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Research Article

EFFECT OF 12 WEEKS AEROBIC TRAINING INTERVENTION ON SERUM INTERLEUKIN-1 BETA IN ASTHMA PATIENTS

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ABSTRACT
Regular exercise training is recognized as a non-pharmacological treatment for systemic inflammation in chronic diseases. In this study, we aimed to assess serum intereleukin-1 beta (IL-1ß) as inflammatory cytokine in response to aerobic exercise program in asthma patients. To achieve this outcome, twenty four adult men with mild to moderate asthma were randomly divided into exercise (n = 12) and control (n=12) groups. All subjects of exercise group completed an aerobic training program for three months (3 time/weekly). Pre and post training of fasting serum IL-1ß and anthropometrical markers were measured of two groups. Paired-samples t-test used to compare values between two measurements. Data showed that aerobic training resulted in significant decrease in serum IL-1ß in exercise group when compared to baseline. All anthropometrical markers improved by exercise program, but not in control group. These data suggest that exercise training for long time can improve systemic inflammation in asthma patients.

Keywords: *Asthma, Aerobic Training, Inflammation*

INTRODUCTION
Several hormonal and metabolic factors are involved in the asthma. Understanding the interactions between these factors and the pattern of their variations in training programs have been the ground for many of the new studies about the treatment of detrimental symptoms of this disease. Asthma is a chronic lung disease of allergic origin. It physiologically appears with narrowing of the respiratory tract and has a large rate of mortality (Figureueroa-Munoz *et al.*, 2001).
Research findings show that cytokine network plays a central role in asthma immunopathology. Bronchial epithelial cells have different functions in cytokine networks, such as IL-1, IL-6 and IL-8, and are believed to play an important role in immunopathology of asthma (Wang *et al.*, 1994; Sousa *et al.*, 1996). Up-regulation of IL-1ß, as an inflammatory cytokine, has been previously reported in asthmatic bronchial epithelial cells compared to healthy subjects (Ana *et al.*, 1997).
IL-1ß is secreted by various tissue cells such as monocytes, tissue macrophages, alveolar macrophages, lymphocytes, mast cells, smooth muscle, and endothelial (Dinarello *et al.*, 1986). This inflammatory cytokine has a wide variety of activities, which been reported to be particularly important in asthma, so that they are also able to stimulate granulocytes, T and B lymphocytes, endothelium, epithelium and hematopoietic cells (Oppenheim *et al.*, 1986). Available evidence show that serum levels of IL-1ß in patients with atopic asthma increases compared to patients with non-atopic asthma and chronic obstructive pulmonary disease (Mahajan *et al.*, 2008). Additionally, IL-1ß stimulates IgE-dependent mast cell activity (Ho *et al.*, 2007; Iikura *et al.*, 2007), which suggests the role of IL-1ß in IgE-associated allergic diseases such as allergic asthma. Thomas (2003) suggested the role of IgE and IL-1ß in asthma (Thomas *et al.*, 2003).
Some studies suggest that the balance in certain cytokines and inflammatory factors through exercise and diet can lead to improved metabolic risk factors (Takizawa, 1998). In this regard, the findings of Hammett (2006) showed that regular exercise has anti-inflammatory effects and reduces levels of inflammatory markers such as IL-1ß (Hammett *et al.*, 2006). But some studies show no short or long-term effects of exercise on inflammatory markers in obese patients or patients with respiratory disease (Bonyadi *et al.*, 2009; Larochelle *et al.*, 2007). Despite numerous and somewhat conflicting scientific findings about the

role of exercise and physical activity on serum levels of IL-1ß and other cytokine in other healthy and patient population, few studies addressed the effects of long-term training programs on serum levels of IL -1ß as an inflammatory cytokine in asthmatic patients. This study aims to investigate the effect of aerobic exercise on serum levels of this cytokine in patients.

MATERIALS AND METHODS

Human Patients: Subjects were aged 34–48 years, sedentary (BMI 27–36 kg/m2, n=24) that participated in this study by accessible sampling and divided into exercise (three month aerobic training) or control (without training) groups. After introduction and awareness of the subjects of the objectives of the study and once they had completed consent forms, the process of test implementation began.

Inclusion and Exclusion Criteria: Inclusion criteria for study groups were determined mild to moderate asthma by spirometry. Participants were included if they had not been involved in regular physical activity in the previous 6 months. All subjects were non-smokers. We also excluded people who had any self reported physician diagnosed chronic disease (arthritis, stroke, diabetes, hypertension, cancer, heart attack).

Anthropometric Measurements: Anthropometric measurements were performed in all study participants before breakfast, with the subject wearing light clothing without shoes. Height of the barefoot subjects was measured to the nearest 0.1 cm. Weight was measured by an electronic balance. Body mass index was measured for each individual by division of body weight (kg) by height (m2).

