



Acute response of serum leptin to short single bout exercise in patients with moderate asthma

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Abstract

Recently, it has been hypothesized that leptin levels is increased during allergic reactions in the airway and may be a role in asthma prevalence, but the mechanisms underlying this response are a matter of some debate. The objective of this study was to evaluate the effect a stepwise incremental bicycle test on a bicycle ergometer on serum leptin in asthma patients and to determine its changes role in response to exercise on respiratory functional in these patients. For this purpose, twenty middle-aged males with moderate asthma participated in this study by accessible sampling. Pre and post training blood samples and respiratory functional test were performed in order to measuring serum leptin and spirometry parameters in all patients. Pre- to post training changes were determined by two-tailed t tests. The bivariate associations between changes in leptin concentrations with respiratory function were examined with the Pearson rank correlation analysis. No significant differences were found in serum leptin by cycling exercise with compared to baseline ($p \geq 0.05$). Compared to pre-exercise, the spirometric marker levels as FEV₁ and FVC increased significantly after cycling exercise ($p < 0.05$). We found no evidence that changes in serum leptin were associated with changes in each spirometry markers in response to exercise test ($p \geq 0.05$). Based these data, we can say, exercise for a session can not affect serum leptin in asthma patients and the change in serum leptin by short-time exercise is not associated with respiratory functional in these patents.

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Introduction

Leptin, a inflammation cytokine, produced mainly by adipose tissue although production has been demonstrated in other tissues, such as the fundus of the stomach, skeletal muscle, liver, placenta (Baltaci *et al.*, 2003), heart (Green *et al.*, 1995), in granulose and cumulus oophorus cells in the human ovaries (Cioffi *et al.*, 1997), in human mammary gland (Smith-Kirwin *et al.*, 1998) and in gastric epithelium (Buyse *et al.*, 2004). In addition to its central action to influence energy homeosetasis, leptin has diverse effects in a number of peripheral tissues (Margetic *et al.*, 2002). The data of a recent study showed that the median serum leptin concentrations of children (especially boys) were significantly higher in those with asthma than in healthy controls even though there was no difference in BMI levels (Guler *et al.*, 2004).

Asthma 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).

Recent observations suggest the presence of an interaction between leptin and the inflammatory system; however, there is no adequate knowledge about the role of leptin in atopic states such as asthma (Gurkan *et al.*, 2004). Recent evidence has shown higher serum levels of leptin in asthmatic children than in healthy controls. Significant correlations with serum leptin levels and BMI, FEV₁ reversibility, and serum total IgE were observed (Guler *et al.*, 2003). A number of studies have demonstrated that serum leptin is increased during allergic reactions in the

airways and may play a role in asthma prevalence (Shore *et al.*, 2005). Although the physiopathological mechanisms underlying these associations are largely unknown.

The question is whether leptin reduction in patients with asthma is associated with improvement in respiratory responses. Although the effect of short or long-term exercise on leptin levels and other inflammatory cytokines in other diseases has been studied repeatedly, and most of these studies report decrease of serum leptin levels in response to exercise (Zaccaria *et al.*, 2002; Olive *et al.*, 2001), some studies have reported conflicting findings (Bouassida *et al.*, 2004; Sari *et al.*, 2007). But, the effect of a single session exercise on serum leptin levels in patients with asthma is less obvious. Hence, the main aim of this study is to determine the effects of one session exercise as a no pharmacologic intervention on serum leptin levels. Also, the relationship between the changes of leptin and respiratory functional in response to exercise test were determined in this patients.

Material and methods

Subjects

In this semi experimental study, twenty middle-aged men (mean age 37.41, range 37-45 yr) with asthma diagnosis participated in the study by accessible sampling. Intensity Illness Demographic characteristics, lifestyle habits (e.g. cigarette smoking), physical activity, and medical history were collected by self-report. All subjects with asthma had moderate disease (intermittent or moderate persistent in severity). Asthma severity was determined from spirometric index (FEV₁), degree of airway hyperresponsiveness, and amount of medication prescribed.

Inclusion or exclusion criteria

All subjects were non-smokers. All participants had not participated in regular exercise/diet programs for

the preceding 6 months. Inclusion criteria for study group were determined as existing asthma for at least 3 years. Participants had no evidence of coronary artery disease; tobacco use; participation in exercise/diet programs; or use of systemic steroids, diabetes treatments, β -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.

Anthropometrical measurements

Anthropometric measurements (body height and weight) were performed with the subjects wearing light underwear and without shoes. Weight was measured by an electronic balance and height by a stadiometer. Height and body mass were measured using a wall-mounted stadiometer and a digital scale, respectively. Body mass index was calculated as body mass (in kilograms) divided by height squared (in square meters).

Spirometry test

Spirometry tests (Minispire model, Made in Italy) were completed immediately before 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.

