



## Resistin response to a short time cycling in asthma patients

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### Abstract

The role of peptide hormones in modulating systemic inflammation are of increasing interest and importance in studies of respiratory diseases. The purpose of this study was to compare serum resistin between asthma and those with non-asthma men and also to evaluate its serum resistin response to a single bout cycling in asthma patients. For this purpose, seventeen adult men with asthma and the same number of healthy subjects matched for age and BMI participated in this study by accidentally samples. Respiratory functional markers and Fasting serum resistin were compared in two groups. Then, respiratory functional markers and serum resistin were measured after a single bout cycling in asthma patients. The data were compared by independent-paired T test. At baseline, respiratory functional markers (FEV<sub>1</sub>, FEV<sub>1</sub>/FVC) and serum resistin in asthma patients was higher than healthy subjects ( $p < 0.05$ ). Exercise protocol resulted in an increase in respiratory function and decrease in serum resistin in studied patients ( $p < 0.05$ ). Based on these data we can say Serum Resistin may be a precise predictor of asthma and one moderate exercise cycling can be improve this inflammation marker these patients.

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## Introduction

Asthma is a condition characterized by variability in airflow obstruction, changes in the level of bronchial responsiveness and airway inflammation (Ebrahim *et al.*, 2012). Accumulating evidence indicated the presence of systemic inflammation in asthma as was previously shown and they have demonstrated an association between systemic inflammation and airway inflammation (Ebrahim *et al.*, 2012; Büyükoztürk *et al.*, 2004; Jousilahti *et al.*, 2002; Enright *et al.*, 1996). The importance of airway inflammation has been well established in patients with asthma. So that, beside the airway inflammation, systemic inflammation may exist in asthma (Jousilahti *et al.*, 2002; Enright *et al.*, 1996). There is considerable evidence that adipose tissue as a metabolically active endocrine organ that is able to secrete a significant number of bioactive peptides that have been termed 'adipokines' such as leptin, adiponectin, Visfatin and interleukins (Kershaw *et al.*, 2004). Resistin is another adipose-derived cytokine first described in 2001 (Steppan *et al.*, 2001). Unlike the expression of resistin in mouse, human resistin is expressed primarily in macrophages but not in adipose (Tomaru *et al.*, 2009).

A positive correlation was observed between Resistin with methacholine and negative correlations with eosinophil count and serum total IgE (Kim *et al.*, 2008). Not only is the presence of cardiovascular disease or diabetes mellitus but also respiratory diseases such as asthma associated with increased plasma resistin levels (Kim *et al.*, 2008). Recently, researchers have reported that in patients with asthma, serum levels of resistin were increased compared with healthy volunteers, and correlated negatively with indices of pulmonary function (Al Mutairi *et al.*, 2011). In addition to compare serum resistin between asthma patients with healthy subjects, this study attempts to evaluate serum resistin response to a single bout cycling in asthma patients.

## Material and methods

The study protocol was approved by the ethics committee of Islamic Azad University. The first aim of this study was to compare serum resistin between seventeen adult men with asthma and the same number of healthy subjects matched for age ( $40 \pm 4$  years) and BMI ( $31 \pm 3$  kg/m<sup>2</sup>) that participated in this study by accidentally samples. Second aim of study was to evaluate serum resistin response to a single bout cycling in asthma patients. After the nature of the study was explained in detail, informed consent was obtained from all participants.

Participants were included if they had not been involved in regular physical activity/diet in the previous 6 months. 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. Inclusion criteria to study for asthma group were as existing asthma for at least 3 years.

At first, the measurements for weight, height, body mass index, respiratory functional markers (FVC: forced vital capacity, FEV<sub>1</sub>: forced expiratory volume in 1 s, FEV<sub>1</sub>/FVC: forced expiratory volume in 1 s / forced vital capacity) and fasting serum resistin were measured after an overnight fast in two groups and compared with each other. Subjects were asked to refrain from tea, coffee, chocolates and caffeinated soft-drinks on 4 hours before Spirometry. Then, asthma patients were completed a incremental bicycle test according to YMCA standard protocol (Tunturi, made in Finland) and measuring of spirometry test and serum resistin were repeated in these patients. This protocol was performed in 5 continues stage without rest between stages and each stage lasted 3 minute. In each stage, intensity was increased according to protocol guideline (Mullis *et al.*, 1999). Subjects were asked to avoid doing any heavy physical activity for 48 hours before blood sampling. Serum

resistin and insulin were measured by ELIZA method respectively using (*Demeditec insulin ELIZA DE2935, Germany*) and (*Biovendora-Laboratoria medicina A.S. Czech*) laboratory kits.

*Statistical analysis*

Statistical analysis was performed with the SPSS software version 15.0. An Independent sample T-test was used to compare the serum levels of all resistin between asthma and non-asthma subjects. Student’s t-tests for paired samples were performed to determine significance of changes in variables by exercise test in asthma subjects. Significance was accepted at  $P < 0.05$ .

**Results**

Anthropometric and spirometry parameters and fasting serum resistin of participants in two groups are shown in Table 1. All values are represented as mean  $\pm$  SD. There were no differences in the age, body weight and body mass index between the two groups (see Table 1). At baseline, serum resistin levels were significantly higher in asthma patients in comparison to healthy subjects ( $p < 0.05$ ). Also, FEV<sub>1</sub>, FVC and FEV<sub>1</sub>/FVC in asthma patients were also significantly lower than those with non-asthma state ( $p < 0.05$ ).

**Table 1.** Mean and standard deviation of anthropometric, spirometry parameters and serum resistin of studied subjects at baseline.

