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Nonpharmologicl effect of exercise on systemic inflammation and respiratory functional in asthma patients

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Abstract

Accumulating evidence has described a positive association between asthma and systemic inflammation. The aims of present study were 1) to compare serum C-reactive protein and respiratory functional between asthma and non-asthma subjects, 2) to determine of acute responses of these variables to a exercise test in asthma patients . For this purpose, a spirometry test and venous blood samples were obtained of 15 adult men with asthma and those without asthma matched for age and sex. Then, these measurements were repeated in asthma patients immediately after a stepwise cycling test. At baseline, serum CRP levels were significantly higher in asthma patients in comparison to healthy subjects. Also, FEV, FVC, FEV/FVC and the other spirometry parameters were lower in asthma patients in comparison to healthy subjects at baseline. No significant differences were found in serum CRP by cycling exercise with compared to baseline in studied patients. Exercise test increased respiratory functional markers (FEV, FVC, FEV/FVC and ...) in studied patients. Although exercise even for a session improves respiratory functional in asthma patients, but is not accompanied with a improving in systemic inflammation in these patients.

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Introduction

Results from several investigations respiratory patients suggest that impaired lung function as measured by FVC or FEV1 is a powerful predictor of heart disease and of mortality due to cardiovascular disease (Sin *et al.,* 2005; Schroeder *et al.,* 2003).

A growing body of literature suggests that the majority of patients with reduced FEV1 have asthma, chronic obstructive pulmonary disease (COPD), or fibrotic lung disease (Mannino *et al.,* 2003). In these conditions, cytokines of inflammatory mediators are over expressed in lung tissue, potentially resulting in systemic low-grade inflammation (Mannino *et al.,* 2003; Barnes *et al.,* 2006). These authors concluded that inflammation is an important pathway between lung disease and vascular disease (Sin *et al.,* 2005; Mannino *et al.,* 2003). Among the inflammatory cytokines, several prospective studies have demonstrated that high-sensitive C-reactive protein (CRP) is an independent predictor of future risk for cardiovascular events among healthy individuals, as well as among patients with acute coronary syndromes. C-reactive protein represents the classical acute-phase protein produced in the liver in response to inflammatory stimuli, and plasma levels of CRP provide a sensitive marker of increased inflammatory activity (Pfützner *et al.,* 2006). On the other hand, it has been previously reported that CRP may be used as a surrogate marker for the airway inflammation in asthma patients (Sahoo *et al.,* 2009), although the psychopathological mechanisms responsible for these observations are largely unknown. Recently, several reports have been reported a positive association between raised CRP levels, current asthma, respiratory impairment and bronchial hyper-reactivity (Kony *et al.,* 2004; Jousilahti *et al.,* 2002). It has been suggested that FEV1 is independently associated with CRP, in agreement with results of previously published studies (O'Connor *et al.,* 1995; Rijcken *et al.,* 1995).

Despite the aforementioned discussion on the role of CRP as an inflammatory cytokine in some chronic diseases, studies on its role in the pathophysiology of asthma are limited. In this study, we seek to answer the question whether the difference in the levels of these inflammatory cytokines between asthma patients and healthy people. However, scientific studies on the role of exercise in the form of short or long sessions on inflammatory cytokine levels have been noted in other chronic diseases, but the effect of exercise on asthma patients has been less frequently studied. Hence, a secondary goal of this study is to determine the acute response of inflammatory cytokine levels and respiratory function in patients with asthma to relatively moderate intensity exercise for a short duration.