Exercise protocol and blood sampling

Then, all participants were completed a single bout cycling exercise (Mullis *et al.*, 1999) on cycle ergometer (Tunturi, made in Finland). Spirometry tests were repeated 30 Min after cycling test. Pre and post training blood samples were taken in order to measuring serum leptin. Serums were immediately separated and stored at -80° until the assays were performed. Serum leptin 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 4.2% and 0.2 ng/mL, respectively.

Statistical analysis

Data were analyzed by computer using SPSS software version 15.0. Kolmogorov-Smirnov test was used to determine of normal status of the data. Pre- to post training changes were determined by two-tailed t tests. The bivariate associations between changes in leptin 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 significant difference.

Results

In this study, we investigate the effect of single bout cycling exercise on serum leptin in males with moderate asthma. Subjects have body weight (89 ± 9 kg), body mass index (29.08 ± 3.14 kg/m²), height (175 ± 9 cm) and abdominal circumference (98 ± 10 cm). Data were expressed as individual values or the mean \pm SD. Serum Leptin concentrations did not change after cycling test when compared to baseline levels (7.01 ± 1.14 vs. 6.78 ± 2.76 , $p \geq 0.05$). FEV₁ levels were significantly increased in response to exercise when compared with baseline levels (78.02 ± 7.14 vs 86.94 ± 9.1 , $P = 0.021$). FVC was also increased in response to cycling test (89.7 ± 7.12 vs

98.58 ± 4.22p = 0.032). We observed no significant correlation between serum leptin levels with FEV1 after exercise test (p = 0.056, r = 0.21, Fig 1). Post exercise serum leptin levels were also insignificant with FVC (p = 0.311, r = 0.21, Fig. 2).

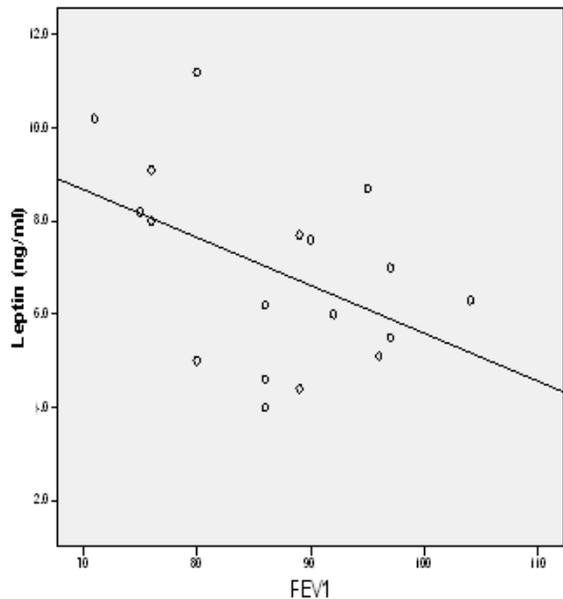


Fig 1. The correlation pattern between serum leptin and EEV1 in studied patients. This illustration indicates no significant association between serum leptin and EEV1 in studied.

Discussion

The present study showed that a single bout cycling exercise does not significant effect on serum leptin in asthma patients. In other words, a session exercise for short time has not anti-inflammatory effect on asthma patients. Asthma is a chronic inflammatory disease and in the last years obesity has also been catalogued as a systemic inflammatory disease considering that adipose tissue is an endocrine organ that produces cytokines that can promote severity of asthma; therefore generating interest in the investigators to perform studies that can relate both conditions (Goodpaster *et al.*, 1999). A large body of evidence suggests an increased risk of incident asthma with an increase in body mass index (Pischon *et al.*, 2006; Izquierdo *et al.*, 2001). Adipose tissue is an endocrine

organ that produces cytokines that can promote severity of asthma; therefore generating interest in the investigators to perform studies that can relate both conditions (Hilda Segura *et al.*, 2007).

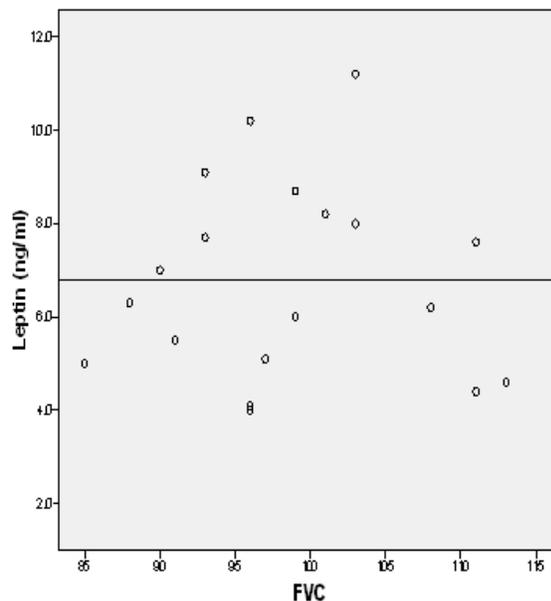


Fig 2. The correlation pattern between serum leptin and FVC in studied patients. This illustration indicates no significant association between serum leptin and FVC in studied patients.

