International Journal of Biosciences (IJB)
ISSN: 2220-6655 (Print) 2222-5234 (Online)
Vol. 1, No. 3, p. 100-106, 2011
http://www.innspub.net

RESEARCH PAPER

OPEN ACCESS

The anti-inflammatory effect of acute exercise in asthma patients

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Received: 14 May 2011
Revised: 22 May 2011
Accepted: 23 May 2011

Key words: Adiponectin, Exercise, Asthma, Airway.

Abstract

To investigate serum adiponectin response to acute cycling exercise and to determine the relationship between Changes in its levels with changes in respiratory function by exercise test. Venous blood samples and spirometry test were performed before and after a single bout l erogometer cycling exercise in order to measuring serum adiponectin, FEV1 and FVC in ninety middle-aged men (35. ±6 years mean ± standard deviation) with moderate asthma diagnosis that participated in this study by accessible sampling. Pre- to post training changes were determined by two-tailed t tests. The bivariate associations between changes in adiponectin concentrations with respiratory function were examined with the Pearson rank correlation analysis. Serum adiponectin was significantly increased in response to cycling exercise when compared with pretest ($P < 0.05$). FEV1 and FVC were also increased following by exercise test. After exercise test, serum adiponectin was positively correlated with FEVI ($r= 0.83$, $p=0.000$). These data suggest that exercise even for one session may be decrease systemic inflammation.

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Introduction

Asthma is a syndrome characterized by intermittent narrowing of the small airways of the lung (Settin *et al.,* 2008). This is a chronic inflammatory disease with pathological changes that occur in the lung such as airway eosinophilia, mucus metaplasia and mucus hypersecretion (Neveu *et al.,* 2010). In these patients, the inflammatory process is orchestrated and regulated by a complex network of mutually interacting cytokines and growth factors, secreted not only by a range of inflammatory cells but also from structural tissue components, including epithelial cells, fibroblasts and smooth muscle cells (Settin *et al.,* 2008).

It has been demonstrated that asthma is associated with disturbance in secretion of some inflammation such as IL-4, IL-5 and IL-13, IL-6 (Georas *et al.,* 2005; Cromwell *et al.,* 1999; King *et al.,* 1998; Deetz *et al.,* 1997) and anti-inflammation cytokine of adipose tissue or the other tissue. It has been suggested that 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 (such as leptin) or anti-inflammatory (such as adiponectin) (Sood *et al.,* 2008). It has been demonstrated that low serum concentrations of adiponectin in some human population may also contribute to the propensity towards asthma (Shore[a] *et al.,* 2006). It was reported that adiponectin receptors are expressed in cultured human airway smooth cells (Shore[b] *et al.,* 2006). On the other hand, recent evidence has shown that a decline in serum adiponectin concentration may contribute to the increased airway smooth muscle mass seen with remodeling in chronic asthma (Shore[c] *et al.,* 2006). It seems that low adiponectin in this patients is associated with high proliferation of airway smooth muscle.

Review of research evidence shows that exercise training increase serum adiponectin in healthy or disease population (Varady *et al.,* 2009; Huang *et al.,* 2007; Tang *et al.,* 2005). Additionally some recent study showed increased serum adiponectin in response to acute exercise (Kraemer *et al.,* 2003). But adiponectin response to acute exercise in asthma patients has not drawn much attention. Therefore, the primary aim was to determine whether serum concentrations of adiponectin increase following an acute cycling in asthma. The secondary aim was to determine whether decrease in serum concentrations is associated with respiratory functional in these patients.

Material and methods

Subjects

Ninety middle-aged men (36 ± 5 years mean ± standard deviation) with asthma diagnosis (Fev1/FVC: 70 ± 3) participated in the study by accessible sampling. Intensity Illness Asthma severity was determined by specialist physicians measuring spirometry indices (Minispire model, Made in Italy). Demographic characteristics, lifestyle habits (e.g. cigarette smoking), physical activity, and medical history were collected by self-report.