We used three parameters to diagnosis of asthma and severity: FEV1, FVC, and FEV1/FVC%. Subjects were instructed to take maximum inspiration and blow into the pre-vent pneumotach as rapidly, forcefully and completely as possible for a minimum of 6 seconds, followed by full and rapid inspiration to complete the flow volume loop. The best of the three trials was considered for data analysis.

Laboratory Assays and Exercise Protocol: In each patient, venous blood sampling and spirometry was performed at first. Blood samples were obtained at rest between 8:00 and 9:00 am from the antecubital vein after overnight fast, serum separated by centrifugation and stored at −80°C until analysis. All participants refrained from any physical activity 48 h before measurements. Serum IL-1ß was determined by ELISA method. The Intra- assay coefficient of variation and sensitivity of the method were 5.1% and 0.3 pg/mL, respectively for IL-1ß.

The measurements of anthropometrical and serum IL-1ß were repeated after aerobic training program.

Aerobic program lasted 3 months (3 days/wk) 60 to 80 % of maximum heart rate. In each session of program started by 10 min of warm up, 30-40 min of aerobic exercise included walking on a treadmill and stationary cycling and 5–10 min of cool down activity. The intensity of the activity of any person was controlled using the Polar heart rate tester (made in the US). In this period, subjects of control group did not participate in exercise program.

Statistical Analysis: Data were analyzed by computer using SPSS software version 15.0. All data were tested for normal distribution by the Kolmogorov-Smirnov test. Independent student t test was used for between groups comparison. Student's paired 't' test was applied to compare the pre and post training values. A p-value less than 0.05 were considered statistically significant.

RESULTS AND DISCUSSION

Results

In this study, the effect of three months aerobic training program on serum IL-1ß was investigated. The baseline levels of spirometry characteristics of the subjects in two groups are shown in Table 1. Based on independent T test, we observed no significant difference in all spirometric markers between two groups at baseline ($p \geq 0.05$). In addition, serum IL-1ß and all anthropometrical markers were similar between two groups at baseline ($p \geq 0.05$).

Data by paired samples T test showed that aerobic training program resulted in significant decrease in serum IL-1ß in exercise group when compared to baseline in exercise($p = 0.000$) group but not in control subjects (Figure 1). All anthropometrical markers were also improved by exercise program when compared to baseline ($p \leq 0.05$) but not in control groups (see table 2 and 3).

Table 1: Mean and Standard deviation of spirometric markers in studied groups at baseline

	Exercise group=1 Control group=2	Mean	Std. Deviation	Std. Error Mean
Forced vital capacity	1	90.0000	9.39052	2.71081
	2	86.5000	8.29567	2.39475
Forced expiratory volume in 1 s	1	77.67	9.509	2.745
	2	76.75	7.412	2..140
FEV1/FVC	1	69.75	3.019	.871
	2	68.75	3.019	.871
Peak expiratory flow	1	80.00	15.148	4.373
	2	78.17	14.314	4.132
FEF %25-%75	1	60.17	15.491	4.472
	2	60.00	14.441	4.169
FEF %75	1	53.83	16.286	4.701
	2	56.17	18.055	5.212

Table 2: Mean and standard deviation of anthropometric and metabolic characteristics of exercise group

		Mean	Std. Deviation	Std. Error Mean
riaP 1	Weight (pre)	92.50	9.793	2.827
	Weight (post)	88.35	10.028	2.895
riaP 2	Abdominal (pre)	102.67	8.606	2.484
	Abdominal (post)	97.67	6.840	1.975
riaP 3	Hip (pre)	103.92	6.156	1.777
	Hip (post)	99.52	6.503	1.877
riaP 4	BMI (pre)	30.49	3.139	.906
	BMI (post)	29.12	3.204	.925
riaP 5	Body Fat % (pre)	30.24	2.563	.740
	Body Fat % (post)	26.967	4.5012	1.2994
riaP 6	Interleukin-1 Beta (pre)	3.367	1.2161	.3510
	Interleukin-1 Beta (post)	1.825	1.3559	.3914

Table 3: Mean and standard deviation of anthropometric and metabolic characteristics of control group

		Mean	Std. Deviation	Std. Error Mean
riaP 1	Weight (pre)	93.042	9.4373	2.7243
	Weight (post)	93.325	9.5722	2.7633
riaP 2	Abdominal (pre)	104.58	11.245	3.246
	Abdominal (post)	104.75	10.695	3.087
riaP 3	Hip (pre)	105.83	8.851	2.555
	Hip (post)	105.33	8.532	2.463
riaP 4	BMI (pre)	30.70	3.088	.892
	BMI (post)	28.44	8.566	2.473
riaP 5	Body Fat % (pre)	30.28	2.831	.817
	Body Fat % (post)	30.125	2.6098	.7534
riaP 6	Interleukin-1 Beta (pre)	3.325	3.0329	.8755
	Interleukin-1 Beta (post)	3.242	2.3228	.6705

