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The effect of chronic aerobic exercise training on serum adiponectin in asthma patients

Eizadi Mojtaba[1], Nazem Farzad[2*], Bananaeifar Abdolali[1], Dooaly Hussein[1]

[1]*Department of Physical Education and Sport Science, South Tehran Branch, Islamic Azad University, Iran*

[2]*Department of Physical Education and Sport Science, Bu-Ali-Sina University, Iran*

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Abstract

Recent evidence has shown that obesity increases the risk of asthma, atopic and autoimmune diseases and it is reported that adiponectin may play an important role in relationship between asthma and obesity. The aim of this study was to evaluate the effects of aerobic exercise training on serum adiponectin in asthma patients. For this purpose, thirty adult obese men with asthma disease divided to experimental and control group by randomly. The experimental group were completed a long term aerobic exercise training for three months (3 time per week) and control group did not participate in exercise program. Fasting serum adiponectin and anthropometrical indexes were measured before and after exercise program. Statistical analysis was performed with the SPSS software version 15.0 using by independent and paired samples T-test. Significance was accepted at $P < 0.05$. Serum adiponectin were significantly increased in response to chronic aerobic exercise program when compared with baseline levels in experimental group ($P = 0.011$). BMI and the other anthropometrical indexes were decreased by exercise training (($P < .05$). FEV1 levels were also significantly increased in response to chronic aerobic exercise program when compared with baseline levels ($P < .05$). All variables in control group remained didn't change. Considering to the findings, we can conclude aerobic exercise training for long time may improve systemic inflammation in asthma patients that is associated with improve respiratory response.

*Corresponding Author: Nazem Farzad ✉ farzadnazem1@yahoo.com

Introduction

Nowadays, obesity is known as an important cause of morbidity and mortality in worldwide. Accumulating evidence indicates that obesity risk factor for type 2 diabetes mellitus, hypertension, atherosclerosis, rheumatoid arthritis and cancer, more so when the weight gain is in and around the abdomen (Mokdad *et al.,* 2004). On the other hand, it was reported that adiposity is a risk factor for asthma, particularly in women (Beckett *et al.,* 2001; Celedon *et al.,* 2001). So, it may alter the severity and control of asthma. A large body of evidence suggests an increased risk of incident asthma with an increase in body mass index (BMI) (Nystad *et al.,* 2004; Flaherman *et al.,* 2006). Recent epidemiologic studies have demonstrated that several mechanisms play key role in the relationship between obesity and asthma. Common genetics (Beuther *et al.,* 2006), obesity related increase in serum levels of proinflammatory adipokines (Scherer *et al.,* 2006) or decrease in anti-inflammatory adiponectin (Yamauchi *et al.,* 2001) and many of the obesity related bio-chemical changes/co-morbidities may contribute.

This hypothesis has been suggested repeatedly that decreased serum concentrations of adiponectin as a anti-inflammatory cytokines in obese humans may also contribute to the propensity towards asthma in this population (Shore *et al.,* 2006). It has been demonstrated that adiponectin inhibits proliferation and migration of cultured vascular smooth muscle cells induced by mitogens (Kondo *et al.,* 2002; Okamoto *et al.,* 2002) and may have similar effects on murine airway smooth muscle (Sood *et al.,* 2008). Consistent with these findings, some recent studies suggest that adipokines may contribute to increased asthma and allergy risk in obese subjects (Nagel *et al.,* 2008). So, a positive significant correlation has been reported between adiponectin with forced expiratory flow (FEF) and forced expiratory volume in 1 second (FEV1) in asthma patients (Kim *et al.,* 2008). Some data suggests that exercise training increases serum adiponectin in obese subjects (Tang *et al.,* 2006; Ceddia *et al.,* 2005), but the role of exercise training on adiponectin in obese men with asthma has not drawn much attention. Therefore, the present study was carried out to investigate serum adiponectin in response to chronic exercise training in adult obese men with asthma.