Inclusion or Exclusion criteria

Inclusion criteria to study for asthma group were as existing asthma for at least 3 years. All subjects with asthma had moderate disease (intermittent or moderate persistent in severity). All subjects were non-smokers and had not participated in regular exercise/diet programs for the preceding 6 months. Participants were non-athletes, non-smokers and non-alcoholics. Participants had no evidence of coronary artery disease; tobacco use; participation in exercise/diet programs; or use of systemic steroids, diabetes treatments, ß-blockers, or thiazides. Subjects with a history or clinical evidence of recent myocardial infarction, congestive heart failure, active liver or kidney disease, growth hormone deficiency or

excess, neuroendocrine tumor, anemia were excluded. Subjects were asked to refrain from tea, coffee, chocolates and caffeinated soft-drinks on 4 hours before Spirometry. Informed consent was obtained from each subject after full explanation of the purpose, nature and risk of all procedures used.

Measurements and protocol

The measurements for weight, height, abdominal and hip circumference and blood pressure were first performed. The weight and height of the participants were measured in the morning, in fasting condition, standing when the participant had thin clothes on and was wearing no shoes. Body mass index (BMI) was calculated using weight divided by squared height. Then, all participants were completed a single bout cycling exercise (Mullis *et al.,* 1999) on cycle erogometer (Tunturi, made in Finland), and underwent a blood sampling and spirometry test before and after exercise. Spirometry tests were completed immediately before and repeated 30 Min after cycling test. Subjects were asked to refrain from tea, coffee, chocolates and caffeinated soft-drinks on 3 hours before Spirometry. The subjects were advised to avoid any physical activity or exercise 48 hours before the exercise test. 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. Calibration of spirometer and all testing protocols were performed as outlined in the instruction manual of the spirometer. Pre and post training blood samples were taken in order to measuring serum adiponectin. Serums were immediately separated and stored at -80° until the assays were performed. Serum adiponectin was determined by ELISA method, using a Biovendor-Laboratorial kit made by Biovendor Company, Czech. The Intra- assay coefficient of variation and sensitivity of the method were 3.9% and 5-50 μg/mL, respectively.

Statistical analysis

Statistical analyses of data were performed using the SPSS software version 15.0. For the descriptive statistics after having checked the normality of the variables using the Kolmogorov-Smirnov test. Pre- to post training changes were determined by two-tailed t tests. The bivariate associations between changes in adiponectin concentrations with respiratory function were examined with the Pearson rank correlation analysis. P value of less than 0.05 was regarded as indicative of a signigcant difference.

Results

In this study, we evaluate serum adiponectin in response to acute exercise on stationary cycling in a group of men with moderate asthma. Subjects have body weight (91 ± 10 kg), body mass index (30 ± 4.11 kg/m2), height (174 ± 8 cm) and abdominal circumference (99 ± 11 cm). Data were expressed as individual values or the mean ± SD. Compared to pre-training, the serum adiponectin levels increased significantly ($P<0.01$) after acute cycling exercise studied patients (5.53 ± 1.2 vs. 6.98 ± 1.9 μg/ml, Fig 1). Increased serum adiponectin by acute exercise test suggest exercise training even for one session can lead to improve systemic inflammation in these patients.

Cycling exercise test also resulted in significant increase in FEVI (74 ± 6 vs. 83 ± 9 %, $p = 0.005$), FVC (86 ± 9 vs. 97 ± 11 %, 0.018), but FEVI/FVC (70 ± 3 vs. 74 ± 6, $p = 0.190$) did not significant change by exercise test. These data suggest that cycling exercise was associated with improve in respiratory function. Increased serum adiponectin after exercise test was most strongly related to improved FEV1 in studied patients ($p = 0.000$, $r = 0.83$, Fig 2).