Materials and methods

The objective of this semi-experimental study was 1) to compare serum CRP and some spirometry markers (FEV1, FVC, FEV1/FVC) as pulmonary functional between adult males with asthma and those without asthma symptoms, 2) to evaluate acute response of these variables to a graded cycling exercise in asthma patients. Participants included seventeen adult men with mild to moderate asthma and the same number non-asthma healthy subjects matched for age (38±5 yrs), weight (88±11 Kg) and sex. Each participant received written and verbal explanations about the nature of the study before signing an informed consent form. Inclusion criteria to study for asthma group were as existing mild to moderate asthma for at least 3 years. Asthma diagnosis and its severity were determined by FEV1/FVC. All participants had not participated in regular exercise/diet programs for the preceding 6 months. Subjects with a history or clinical evidence of impaired fasting glucose or diabetes, orthopedic abnormalities, recent myocardial infarction, congestive heart failure, active liver or kidney disease, neuroendocrine tumor and anemia were excluded. All subjects were non-smokers. At first, body weight and height were measured with the subject wearing light clothes. BMI was calculated as weight (kilograms) divided by height squared (square meters).

At baseline, blood samples were taken between 8:00 and 9:00 a.m. after 10 to 12 hours overnight fast to measure fasting serum CRP in asthma and non-

asthma subjects. Also, Spirometry test was performed for measuring FEV1, FVC and FEV1/FVC in all subjects. Subjects were asked to refrain from tea, coffee, chocolates and caffeinated soft-drinks on the day of recording Spirometry.

For this purpose, we compared some markers indicative of pulmonary function as FEV1, FVC, Maximum voluntary ventilation (MVV) and FEV1/FVC between adults obese men (36 ± 6) with asthma (n = 16) and without asthma (n = 14) by resting spirometry test. In next stage, asthma patients were completed a single bout graded cycling exercise and serum CRP were measured immediately after exercise test in these patients. Also spirometry test was repeated after half hours (30 min of recovery) after test. The subjects were advised to avoid any physical activity or exercise 48 hours before the exercise test. Cycling exercise test was a YMCA standard test on leg ergometery cycle (Tunturi, made in Finland) in 5 continues stage without rest between stages (Mullis *et al.,* 1999).

Table 1. Mean and standard deviation of anthropometrical and spirometry markers and serum CRP of asthma and non-asthma participants.

Group	Healthy	Asthma patients	
Variable		Pretest	post-test
Weight (kg)	90 ± 10	88 ± 11	88 ± 11
Height (cm)	174 ± 7	175 ± 8	175 ± 8
Age (year)	37 ± 5	38 ± 5	38 ± 5
BMI (kg/m2)	29.7 ± 3.8	28.7 ± 3.5	28.7 ± 3.5
FVC (%)	94 ± 6.9	79 ± 5.6	84 ± 7
FEV1 (%)	90 ± 7.6	73 ± 3.9	79 ± 5.6
FEV1/FVC (%)	85 ± 7.2	68 ± 3.2	73 ± 7.2
Serum CRP (ng/mL)	1527 ± 318	2779 ± 365	2693 ± 411

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

Statistical analyses

All values are represented as mean ± SD. Data were analyzed by computer using SPSS software version 15.0. The Kolmogorov-Smirnov test was applied to determine the variables with normal distribution. An Independent sample T-test was used to compare all variables between asthma and none-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

Baseline levels of anthropometrical indexes, spirometry parameters and serum CRP of two groups are shown in Table 1. All values are represented as mean ± SD. The finding of independent T test showed no significant difference in anthropometrical parameters between two groups ($p \geq 0.05$). At baseline, serum CRP levels were significantly higher in asthma patients in comparison to healthy subjects ($p = 0.007$). Asthma patients also had lower levels of FEV1, FVC and FEV1/FVC than healthy subjects ($p < 0.05$).

Based on paired T test data, we observed no significant change in serum CRP by exercise test in studied patients ($p = 0.211$, Fig 1). Compared to pre-exercise, FEV1 increased significantly after exercise test ($p = 0.021$). In addition, FVC and FEV1/FVC as respiratory functional were significantly increased in response to cycling exercise in studied patients ($p \leq 0.05$).

