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Therapeutic effect of aerobic exercise training on serum resistin in asthma patients

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Abstract

Previous studies were reported higher adipokine resistin on asthma patients. The objective of this study was to estimate the effects of aerobic exercise program on serum resistin in asthma patients. For this purpose, twenty four adult men with chronic asthma aged 37 ± 6 were participated in this study and divided into exercise or control groups by randomly. Subjects in exercise group were completed an aerobic exercise program for three month, three times per week and control subjects was banned of exercise in this period. Pre and post training of anthropometrical markers and fasting serum resistin were measured in two groups. Exercise program resulted in significant decrease in serum resistin, body weight, BMI and body mass index in exercise group. All variables remained without change in control group. Based on this data, we can say aerobic training is associated with loss weight can be improve inflammation profile in asthma patients.

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Introduction

Increasing evidence suggest that the airway inflammation is associated with the recurrent episodes of wheezing, breathlessness, chest tightness and the nocturnal cough (Sahoo *et al.,* 2009). Among respiratory diseases, asthma is a chronic inflammatory disorder of the airways in which mast cells, eosinophils and T-lymphocytes play a pivotal role (Sahoo *et al.,* 2009). According to a general definition by the National Heart and Lung Institute and World Health Organization it was stated that "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).

It has been previously reported that adipokines may contribute to increased asthma and allergy risk in obese subjects (Nagel *et al.,* 2008), but little is known about the underlying mechanisms.

Leptin, adiponectin, resistin and adipsin named Adipokines are protein mediators secreted by adipocytes and macrophages within the adipose tissue (Fantuzzi, 2005). Among adipokines, resistin a member of a secretary protein family known as resistin-like molecules (RELMs), is a protein with proinflammatory properties may play a pivotal role in inflammation and process of inflammation-related diseases (Shanshan *et al.,* 2006).

Despite other adipokines, there are only a few publications on resistin in human asthma with conflicting results (Larochelle *et al.,* 2007; Kim *et al.,* 2008; Arshi *et al.,* 2010). In this regard, some but not all recent study suggested that resistin may have a protective effect against asthma (Kim *et al.,* 2008), while Larochelle *et al.* (2007) reported higher resistin levels in asthmatics and the levels were increased with disease severity (Larochelle *et al.,* 2007). A recent finding by Sirpa *et al.* (2011) was showed that resistin is positively related with asthma (Leivo-Korpela *et al.,* 2011).

Aerobic physical training with low and moderate intensities has been known to modulate immune responses (Pedersen *et al.,* 2000; Woods *et al.,* 2000; Ceddia *et al.,* 2000). The beneficial effects of exercise and regular physical activity on systemic levels of other adipokines such as leptin and adiponectin have been reported repeatedly (Jung *et al.,* 2008; Kelly *et al.,* 2007). Despite the known effects of physical exercise on healthy individuals, limited studies have investigated the effect of exercise program for short or long term on inflammatory responses in respiratory diseases such as asthma. This question has also been raised whether exercise training for long-time as a non-pharmacologic therapy, can affect serum resistin in asthma patient.

Material and methods

This study was aimed to estimate the effect of long term exercise training on serum resistin in asthma patients. The study included twenty four non-trained adult men with mild to moderate asthma (37 ± 6 yrs; BMI, 31 ± 3.1 kg/m2; 173 ± 2.31 kg) who consented to participate. Then the subjects were divided into exercise (3 days/week for 3 months) and control group by accidentally. Spirometry test was performed for diagnosis of asthma severity. Subjects were asked to refrain from tea, coffee, chocolates and caffeinated soft-drinks on 4 hours before Spirometry.

Inclusion criteria to study were as existing moderate asthma for at least 3 years. Subjects of two groups were reported to be non-smokers and non-athletes. Patients with known history of acute or chronic respiratory infections which may interfere with lung function tests, neuromuscular disease, cardiopulmonary disease and those who had undergone chest surgery or other major operations were excluded. None of the participants had ongoing cardiovascular disease, infections, renal diseases, hepatic disorders, use of alcohol.

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. Anthropometrical markers were measured before exercise program. Height of the barefoot subjects was measured to the nearest 0.1 cm. Weight was measured by an electronic balance. Waist and hip circumferences were measured with the subject standing erect with arms at the sides and feet together, wearing only underwear. Te measurer placed an inelastic tape around the subject, without compressing the skin, on a horizontal plane at the level of the last false rib and the buttocks, respectively. Te measurement was recorded to the nearest 0.1 cm. BMI was calculated as weight (kg)/height (m2).

In next stage, blood samples were collected after a 12-hour overnight fast in all subjects to assess serum resistin. All participants refrained from any severe physical activity 48 h before measurements. Blood samples were dispensed into EDTA-coated tubes and centrifuged in order to separate serum. Samples were frozen and stored (- 80°C) until analysis in the same assay. Serum resistin (Biovendor-Laboratoria medicina a.s. Czech) was quantified using commercially available enzyme-linked immunosorbent assay kits. The inter- and intra-assay coefficients of variance were 5.2 and 3.4% for resistin. All blood sampling and anthropometrical measurement were repeated at the end after exercise program (48 hour after lasted exercise session).

Aerobic exercise program lasted 3 months (3 days/week) at 60-80% of maximal heart rate. 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. The intensity of the activity of any person was controlled using the Polar heart rate tester (made in the US).

