite its low serum concentrations, IgE has high immunological activity due to the large number of receptors it has on mast cells and basophils (Bousquet *et al*., 2003). The binding of IgE to its receptors in these cells creates a cross-link between allergen and IgE molecules, and thereby, starts inflammatory reactions through the release of a number of inflammatory mediators such as histamine and leukotrienes (Arshad *et al*., 2001). IgE is known to have a key role in the initiation of both allergic and non-allergic asthma (Powe *et al*., 2003; Ying *et al*., 2001).Its importance has also been reported in some other chronic diseases such as cardiovascular diseases (Busse *et al*., 2001; Szczeklik *et al*., 1998). The plasma IgE levels in patients with myocardial infarction has been reported to be almost double compared to those in the angina pectoris patients or those without coronary artery disease. Some studies have also noted that mast cells, which are the primary targets of IgE, have an important role in obesity-related diseases such as type 2 diabetes (Wang *et al*., 2011; Patrícia *et al*., 2011) as the removal of mast cells in animal species was associated with the reduced incidence or severity of type 2 diabetes (Liu *et al*., 2009). Several studies have been conducted aiming at determining the effect of the internal or external interventions IgE level in respiratory or allergic diseases such as asthma or COPD. In this context, the role of exercise or physical therapy is important too. However, the findings on the IgE response in these populations are often contradictory as studies have indicated the beneficial effects of exercise (Eizadi *et al*., 2011; Aldred *et al*., 2010; Moreira *et al*., 2008), and some others have showed that exercise has no effect on IgE levels in obese individuals or asthmatic patients (Eliakim *et al*., 1997; Eizadi *et al*., 2014).

The effect of exercise on serum levels of IgE in patients with type 2 diabetes has not been addressed much. Hence, this study aimed at determining the effects of aerobic exercise on IgE levels in type 2 diabetics.

MATERIALS AND METHODS
Subjects were twenty four adult males with type II diabetes matched for age 44 ± 6 year, body weight 92 ± 6 kg and BMI 31 ± 3 kg/m2. The subjects were nonsmokers and physical impairment affecting their performance. All participants reported being weight stable (±1kg) for 6 months prior to the study and engaged in physical activity less than once per week. Subjects with diagnosed other metabolic diseases were excluded. Anthropometrical markers and fasting serum IgE were measured before exercise program and repeated at 2 days afters lasted session of exercise. A

medical history to retrieve information about health status, current medications and a physical examination including height, weight, and waist circumference were performed before study. Weight and height were measured in the morning, in fasting condition, standing, wearing light clothing and no shoes. Body mass index (BMI) was calculated by dividing body mass (kg) by height in metres squared (m2). Abdominal obesity and hip circumference were determined in a standing position at the end of normal expiration and ratio between them (AHO) was calculated for each subjects.
Patients asked to does not use medicine or hormone preparations that affect the carbohydrate and lipid metabolism at 12 before blood samples and those unable to avoid taking hypoglycemic drugs or other therapeutic drugs within 12 hours before blood sampling were excluded. For measure serum IgE, blood samples were collected after an overnight fast at 8.0 am. The Intra- assay coefficient of variation for IgE (Monobind Inc, CA 92630, USA).and sensitivity of the method was 1.95% and 3.52 IU/mL, respectively.

Exercise protocol

The exercise protocol included aerobic exercise training lasted for three months and three sessions per week. Each session lasted for 45-60 minutes and with intensity of 55-75 percent of maximum heart Rate (HRmax). Exercise intensity and exercise volume at initial training sessions was in at least of mentioned range.The exercise intervention program was based on current health promotion recommendations for weigh lose and improving physical fitness. Target heart rate was monitored by polar telemetry. Recommendations for modification of individual exercise regimens were made as needed to ensure exercise goals were obtained.

Statistical analysis

The average and standard deviation of data were calculated after checking the data distribution normalcy using Kolmogorov-Smirnov test and Homogeneity of variance method. Data were analyzed by computer using the Statistical Package for Social Sciences (SPSS) for Windows, version 15.0. The comparison of between means groups and Homogeneity of groups examined using Independent test. Paired t test was used to determine the mean differences between baseline and post-training values on serum IgE and anthropometric variables. The level of significance was set at $P< 0.05$.

RESULTS

Characteristics for the subjects at baseline (before intervention) and post training are described in Table 1. Overall, the subjects of two groups were adult-aged, and obese or overweight. Neither fasting glucose nor insulin was significantly different between two groups at baseline. We also did not significant difference in all anthropometrical markers between two groups at baseline ($p \geq 0.05$) (see table 1). Serum IgE was also same in two groups at baseline ($p = 0.07$). Based on data of paired t test, aerobic training program resulted a significant decrease in body weight ($p = 0.001$) and BMI ($p = 0.004$). Compared to pre-training, abdominal circumference and body fat percentage decreased significantly in experimental group ($p < 0.05$) but not in the control subjects (Fig 1). Results indicated no change in serum IgE between the beginning and end of exercise training in experimental ($p = 0.846$). In contrast, fasting glucose concentration decreased by exercise program when compared with baseline ($p = 0.001$, Fig 2).