Material and methods

In present semi-experimental study, we aimed to investigate the effect a chronic aerobic exercise training program for three months (3 days/week for 12 weeks) on serum adiponectin in adult obese men with mild to moderate asthma. For this purpose, thirty adult obese men (age 38±5 yrs, body mass index 31.08±14 Kg) participated in this study by accessible sampling and divided to experimental and control groups by randomly. After the nature of the study was explained in detail, informed consent was obtained from all participants.

Asthma severity was determined from spirometric index (FEV1), degree of airway hyperresponsiveness, and amount of medication prescribed. So that, forced expiratory volume in 1 s (FEV1) and forced expiratory volume in 1 s / forced vital capacity (FEV1/FVC) were measured by Spirometry tests (Minispire model, Made in Italy) in order to asthma diagnosis as well as to determine the asthma severity. Patients were asked to avoid having tea or coffee as well as other airways dilator food for at least 4 hours prior to spirometry test. History of asthma and medication were recorded by a specialist physician. Minimum age of getting affected by asthma is 5 years old.

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, growth hormone deficiency or excess, neuroendocrine tumor, anemia were excluded. All subjects were non-smokers and had not participated in regular exercise/diet programs for the preceding 6 months. In addition, exclusion criteria

included inability to exercise and supplementations that alter carbohydrate-fat metabolism.

All measurements were performed before and after exercise program in experimental and control groups. The measurements for weight, height, abdominal and hip circumference were first performed. 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. Abdominal circumference and hip circumference were measured in the most condensed part using a non-elastic cloth meter. Body Mass index (BMI) was calculated using the formula body weight/height2 in terms of kg/m^2. Visceral fat and body fat percentage was determined using body composition monitor (OMRON, Finland).

Table 1. Mean and standard deviation of anthropometrical and biochemical variables of experimental and control groups in baseline and after intervention.

variables	Control group		Experimental group	
	Baseline	post-exercise	Baseline	post-exercise
Weight (kg)	95 ± 9	95 ± 7	94 ± 7	90 ± 8
Height (cm)	174 ± 6	174 ± 6	175 ± 5	175 ± 5
Age (year)	38 ± 5	38 ± 5	37 ± 6	37 ± 6
abdominal circumference (cm)	104.11 ± 9	104.98 ± 8	105.75 ± 9.30	101.3 ± 6.4
Hip (cm)	105.4 ± 5.6	105.6 ±6.3	106.7 ± 6	102.9 ± 5.3
AHO (Ratio)	0.993 ± 0.11	0.994 ± 0.12	0.991 ± 0.12	0.984 ± 0.13
BMI (kg/m2)	31.45 ± 2.32	31.45 ± 2.65	30.71 ± 2.14	29.41 ± 3.56
Body fat (%)	29.11 ± 3.21	29.45 ± 2.63	28.68 ± 3.21	25.01 ± 5.12
FEV1 (%)	76.5 ± 5	75.3 ± 6	76 ± 5	83 ± 6.3
FEV1/FVC	68.3 ± 4	68.2 ± 5.6	69.6 ± 6.2	76.3 ± 7.2
Adiponectin (µg/ml)	7.21 ± 2.11	7.45 ± 2.62	7.44 ± 2.3	9.11 ± 3.6

***FEV1**, forced expiratory volume in 1 s; **FEV1/FVC:** forced expiratory volume in 1 s / forced vital capacity*
***BMI**, body mass index; **AHO**, Abdominal to hip circumference ratio*

After anthropometric measurements, the individuals in the experimental and control groups were asked to attend Hematology Lab following12 hours of overnight fasting, between the hours of 8 to 9 am for blood sampling in order to measuring serum adiponectin. Serums were immediately separated and stored at -80° until the assays were performed. Subjects were instructed to refrain from intense physical activity for 48 h before testing.