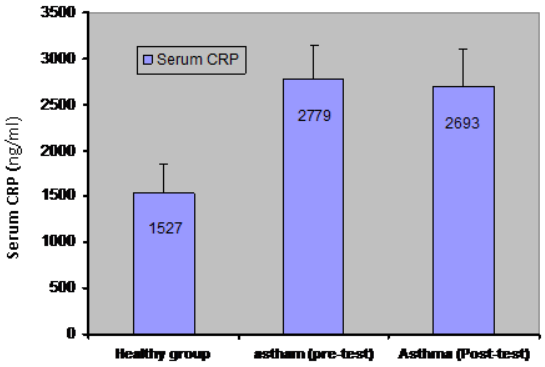

Fig. 1. The changes pattern of serum CRP concentration in asthma and those without asthma symptoms. No significant change in serum CRP was found by exercise test in studied patients.

Discussion

In present study, we observed higher serum CRP as an inflammatory cytokine in asthma patients compared to healthy subjects. In addition, respiratory functional in these patients was significantly lower than healthy subjects. Reported studies have found an inverse relationship between lung function and markers of systemic inflammation (Amina *et al.,* 2010).

It is also important to note that asthma is a syndrome characterized by intermittent narrowing of the small airways of the lung (Settin *et al.,* 2008). It has been demonstrated that inflammation mechanism play important role in pathogenesis of impaired airway in respiratory diseases (Eizadi[a] *et al.,* 2011). These findings suggest that 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). High sensitivity C-reactive protein is an inflammatory cytokine known to be related to inflammation diseases and elevated immunoglobulin E (IgE) is considered as an objective marker of allergy and has been associated with a number of respiratory disorders (Eizadi[a] *et al.,* 2011). It is an acute phase response protein markedly increased in both inflammatory and infectious diseases (Safiullah *et al.,* 2010). It has been previously reported that asthma is an inflammation disorder and date in this area support the hypothesis that the measurement of serum levels of CRP may be useful tool for detecting systemic inflammation in asthma (Eizadi[b] *et al.,* 2011). A number of independent studies have indicated an inverse relationship between lung function and markers of systemic inflammation (Amina *et al.,* 2010).

In this context, the authors suggest that Increased CRP levels are strongly and independently associated with respiratory impairment and more frequent bronchial hyper responsiveness (Amina *et al.,* 2010). Although several studies have suggested an inverse relationship between lung function and markers of systemic inflammation, limited studies has reported a relationship between lung function and CRP levels (Kony *et al.,* 2004). Also, a significant negative correlation was found between serum CRP with each of FEV1 as a respiratory functional marker in asthma patients (Eizadi[b] *et al.,* 2011).

In cross-sectional epidemiologic studies higher aerobic fitness has been associated with lower CRP levels (LaMonte *et al.,* 2002; Church *et al.,* 2002). These latter findings as well as a report suggesting that frequent habitual exercise may contribute to reduced levels of CRP (Albert *et al.,* 2003). On the other hand, numerous studies have reported an association between the level of physical activity and respiratory function (Pelkonen *et al.,* 2003). To support these data, our study showed that exercise for one session increases respiratory functional markers such as FEVC, FVC and FEV1/FVC in studied asthma patients. In this area, Data from a recent observational study indicate that men who remained in the active life style during the follow-up (19 months) showed 50 ml improvement in their FEV1 and 70 ml in their FVC, whereas subjects who remained in sedentary life style had 30 and 20 ml reduction in their FEV1 and FVC, respectively (Garcia-Aymerich *et al.,* 2007). In another study, it has been indicated that intensive swimming prepuberty enhances static and dynamic lung volumes (Courteix *et al.,* 1997).

In the present study, In spite of a significant increase in respiratory function in response to a single bout of cycling exercise in asthma patients, the results showed that this exercise test was associated with no significant changes in levels CRP. In fact, the findings show that short-term exercise does not lead to changes in these inflammatory cytokines. However, considering the findings of other studies that have been reported acute increase in CRP or other inflammatory cytokines in response to exercise, it can be concluded that a relatively moderate-intensity exercise of short duration, although not stimulating inflammatory response, leads to temporary improvement of respiratory function in asthmatic patients. Based on this information, this study supports beneficial effects of exercise on respiratory function for a single session without any stimulatory effect on inflammatory mediators in patients with asthma to which most studies have pointed as an inflammatory disease.

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