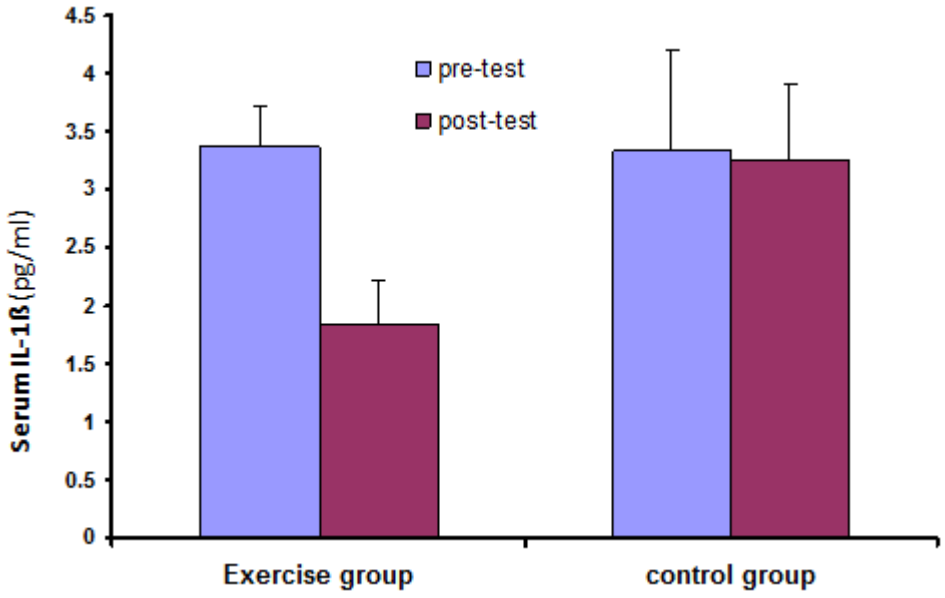

Figure 1: Pre and post training of serum IL-1ß in study groups

Discussion

Although some previous studies suggested ineffectiveness of different training programs on serum levels of inflammatory and anti-inflammatory cytokine in healthy or patients and athletes or non-athlete populations, findings of this study supports the beneficial effects of aerobic training on cytokine profiles in asthmatic patients. As the findings of this study indicate that aerobic exercise three times a week for three months significantly reduces the serum levels of IL-1ß in men with mild to moderate asthma. In other words, the findings support the anti-inflammatory properties of exercise in patients.

Although the molecular mechanisms by which IL-1ß affects asthma or respiratory tracts inflammation is not well known, literature indicated that the expression of IL-1ß in macrophages and epithelial bronchial

increases in asthmatic patients (Wang *et al.,* 1994). Alveolar macrophage secrets IL-1ß in response to certain stimuli, and the production of this cytokine can affect production and secretion of other inflammatory cytokines such as TNF-α, IL-6, IL-8 and adhesion molecules in smooth muscle cells of respiratory pathways, epithelial cells, and endothelial cells (Aya *et al.,* 2010).

However, evidence about the direct role of IL-1ß in the pathology of asthma have been concluded from studies in which administration of IL-1ß in rats led to inflammatory changes such as increased numbers of neutrophils in alveolar-bronchial fluid and increased response of air pathways to bradykinin (Tsukagoshi *et al.,* 1994). Studies on macrophages of asthmatic patients have shown that IL-1ß expression in macrophages increases the levels of IL-1ß in the alveolar-bronchial fluid compared to healthy individuals (Broide *et al.,* 1992).

However, how exercise reduces the levels of this inflammatory cytokine in these patients is not yet fully understood. Anti-inflammatory properties of long-term aerobic exercise in other healthy or patient populations and less in asthmatic patients have been reported by some studies. As some recent studies noted a significant reduction in inflammatory cytokine after three months of aerobic or resistance training in obese women (Phillips *et al.,* 2012; Rosety-Rodríguez *et al.,* 2013). However, some studies reported ineffectiveness of long-term training programs on inflammatory and anti-inflammatory cytokine (Riesco *et al.,* 2013; Oh *et al.,* 2013).

It is possible that the reduction in serum levels of IL-1ß in patients is rooted in exercise-induced weight loss. Because each of the indexes of obesity, such as body weight, body mass index, and body fat percentage significantly decreased in response to exercise. In this regard, some literature has noted a relationship between obesity and asthma (Hancox *et al.,* 2005). It seems that obesity-induced damage to respiratory performance and mechanisms increases resistance of the respiratory tract. In other words, asthma is an inflammatory disease, and research findings indicate that obesity is a cause of increasing inflammatory symptoms (Visser *et al.,* 2001). In the present study, however, patients were placed in the category of obese people, and most of them were overweight or had body mass index near to obesity. Exercise program led to a significant reduction in them. On the other hand, literature have showed that adipose tissue and also adipose tissue macrophages secret IL-1ß, it is possible that reduction in body fat percentage in response to training program lead to a reduction in the secretion of this cytokine and its systemic levels. In this regard, some literature has noted the lack of variations in cytokines in the absence of weight loss even after 12 months of training (Bouchonville *et al.,* 2013).

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