After all measurements, the experimental group participated in an aerobic exercise program (60 min, 3 days/week for 12 weeks, %60-80 HRmax). Each session started by 15 min of flexibility exercises, 30-40 min of aerobic exercise 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. The intensity of the activity of any person was controlled using the Polar heart rate tester (made in the US). Finally, all measurements of blood sampling, spirometry and anthropometrical indexes were repeated in 48 hours after lasting session of exercise.

Statistical analyses

Data were expressed as individual values or the mean ± SD. Statistical analysis was performed with the SPSS software version 15.0. Baseline characteristics were compared by using independent t-tests in the case of normal distribution of data sets, and using the Kolmogorov- Smirnov's test when at least in one of the data sets the normal distribution was excluded. Student's t-tests for paired samples were performed to determine whether there were signigcant within-group changes in the outcomes. P value of <0.05 was accepted as significant.

Results

Baseline and post training serum adiponectin levels, anthropometrical indexes and spirometry parameters of two groups are shown in Table 1. Data were expressed as individual values or the mean ± SD. At baseline there were no differences in the serum adiponectin, spirometry markers and all anthropometrical indexes as age, body weight or BMI, body fat (%) and abdominal circumference between the two groups (Table 1).

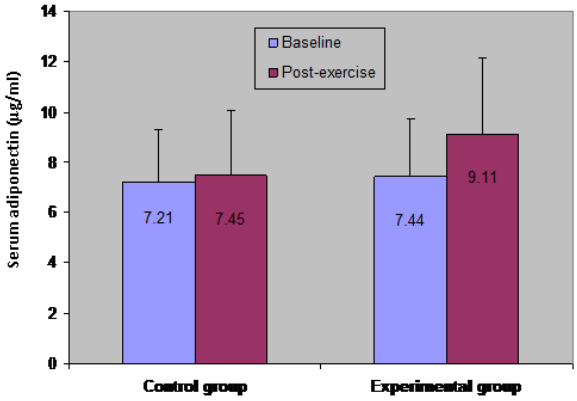

Fig. 1. The changes pattern of serum adiponectin concentration in control and exercise groups of studied subjects. Aerobic exercise leads to significant increase in serum adiponectin in exercise group, while this variable remained without change in control group.

The statistical finding of paired T-test showed that fasting serum adiponectin was significantly increased by exercise program in experimental group (p = 0.011, Fig 1). FEV1 levels were also significantly increased in response to exercise program when compared with baseline levels (P = 0.019). Exercise training resulted in significant decrease B<I (p = 0.033), body fat percentage (p = 0.028), abdominal circumference (p = 0.23) and visceral fat (p = 0.33) in experimental groups.

Discussion

The major finding of this investigation was that long-term aerobic exercise led to improvement serum adiponectin. In the other words, serum adiponectin increased by three months aerobic exercise (3 times/weekly) in asthma patients studied. Our study also showed that FEV1 and anthropometrical indexes such as BMI, body weight and body fat percentage decreased by aerobic exercise training. A number of independent studies have indicated adiposity is a stronger risk factor for asthma (Beckett *et al.,* 2001; Celedon *et al.,* 2001). In fact, Aadipose tissue produces and releases a variety of pro-inflammatory and anti-inflammatory factors that may play a role in the development of a number of inflammatory conditions such as cardiovascular disease, type 2 diabetes and possibly asthma, although their pathogenic role is far from proven (Fantuzzi, 2005). Among them, adiponectin is an anti-inflamatory cytokine that is associated with obesity and asthma (Shore, 2006).There is considerable evidence that Adiponectin inhibits inflammatory gene expression in a variety of cell types, inhibits or modulates nuclear factor kB (NF-kB), and augments expression of anti-inflammatory genes, including the IL-1 receptor antagonist gene (Shibata *et al.,* 2004; Yokota *et al.,* 2000). Although central (visceral) adipocytes are the most important source of adiponectin (Steffes *et al.,* 2004), the serum adiponectin concentration does not increase with obesity in the way the serum leptin concentration does. On the contrary, there is a tendency for a reduced serum adiponectin concentration in obese subjects (Arita *et al.,* 1999). It is reported that adiponectin may play an important role in relationship between asthma

and obesity (Shore *et al.,* 2006). These authors noted that serum adiponectin is reduced during pulmonary allergic reactions and that adiponectin attenuates allergic airway inflammation and airway hyperresponsiveness in mice (Shore *et al.,* 2006).