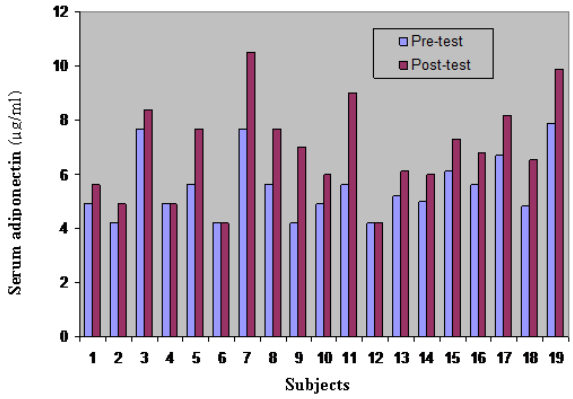

Fig 1: Serum adiponectin before and after cycling test in studied patients. Serum adiponectin levels exhibited a statistically significant increase at the end of cycling exercise when compared to pre-test values. Each number on the horizontal axis represents one subject.

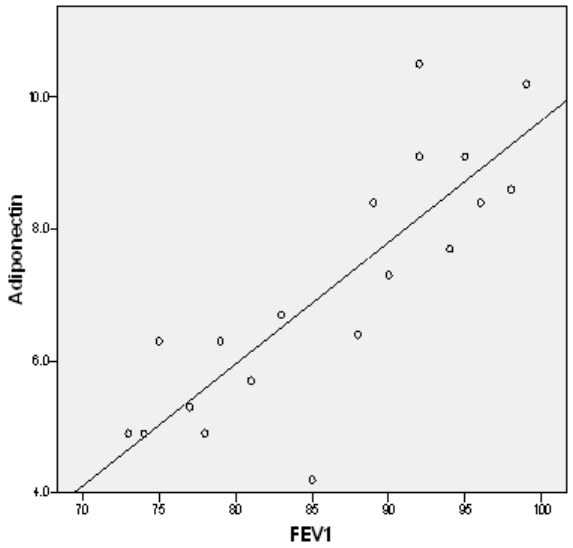

Fig 2. The correlation pattern between serum adiponectin and FEV1 in studied patients. This illustration indicates increased serum adiponectin after exercise test is most strongly related to improved FEV1 in studied patients.

Discussion

In present study, we observed increased serum adiponectin by single bout short-time cycling exercise in middle-aged adult men with moderate asthma. Adiponectin (ACRP30/AdipoQ) is a 30 kDa protein specifically expressed in adipocytes, plasma levels of which negatively correlate with adiposity, insulin resistance, coronary artery disease and dyslipidemia in both mice and humans (Kershaw *et al.,* 2004; Havel *et al.,* 2004; Shimada *et al.*, 2004). This anti-inflammatory cytokine is thought to directly affect a wide variety of target cells, including hepatocytes, myocytes, endothelial cells, macrophages and smooth muscle cells; AMPK has been identified as a key intracellular mediator of adiponectin function (Shimada *et al.,* 2004; Nawrocki *et al.,* 2004).

No control group (healthy group) is one of the limitations of this study. But, some previous studies reported serum adiponectin in asthma patients is lower than healthy subjects (Sood *et al.,* 2008). In this area, a recent study has demonstrated that serum adiponectin is reduced during pulmonary allergic reactions and that adiponectin attenuates allergic airway inflammation and airway hyperresponsiveness in mice (Shore[a] *et al.,* 2006). It is also reported that high serum adiponectin concentration may protect against current asthma (Sood *et al.,* 2008). Adiponectin response to different exercise training in asthma patients has received limited attention. But review of research evidence on other healthy and diseases populations show that adiponectin responses and adaptations differ in acute and chronic exercises. It is reported that serum adiponectin level was not modified during short term exercise, but physical training increased it in 38% of randomized controlled trials (Impson *et al.,* 2008).

