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Effects of cycling test on serum interleukin 6 and lipid profile in asthma patients

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Abstract

Accumulating evidence indicates that asthma is associated with systemic inflammation. It was previously reported that circulating interleukin 6 (IL-6) in asthma patients is significantly higher than normal people. This study aimed 1) to compare serum IL-6 and lipid profile between asthma patients and those without asthma, 2) to determine the effect of a single bout exercise test on mentioned variables in asthma patients. For this purpose, serum IL-6 and lipid profile such as triglyceride (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL) and high density lipoprotein cholesterol (LDL) were measured in fifteen adult males with moderate asthma and fifteen healthy men matched for age and body weight. Then the measurements of these biochemical variables were repeated immediately after a stepwise cycling exercise test in asthma patient. Statistical analysis was performed with the SPSS software version 15.0. A p-value less than 0.05 were considered statistically significant. At baseline, asthma patients have higher serum IL-6 than healthy people, while there was not significant difference in lipid profile markers between two groups. Exercise test resulted in no significant change in serum IL-6 in asthma patients. Also, lipid profile markers were not affected by exercise test in studied patients. Finally, it should be acknowledged that acute exercise can not affect serum IL-6 as an inflammatory cytokine or lipid profile in moderate asthma patients.

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Introduction

This hypothesis has been repeatedly that impaired respiratory function or reduced FEV1 (forced expiratory volume in one second) have closely related with cardiovascular risk factors, atherosclerosis, arterial stiffness, cardiovascular disease and mortality, although the physiopathological mechanisms underlying these associations are largely unknown (Zureik *et al.,* 2001). Although some studies have pointed out repeatedly that Smoking and sedentary are main causes of low respiratory function but some recent studies suggested that systemic inflammation is a key factor of Respiratory damage in asthma patients or other respiratory disease. So that, some authors established that reduced lung function has been associated with various inflammation sensitive plasma proteins (Kony *et al.,* 2004; Mendall *et al.,* 2000). In this area, a recent study stated that IL-6 and TNF–Alfa, which are elevated in obese people, are thought to be important agents in the pathophysiology of asthma (Ford, 2005). This is because IL-6 is an effective stimulus of hepatic C reactive protein (CRP), its concentration may be regarded as a proxy for IL-6 activity (Ford, 2003).

Whether some cytokines secreted by adipose tissue such as IL-6 are biologically active in lung tissues is not fully understood. On the other hand, although the role of IL-6 in the incidence of asthma is not known completely, IL-6 concentrations were higher in BALF from patients with status asthmatics than from control subjects (Tillie *et al.,* 1999).

Numerous pharmacological treatments such as the use of inhaled corticosteroids suggested reducing airway resistance in asthma patients. But whether exercise also improves the symptoms of asthma in these patients? Although Information about the role of different types of exercise on IL-6 and other cytokines in asthma patients is limited, but in a study, moderate-intensity constant-work-rate exercise (11 min at 40% of pretraining peak work-rate) led to increase in TNF-alpha levels without any changes IL-6 levels in COPD patients (Rabinovich *et al.,* 2003). In this study, we aimed to investigate the effect of a session exercise test on ergometry cycle on serum Il-6 in males with asthma symptoms.

Subjects and methods

Participants included 16 middle-aged men moderate asthma (age, 41 ± 3.8 years; BMI, 31.84 ± 3.9 kg/m2, mean ± standard deviation) and same numbers of non-asthma healthy subjects matched for age, sex and BMI. Informed consent was obtained from each subject after full explanation of the purpose, nature and risk of all procedures used. The study protocol was approved by the ethics committee of exercise physiology of Islamic Azad University, Iran. Inclusion criteria to study for asthma group were as existing moderate asthma for at least 3 years. Neither the asthma nor non-asthma had ongoing cardiovascular disease, infections, renal diseases, hepatic disorders, use of alcohol, and use of nonselective β blockers and presence of malignancy. Participants were non-athletes, non-smokers and non-alcoholics.

Participants were included if they had not been involved in regular physical activity/diet in the previous 6 months. Neither the asthma nor none-asthma had ongoing cardiovascular disease, infections, renal diseases, hepatic disorders, use of alcohol, and use of nonselective β blockers and presence of malignancy. Weight and height of the participants were measured by the same person when the participant had thin clothes on and was wearing no shoes. Height was measured on standing while the shoulders were tangent with the wall. BMI was calculated as weight in kilograms divided by the square of height in meters (kg/m2).

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. Subjects were instructed to refrain from caffeine consumption and intense physical activity for 24 h before testing.

This study aimed 1) to compare serum IL-6 and lipid profile between asthma patients and those without asthma, 2) to determine the effect of a single bout exercise test on mentioned variables in asthma patients. For this purpose, serum IL-6 and lipid profile such as triglyceride (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL) and high density lipoprotein cholesterol (LDL) were measured in asthma and non-asthma subjects. Then the measurements of these biochemical variables were repeated immediately after a stepwise cycling exercise test in asthma patient. Exercise test was performed according to YMCA protocol on ergometry leg cycle (Mullis *et al.,* 1999). 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.

HDL-cholesterol, LDL-cholesterol, TG and TC were measured directly with enzymatic methods (Randox direct kits, Pars Azmoon, Iran). Serum IL-6 was determined by ELISA method, ((Enzyme-linked Immunosorbent Assay for quantitative detection of human IL-6). The Intra- assay coefficient of variation and sensitivity of the method were 3.4% and 0.92 pg/mL, respectively.