Data analysis

Statistic analysis was done with SPSS 15.0 for Windows. Normal distribution of data was analyzed by the Kolmogorov-Smirnov normality test. Independent sample T-test was used to compare the serum levels of all variables between two groups at baseline. Student's paired 't' test was applied to compare the pre and post training values. A p-value of less than 0.05 was considered to be statistically significant.

Results

Anthropometric and spirometry characteristics of the study participants are described in Table 1. The data were reported as mean and standard deviation. At baseline, there was no difference between all anthropometrical markers between two groups. We did not also any difference in respiratory functional markers between two groups at baseline. Baseline and post training resistin levels and anthropometrical indexes of two groups are shown in Table 2. Compared to pre-training, the serum resistin levels decreased significantly after aerobic exercise program in exercise group ($p = 0.002$) but not in the control groups. Furthermore, exercise program resulted in significantly decrease in body weight ($p = 0.025$), BMI ($p = 0.017$) and abdominal circumference ($p = 0.000$).

Main finding of our study was decreased serum resistin after exercise program when compared to baseline in exercise group. Indeed, three months aerobic exercise for 3 times weekly led to a significant decrease in this inflammatory adipokine in adult asthma patients. Furthermore, our exercise program was associated with weigh lose and decreased BMI or body fat percentage in studied patients.

Based on the available information, asthma is a chronic disease characterized by allergic airway inflammation with increased mucus production and lung epithelium remodeling, intermittent airway obstruction and airway hyperresponsiveness (Arm et al., 1992). Most recently, the role of inflammation in the pathogenesis and disease progression of asthma has received considerable attention. So that, in recent years, the recognition of bronchial asthma as an inflammatory disease led to a search for soluble

markers that would be useful in assessing airway inflammation (Yokoyama et al., 1997).

Table 1. Mean and standard deviation of spirometry characteristics of the study participants.

Variable	Mean	Standard deviation
FVC (%)	87.25	8.95
FEV1 (%)	75.67	8.85
FEV1/FVC (%)	68.08	2.94

FEV1, forced expiratory volume in 1 s; FEV1/FVC: forced expiratory volume in 1 s / forced vital capacity, BMI, body mass index

Table 2. Baseline and post training resistin levels and anthropometrical indexes of two groups.

Variables	Control group		Exercise group	
	Baseline	post-exercise	Baseline	post-exercise
Weight (kg)	94.1 ± 8.6	93.8 ± 3.3	93.1 ± 10.8	90.63 ± 13.75
Abdominal circumference (cm)	106.3 ± 9.8	106.1 ± 4.3	105 ± 10.6	103 ± 10.7
Hip (cm)	106 ± 7.5	105.9 ± 6.8	105.6 ± 7.9	104.7 ± 9.05
AHO (Ratio)	1.003 ± 0.03	1.002 ± 0.02	0.99 ± 0.04	0.98 ± 0.43
BMI (kg/m2)	31.02 ± 3.6	30.91 ± 3.4	31.2 ± 3.3	30.33 ± 4.08
Resistin (ng/ml)	5.44 ± 1.04	5.38 ± 1.12	5.20 ± 1.07	4.30 ± 1.23

BMI, body mass index; AHO, Abdominal to hip circumference ratio

Resistin belongs to the RELM/FIZZ family that includes three additional cysteine-rich secretory proteins that share homology with resistin (Akshay et al., 2013). Animal studies have provided evidence indicating that resistin and resistin-like molecules may induce inlammation, angiogenesis, and smooth muscle cell proliferation, all processes that are relevant to asthma pathogenesis (Fang *et al.,* 2012; Jamaluddin *et al.,* 2012). Recent epidemiologic studies have demonstrated that steroid-treated patients with moderate to severe asthma had higher levels of resistin than controls, and resistin levels were increased with increasing disease severity (Larochelle *et al.,* 2007). In a present study, we found that baseline resistin concentrations correlated with anti-inflammatory effects of inhaled fluticasone suggesting that resistin may be a feature and biomarker of steroid-sensitive phenotype of asthma (Leivo-Korpela *et al.,* 2011). It was reported that the expression of resistin itself has been reported to be enhanced by inflammatory factors like IL-1, IL-6, TNF-a (Kaser *et al.,* 2003; Silswal *et al.,* 2005).

Beneficial effects of exercise training on adipokines or adipocytokines such as resistin were repeatedly reported by previous studies in health or diseases population (Rubinb *et al.,* 2008; Tang *et al.,* 2005). These studies was also supported a relationship between hormonal or inflammatory markers with each other in response to exercise training (Sheu *et al.,* 2008; Skilton *et al.,* 2006). Nevertheless, there are limited publications regarding resistin response to exercise training in human asthma. To support some previous finding on other population, our study showed that aerobic exercise program can be improving serum resistin in adult men with asthma.

Finally, the decrease in serum resistin in the present study may be attributed to changes of other such hormonal factors as adipokines or inflammatory cytokine such as IL-1, IL-6, TNF-a, because some previous studies, support significant changes of these hormonal factors or inflammatory mediators in response to a variety of training programs in healthy subjects or patients (Sheu *et al.,* 2008; Skilton *et al.,* 2006). However, since most subject patients in the present study are overweight or obese and the exercise program has brought about weight loss and with lowered levels of body fat, the significant reduction in serum resistin seems to have occurred

partly in response to reduced body fat levels; as adipose tissue is one of the most important tissue from which resistin is secreted. Hence, given the findings of the present study and citing those of previous studies it can be concluded that weight loss and reduced body fat levels in response to the long-term training program in this study is one the most important factors in decrease of resistin levels in asthmatic patients studied.

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