In a recent study, adiponectin concentration was measured prior to exercise, immediately after as well as 24 and 48 h after exercise. Authors noted that there were no significant changes in adiponectin across time. The results of mentioned study indicated that a submaximal aerobic exercise did not result in significant changes in adiponectin up to 48 h post-exercise in overweight subjects (Jamurtas *et al.,* 2006). In a recent study, the plasma adiponectin response to a maximal 6000 m rowing erogometer test was unchanged immediately after exercise when uncorrected for plasma volume changes but was

decreased when adjusted for plasma volume changes. Adiponectin concentrations rose significantly above the pre-exercise value after 30 min of recovery (in both uncorrected and corrected for plasma volume expressions) (Jurimae *et al.,* 2005). In this area, authors suggested that 30 min of heavy continuous running does not stimulate an increase in the production and the release of adiponectin, and that the small increases in adiponectin concentrations resulting from the exercise may be attributed to normal plasma volume shifts (Kraemer *et al*., 2003). It is likely, increased serum adiponectin in our study follow of this pattern.

In Our study, cycling exercise were also increases functional respiratory such as FEV1 and FVC in studied patients. Additionally, a positive significant correlation was observed between serum adiponectin and FEV1 after cycling exercise in present study. These finding support this hypothesis that low systemic inflammation is associated with improve in respiratory functional.

Recently, a protective role for adiponectin in cardiomyopathy was demonstrated: adiponectin deletion enhances cardiac hypertrophy, whereas overexpression attenuates it (Shibata *et al.,* 2004). Adiponectin also demonstrates anti-inflammatory effects and down-regulation of vascular smooth muscle cell proliferation (Ouchi *et al.,* 2003). The activity of adiponectin is mediated by at least 2 cell membrane receptors (AdipoR1 and AdipoR2) (Shin *et al.,* 2008). This is likely, decreased adiponectin or its receptors in airway are associated with high airway resistance.

Hyperplasia and hypertrophy of airway smooth muscle (ASM) are characteristic features of airway remodeling in asthma (Shin *et al.,* 2008). Although ASM cells expressed adiponectin receptors, they did not secrete adiponectin. It is, therefore, possible that adiponectin plays a role through its receptors. (Shin *et al.,* 2008). Although adiponectin did not suppress the proliferation of ASM cells, it appeared to act on adiponectin receptors and cause anti-allergic reactions (Shin *et al.,* 2008). It was reported that adiponectin attenuated allergen-induced airway inflammation and hyperresponsiveness in mice (Shore[a] *et al.,* 2006; Shore *et al.,* 2005).

Although most studies have pointed to the fact that short-term exercise is not associated with decreased body weight or reduced body fat levels or those sports activities that do not changes energy expenditure do not change the inflammatory or anti-inflammatory cytokine levels, the present study showed that one session exercise for short-time significantly increased serum adiponectin concentration in patients with asthma. In confirmation of some previous studies, increased levels of adiponectin in the present study may be attributed to changes in plasma volume. But it does not seem that 15 minutes of sub-maximal biking exercise in this study to have resulted in marked changes in plasma levels. Hence, increased serum adiponectin in the present study can be attributed to other factors such as intensity of exercise or methodology and the initial levels of serum adiponectin concentrations.

It is likely that exercise, even for short-time, reduces the concentration of inflammatory cytokines or systemic inflammation in people with some kind of disorder of these cytokines not in healthy or athlete individuals who have normal concentrations of these cytokines. On the other hand, the simultaneous increase of adiponectin and FEV1 in response to cycling exercise in this study indicates that reduced inflammatory responses due to exercise is associated with increased respiratory function in patients with asthma. Although longitudinal studies have shown that increased adiponectin levels are associated with reduced proliferation of smooth muscle in blood vessels and respiratory pathways. But increased serum adiponectin levels in our study do not seem to

have affected the proliferation of these cells, because adiponectin response to one session exercise seems to be acute. But the significant correlations between increased adiponectin levels and FEV1 in this study somehow support the possible role of adiponectin in respiratory responses even after one session exercise. Increased levels of adiponectin as an anti-inflammatory cytokines may have directly or indirectly affected respiratory function, because some studies have suggested that adiponectin affects inflammation of the respiratory airway caused by certain allergens. In addition, the findings of a recent study showed that treatment with adiponectin by long-term injection of adiponectin to asthma patients would lead to reduced allergic response in these patients' respiratory airway (Shore[a] *et al.,* 2006).

Acknowledgements: The authors of this paper wish to acknowledge all asthma patients participated in this study.

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