Table 1: **Pre and post training levels of anthropometrical and clinical markers of two groups of two studied groups.**

Variables	**Experimental group**		Control group	
	Pre-training	**post-training**	Pre-training	post-training
Age **(year)**	*43.8 (6.71)*	*43.8 (6.71)*	*43.5 (4.89)*	***43.5 (4.89)***
Height **(cm)**	*172 (4.9)*	*172 (4.9)*	*172 (2)*	***172 (2)***
Weight **(kg)**	*91.5 (6.3)*	*88.5 (7.3)*	*91.6 (5.3)*	***91.7 (5.1)***
Waist **(cm)**	*104 (8.1)*	*99.8 (7.7)*	*101 (5.7)*	***102 (5.6)***
Hip **(cm)**	*102 (3.9)*	*99.9 (4.6)*	*101 (5.8)*	***100 (5.7)***
BMI **(kg/m2)**	*31 (2.4)*	*29.9 (2.7)*	*30.9 (2)*	***30.94 (1.97)***
Body fat **(%)**	*30.5 (2.1)*	*29.9 (1.8)*	*30.1 (1.2)*	***30 (1.3)***
Visceral Fat	*13.4 (1.7)*	*11.5 (1.4)*	*13.4 (1.1)*	***13.3 (1.1)***
Serum IgE **(IU/ml)**	*138 (94)*	*143 (80)*	*147 (52)*	***155 (42)***
FBS **(mg/dl)**	*242 (66)*	*187 (46)*	*236 (37)*	***229 (24)***

DISCUSSION

In the present study, serum levels of IgE did not significantly change in response to exercise. Based on these findings, it can be stated that, three months of aerobic training did not affect the serum levels of IgE in type 2 diabetic patients. Similar to other immunoglobulins, IgE is produced by B cells and plasma cells. Due to the high absorption ability of mast cells on IgE, IgE circulating levels are significantly lower than those of other immunoglobulins. However, its synthesis level by its producing cells is far lower. It has been found that IgE levels are often elevated in allergic condition, and increased IgE levels increases the severity of allergic, inflammatory, and infectious diseases too. The most common reason for its elevation is allergy, especially in industrialized countries. Parasitic infections are known to be most common reason for its elevation in developing countries (Winter *et al*., 2000). IgE and mast cells play an important role in the immune system. Researchers have noted that obesity is associated with allergic symptoms or increased IgE levels (Schachter *et al*., 2003: Xu *et al*., 2000). On the other hand, IgE molecules affect the mast cells and cause them to stimulate histamine, leukotrienes and cytokines that play an important role in the inflammatory response and the contraction of the vascular smooth muscle cell (Szczeklik *et al*., 1988; Busse *et al*., 2001). For example, it is known that IgE stimulates the mast cells to increase the secretion of CRP as an inflammatory cytokine in the cells (Erdogan *et al*., 2003). Cytokines, such as IL-4 and IL-13, produce the early signals of B cells to create IgE isotopes, which in turn, have a special importance in the production of other cytokine and inflammatory processes (Busse *et al*., 2001). Mast cells are of the main tissues responsible for allergic responses and asthma (Theoharides *et al*., 2006; Bradding *et al*., 2006), however, some studies have shown that these cells are of particular importance in obesity-related diseases such as type 2 diabetes. The mice lacking mast cells or those exposed to mast cell inhibitors, such as cromolyn or Ketotifen, are protected against type 2 diabetes (Liu *et al*., 2009).

It is known that allergic cells play a role in the apoptosis of vascular cells through the release of trypase (Zhang *et al*., 2011) and cerine protease chymase (Sun *et al*., 2009) by mast cell. On the other hand, one of the main mechanisms of mast cells is the binding of IgE to some specific receptors that have high absorption ability (Wang *et al*., 2011). The response of mast cell receptors to IgE is the secretion of histamine, mast cell proteases, some cytokines and chemokines (MacGlashan *et al*., 1998). Some of these mediators, such as inflammatory cytokines, are associated with type 2 diabetes (Pickup *et al*., 2004; Wellen *et al*., 2005). Studies suggest a close association between IgE levels and obesity (IgE, 2009). These studies noted that IgE levels were significantly higher in the obese individuals than those with normal weight (Visness *et al*., 2009). However, fat mass has been introduced as a predictor of IgE levels in obese individuals (Vieira *et al*., 2005). Hence, it is thought that weight loss in obese subjects is associated with decreased levels of IgE. It should be noted that the majority type 2 diabetics are categorized as obese. In this study, all the diabetics were overweight or obese. However, the exercise-induced weight loss was not associated with reduced serum levels of IgE in these patients. These findings pointed out that apart from the obesity factor, other factors are also affective in the increased levels of IgE in diabetic patients. In support of these findings, some studies reported no change in IgE levels after short-term exercise test (Eliakim *et al*., 1997) or long-term training programs (Eizadi *et al*., 2014). However, some studies reported the reduced levels of IgE in response to short or long-term training programs. For instance, 12-week exercise training led to a significant reduction in IgE levels of asthmatic patients (Moreira *et al*., 2008). In two other studies conducted in the form of moderate-intensity exercise tests, IgE levels were reduced in asthmatic patients (Eizadi *et al*., 2011; Aldred *et al*., 2010). Given these conflicting evidence, conducting further studies is recommended to determine the significance of IgE in the pathophysiology of type 2 diabetes and the effects of other short-term and long-term training programs.

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