Our study also showed that Changes in serum adiponectin induced by aerobic exercise training were significantly negative related to the changes in BMI or body fat percentage. In the other words, increased serum adiponectin after training was most strongly related to decreased BMI or body fat percentage. To support this finding, there is evidence that adiponectin mRNA expression in adipocytes decreases in obesity and increases again with weight loss (Milan *et al.,* 2002; Kern *et al.,* 2003), and adiponectin levels are inversely related to body mass index (Hotta *et al.,* 2001; Engeli *et al.,* 2003). Furthermore, morbidly obese asthmatic subjects studied after weight loss demonstrates decreased severity and symptoms of asthma (Hakala *et al.,* 2000). A recent study demonstrated that consistent weight loss in severely obese patients with asthma is associated to improvement in respiratory symptoms and lung function (Maniscalco *et al.,* 2008). To support these data, studies have found that obesity precedes and predicts the onset of asthma (time effect), that increased obesity leads to more severe asthma (dose-response effect), that weight reduction (by diet or gastric bypass) improves asthmatic symptoms, and that obesity co-occurs with intermediate asthma phenotypes (obese young girls undergoing early menarche) (Castro-Rodríguez, 2007).

The known anti-inflammatory effects of adiponectin in both mice and humans and the prevention of both allergen-induced airway responsive-ness and airway smooth muscle proliferation in murine models has led to the hypothesis that the decreased serum concentrations of adiponectin in obese humans may contribute to the propensity towards asthma in this population (Shore[a] *et al.,* 2006). A recent study indicates that treatment with exogenous adiponectin inhibits allergic responses in the airways also indicate that allergen challenge inhibits adipose tissue adiponectin expression and pulmonary adiponectin-binding protein expression (Shore *et al.,* 2006). Referring to the role of anti-diabetic, it is likely alterations in systemic adiponectin might play a role in the asthmatic diathesis not only in obese individuals but also in healthy lean subjects.

It has been demonstrated that airway smooth muscle (ASM) cells expressed adiponectin receptors (Shore[a] *et al.,* 2006), but they did not secrete adiponectin. It seems that adiponectin plays a role through its receptors. It has been hypothesized that a decline in serum adiponectin concentration in obese subjects may contribute to the increased airway smooth muscle mass seen with remodeling in chronic asthma (Shore[b], 2006). In other word, considering to adiponectin has an anti-inflammatory effect and its levels declines in obesity, these anti-inflammatory effects might inhibit ASM cell proliferation. A number of studies have demonstrated that adiponectin attenuated allergen-induced airway inflammation and hyperresponsiveness in mice (Shore *et al.,* 2006).

Overall, according to previous studies it is concluded that obesity is associated with increased asthma prevalence. In other words, obese individuals are more prone to asthma than people with normal weight. It seems that lowered levels of adiponectin or its receptors in airway of obese people somehow leads to increased proliferation of smooth muscles of respiratory pathways wall which leads to resistance to air flow by narrowing of the respiratory pathways. In other words, reduced adiponectin in both obese subjects and patients with asthma is associated with narrowing of the respiratory pathways. Besides exercise as a non-pharmacologic treatment leads to increased serum adiponectin levels. Inverse relationship between serum adiponectin levels with lower body mass index or body fat percentage indicates

that if prolonged exercise is accompanied with weight loss and reduction of body fat percentage, it leads to an increase in adiponectin levels. On the other hand, the concurrent increase of FEV1 (indicator of asthma severity) alongside the increase of adiponectin in response to exercise in this study, supports to some extent the role of adiponectin in the respiratory pathways resistance in patients with asthma.

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