Animal experiments have evaluated the effects of leptin on airway inflammation in response to both allergic and nonallergic exposures and suggest that airway inflammatory response is enhanced by both endogenous and exogenous leptin (Beuther *et al.*, 2006). In fact, leptin is released from fat cells and other tissues, and may exacerbate airway inflammation in asthma. It induces pulmonary inflammation after ozone exposure in mice (Shore *et al.*, 2003) and augments Airway hyperresponsiveness (AHR) in ovalbumin-sensitized mice (Shore *et al.*, 2005). Leptin induces cell proliferation in hematopoietic cells (Huang *et al.*, 2000) and human umbilical vein endothelial cells (Park *et al.*, 2001). However, it is not clear whether leptin influences Airway smooth muscle (ASM) proliferation and cytokine production by ASM cells. But some study

reported that leptin receptors also exist in human lung tissue, and leptin may have stimulatory effects on the proliferation of cells of a human cell line through its specific leptin receptor (Tsuchiya *et al.*, 1999). It was reported that Leptin may provide a link between inflammation and T-cell function in asthma (Guler *et al.*, 2004).

In recent years, generally, it has been demonstrated that serum leptin concentrations are a predictive factor for asthma in children, especially in boys, independent of BMI (Guler *et al.*, 2004). Additionally, the finding of a recent study showed higher serum leptin in children with asthma than none asthma subjects (Guler *et al.*, 2004). Despite this evidence, little is known about the association between leptin concentrations and asthma in adults and its response to differ exercise in these patients.

Although, leptin response to exercise training in the other diseases has been repeatedly studied, but the effect of differ exercises particularly one session exercise on serum leptin in asthma patients has not been fully studied. In this area, another study showed that 45 minutes walking reaching 60–80% of the maximal heart rate did not determine a change in the leptin level, but led to a decrease of the insulin resistance (Yang *et al.*, 2001). There is considerable evidence that, decreases of leptin values may be registered after prolonged physical exercise, over 60 minutes duration, which determines the stimulation of free fatty acids release or after exercise that generates an energy expenditure higher than 800 kcal (Højbjerg *et al.*, 2007). In other words, most training studies which improve fitness levels and affect body composition could decrease leptin or the other inflammation cytokines concentrations.

Despite these date, in trained rowers, it was registered a leptin value decrease, immediately after stopping maximal 30 minutes physical

exercise (Yang *et al.*, 2001). Also, this was decreased in the case of middle-aged, sedentary subjects after 20 minutes of rapid running (Gao *et al.*, 2007). Our study finding showed no significant changes in serum leptin follow cycling test when compared to pretest values. The insignificant decrease in serum leptin in the present study may be attributed to low energy expenditure during exercise. Because, some previous studies have also emphasized that a short-term exercise would reduce or change levels of inflammatory cytokines only when it take noticeable energy consumption over 800 Kilocalories (Højbjerg *et al.*, 2007). It is also possible that the serum leptin response to exercise protocol in the study is a delayed response; not an acute response. So that, it was reported a decline in leptin concentrations in trained rowers 30 min after maximal rowing exercise (30 min) (Jurimae *et al.*, 2). These finding was also confirmed by some previous studies (Olive *et al.*, 2001). The question is whetho05er leptin response to acute exercise in asthma patients follows this pattern. It must be noted that the absence of a control group (Healthy individuals) is one of the main limitations of this study. Hence, it is possible that baseline serum leptin level in asthmatic patients studied is not very much different from the normal levels in healthy individuals. Because in some previous studies, no significant differences in baseline serum leptin levels between healthy subjects and patients with asthma has been observed (Kim *et al.*, 2008; Erel *et al.*, 2007). The insignificant decrease in serum leptin levels in response to exercise in the present study may be attributed to moderate asthma of the patients.

Despite a lack significant change in serum leptin in our study, we observed increased FEV1 and FVC in response to single bout cycling exercise in these patients. These data suggest that one session exercise, in the absence of improvement in systemic inflammation, lead to improve in respiratory function in asthma patients. In addition, we found no evidence that changes in serum leptin were associated with changes in each spirometry markers in response to

exercise test. Our data are consistent with the observation by Guler et colleagues that they did not find any correlation between leptin levels and spirometric parameters (Guler *et al.*, 2003). Accordance with the conclusions of some previous studies, this result must be interpreted with caution, because FEV₁ is a lung volume index, which is a function of height, a parameter that is also included in the derivation of BMI (Guler *et al.*, 2003). On the other words, although FEV₁ is considered a measure of asthma severity, it is not consistently related to inflammation or symptoms and is affected by multiple factors. On the other hand, it is probably that lack a significant relation between them to be due to low number of participants who have participated in this study. Despite the lack of effect on serum leptin levels, it is likely that exercise affect airway resistance or respiratory function by change in the other inflammatory or anti-inflammatory cytokines. Further studies are necessary to elucidate the significance of serum leptin concentration in asthma pathophysiology.

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