Variables	Healthy subjects	Asthmatic patients
Age (year)	40 $\pm$ 4.8	39 $\pm$ 4.3
Height (cm)	175.2 $\pm$ 5.6	176.3 $\pm$ 7.4
Weight (kg)	96 $\pm$ 8.3	97 $\pm$ 7.4
Body mass index (kg/m <sup>2</sup> )	31.27 $\pm$ 3.14	31.20 $\pm$ 4.11
FVC (%)	94 $\pm$ 6.3	82 $\pm$ 4.3
FEV <sub>1</sub> (%)	92 $\pm$ 9.5	75 $\pm$ 3.2
FEV <sub>1</sub> /FVC	86 $\pm$ 7.6	69 $\pm$ 5.2
Resistin (ng/ml)	2.41 $\pm$ 0.65	5.16 $\pm$ 1.36

*FVC, forced vital capacity; FEV<sub>1</sub>, forced expiratory volume in 1 s; FEV<sub>1</sub>/FVC: forced expiratory volume in 1 s / forced vital capacity; MVV: Maximal voluntary ventilation*

Compared to pre-cycling, FEV<sub>1</sub> increased significantly after exercise program in patients ( $p = 0.014$ ). Exercise protocol was also resulted in a decrease in serum resistin in asthma patients ( $p = 0.022$ , Fig 1). FVC and FEV<sub>1</sub>/FVC levels were significantly increased in response to acute exercise when compared with baseline levels ( $P < 0.05$ ).

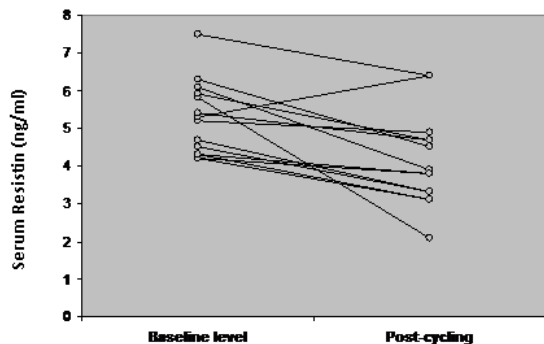
**Discussion**

In present study, we observed that serum resistin in asthma patients was significant higher those non-asthma subjects. In addition, the respiratory functional markers in these patients were higher that normal subjects. The major finding of this

investigation was that one cycling exercise resulted in significant decrease in serum resistin in patients. This exercise protocol was also accompanied with increase in respiratory functional in studied patients.

There is considerable evidence that the proinflammatory adipokines (leptin, resistin) and antiinflammatory (adiponectin) may be causally associated with asthma, however, the precise mechanisms of any association between them have not yet been established. Data from a recent observational study indicate that resistin is involved in pathological processes leading to CVD including

inflammation, endothelial dysfunction, thrombosis, angiogenesis and smooth muscle cell dysfunction (Leivo-Korpela *et al.*, 2011). On the other hand, it has been established that resistin is significant predictive factor for asthma. Accumulating evidence indicates a complex interaction between the inflammatory state and adiposity, allergy and asthma (Arshi *et al.*, 2010).



**Fig. 1.** This fig indicates a significant decrease in serum resistin in response to an exercise cycling in studied patients.

Possible roles for resistin in inflammation disorders such as atherosclerosis and cardiovascular disease, non-alcoholic fatty liver disease, rheumatic diseases, inflammatory bowel disease, and chronic kidney disease and asthma have already been demonstrated. Additionally, resistin as an inflammatory adipokines can modulate several molecular pathways involved in metabolic, inflammatory, and autoimmune diseases (Filková *et al.*, 2009). Patients with COPD, acute and stable asthma have significantly higher resistin than control subjects (Al Mutairi *et al.*, 2011). Recently, researchers have reported that patients with asthma have higher levels of resistin, and resistin levels were increased with disease severity in the asthma cohort (Larochelle *et al.*, 2007). In a recent study, resistin showed significant inverse correlations with FEV1%; FEV1/FVC% in asthma patients (Al Mutairi *et al.*, 2011). Interestingly, it was reported that resistin increases the production of proinflammatory factors IL-6 and TNF- $\alpha$  and that was inhibited by fluticasone in asthma patients (Leivo-Korpela *et al.*, 2011).

The positive role of short or long-term exercise on inflammatory or anti-inflammatory cytokine levels in patients with metabolic disorders such as diabetes or heart disease, and metabolic syndrome and cardiovascular patients has been repeatedly reported (Tang *et al.*, 2005; de Salles *et al.*, 2010). Although some studies have reported exercise not to affect the serum levels of these inflammatory markers in patients or normal subjects (Huang *et al.*, 2007). Some studies in this field have noted decreased serum levels of resistin in obese patients or those with obesity-related diseases in response to physical activity (Valsamakis *et al.*, 2007), and some have reported no effect of prolonged exercise (Elmarakby *et al.*, 2010; Eizadi *et al.*, 2011) or single-session exercise (Kelly *et al.*, 2007) on the inflammatory markers. However, the role of exercise on resistin serum levels in patients with asthma, has received little attention. Although most studies point out that exercise is associated with acute increase of serum or plasma levels of inflammatory cytokines; the findings of this study showed that a single bout of exercise would decrease levels of resistin as an inflammatory marker in asthmatic patients. In this regard, although the reason for the occurrence of this phenomenon can not be explained with certainty, it seems that the low intensity exercise in the protocol used in this study, has not only failed to increase the serum levels of this inflammatory marker, but has significantly decreased it. However, in this study, physical activity was associated with significant improvement of respiratory function in the subjects which can be considered a reason confirming the type of exercise protocol effective in improving inflammatory or respiratory markers.

Based on the present findings, it can be noted that a moderate-intensity physical activity not only leads to improved respiratory function in asthmatic patients but is associated with reduction of systemic inflammation in these patients.

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