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 variables between asthma and none-asthma subjects. Student's paired 't' test was applied to compare the pre and post training values in asthma patients. A p-value < 0.05 was considered to be statistically significant. All values are represented as mean ± SD.

Table 1. Mean and standard deviation of anthropometric and metabolic characteristics of studied subjects.

Variables	Non-asthmatic	Asthmatic (pretest)	Asthmatic (Post-test)
Age (year)	40 ± 5.3	41 ± 3.8	------
Height (cm)	175 ± 6.3	174 ± 7.1	------
Weight (kg)	98.3 ± 9.8	96.4 ± 7.8	------
Body mass index (kg/m²)	32.09 ± 4.6	31.84 ± 3.9	------
FVC (%)	96 ± 7.63	83 ± 4.9	------
FEV1 (%)	87 ± 7.3	73 ± 6.8	------
FEV1/FVC	79 ± 5.3	67 ± 4.8	------
IL-6 (pg/ml)	4.5 ± 1.2	5.7 ± 1.3	5.1 ± 1.14
LDL (mg/dL)	180 ± 23	175 ± 41	178 ± 38
TC (mg/dL)	160 ± 33	163 ± 38	166 ± 39
TG (mg/dL)	105 ± 21	100 ± 23	103 ± 25
HDL (mg/dL)	44 ± 5.6	42.6 ± 4.4	46.5 ± 5.6

FVC, forced vital capacity; FEV1, forced expiratory volume in 1 s;
FEV1/FVC: forced expiratory volume in 1 s / forced vital capacity; MVV: Maximal voluntary ventilation
LDL, Low density lipoprotein; HDL, High density lipoprotein; TG, Triglyceride; TC, Total cholesterol

Results

First aim of present study was to compare serum IL-6 and lipid profile markers between asthma and non-asthma subjects. Anthropometric and metabolic characteristics of the study participants in the asthma and non-asthma groups are shown in Table 1. The data of independent T test showed that, although serum IL-6 in asthma patients was higher than healthy subjects, but is not significantly from statistical perspective (p = 0.087). But, we did not observe significant difference in all lipid profile markers (LDL, HDL, TG, TC) between asthma patients and healthy groups at baseline ($p \geq 0.05$). On the other hand, all spirometry markers (FEV1, FVC, and FEV1/FVC) were significantly higher in asthma patients in comparison to healthy subjects at baseline ($p \leq 0.05$).

By statistical data by paired sample T test, no significant differences were found in serum IL-6 by cycling exercise with compared to baseline ($p = 0.211$). Additionally, there were no significant changes in LDL cholesterol, total cholesterol and triglyceride by exercise test in studied patients ($p \geq 0.05$). Compared to pre-exercise, HDL cholesterol increased significantly after exercise test ($p = 0.028$).

Discussion

In present study, baseline serum of IL-6 was higher than non-asthma subjects but insignificantly. Although it appears that this minor differences is important from clinical perspective. Airways hyper-responsiveness is an important characteristic of asthma that is associated with the exaggerated narrowing of the airways in response to provocative agents. In the other words, asthma is a syndrome characterized by intermittent narrowing of the small airways of the lung, with subsequent airflow obstruction and symptoms of wheeze, cough and breathlessness (Settin *et al.,* 2008). Recognition of asthma as an inflammatory disease led to a search for soluble markers that would be useful in assessing airway inflammation. Inflammatory processes in asthma is orchestrated and regulated by a by an extensive network of cytokine 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).

Increasing evidence suggests that IL-6 as an inflammatory cytokine is up-regulated in the airway and systemic circulation of asthmatic patients (Kishida *et al.,* 2007; Rogers, 2004). Although increased circulating IL-6 was reported in asthma patients (Neveu *et al.,* 2009), no direct evidence is currently available regarding this hypothesis. Recent studies have shown that IL-6 influences pathological changes within the airway that results in increased airflow resistance (Neveu *et al.,* 2009).

Despite the study's findings, some earlier studies reported higher levels of leptin and IL-6 in asthmatic patients when compared with those without asthma symptoms (Shore *et al.,* 2005; Lacy *et al.,* 1998). It has been demonstrated that the airway inflammation caused by antigen inhalation could similarly increase the circulating levels of IL-6 (Yokoyama *et al.,* 1997). However, some previous studies data and our finding (Partially) support higher serum Il-6 in asthma patients than healthy people, but the data on present study showed that this inflammation cytokine did not change in response to exercise teat in these patients. The finding of present study also showed no significant difference in lipid profile between pre and post-exercise test. Of course, no change in inflammatory cytokines in response to single bout exercise with short time was observed in other chronic diseases in some previous studies (Eizadi *et al.,* 2011).

No change in serum levels of this inflammatory cytokine in response to this exercise model in subject patients is controversial; because if one exercise session is considered a stimulus to increase the secretion of inflammatory cytokines, it is expected that the intended exercise activity is associated with significant increase of this cytokine. It is also possible that the lack of significant changes in Il-6 following an exercise session is rooted in lipid profile markers remaining unchanged. Because the main source of release of both of these variables is body fat reserves. However, although the levels of Il-6 have not changed in response to this exercise test it is possible that the reaction of Il-6 to this exercise is a delayed response; so it is likely that once the levels of inflammatory cytokines had been measured in the recovery period after exercise, the change would have been significant. Finally, based on the findings of this study it might be concluded that a relatively moderate-intensity cycling exercise would not lead to changes in levels of Il-6 as an inflammatory cytokine and a marker of lipid profile which was associated with no asthmatic attacks in the subject patients.

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