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Acute exercise has not an anti-inflammatory property in respiratory patients

Sedghi Hussein*, **Pourtoeiserkani Mohammad**, **Dooaly Hussein**, **Daraei Shokrabad Firooz**

Department of Physical Education and Sport Science, Central Tehran Branch, Islamic Azad University, Iran

Abstract

Proinflammatory cytokines including interleukin -1 beta (IL-1ß), a protein produced by various cells, has been involved in pathophysiology of respiratory disorders. To evaluate serum response of IL-1ß to acute exercise, seventy males with mild to moderate asthma Aged 35 to 45 years participated in this study and its serum levels were measured before and immediately after a single bout cycling test. 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 $P < 0.05$. No significant differences were found in this cytokine by cycling exercise with compared to baseline. Based on this data, we can say on short-time exercise has not an anti-inflammatory properties in asthma patients.

*Corresponding Author: Sedghi Hussein ✉ sedghi2001@yahoo.com

Introduction

Previous investigations have described that Impaired inflammatory cytokine is associated with chronic disorders, While the mechanisms underlying these inflammation-associated changes in airway responsiveness remain to be elucidated. Cytokines are extracellular signaling proteins usually less than 80 KD in size. These mediators secreted by fatty tissue and other tissues play a key role in the co-ordination and persistence of inflammation in obesity, obesity related diseases and respiratory diseases such as asthma, although the precise role of each cytokine are not completely understood (Chung *et al.,* 1999).

Current evidence suggests that inflammatory cytokines such as interleukin-1, tumor necrosis factor-alpha (TNF-alpha) and IL-6 are important in the induction of inflammatory responses (Takizawa, 1998). Among them Interleukine-1beta (IL-1ß) is a pivotal cytokine that is centrally involved in both local and systemic immune responses (Whelan *et al.,* 2004). It has been previously reported that IL-1β is a regulator of the body's inflammatory response and is produced after injury, infection and antigenic challenge (Maedler *et al.,* 2009). Recent epidemiologic studies have demonstrated that dysregulated synthesis and prolonged release of IL-1ß in chronic inflammatory conditions, such as inflammatory bowel disease, psoriasis and rheumatoid arthritis, may contribute to the pathogenesis of these diseases (Dinarello, 1998). Accumulated evidence suggest that IL-1ß may be involved in in the early phase of both the inflammatory response and altered airway responsiveness of an asthma patient, and elevated levels of IL-1ß protein have been shown to be present in the airways of patients with asthma (Borish *et al.,* 1992; Pujol *et al.,* 1990). Animal and preliminary human research has also suggested IL-1ß as one of the key molecules responsible for induction of altered airway responsiveness in experimental asthma according to

its direct action on the ASM (Hakonarson *et al.,* 2002; Hakonarson *et al.,* 1999).

Conflicting data are available about the role of different types of physical activities exercise training on inflammatory cytokines such as IL-1ß in chronic diseases such as asthma patients. So, some of them supports the beneficial effects of exercise training on IL-1ß (Gomez-Merino *et al.,* 2007; Eizadi *et al.,* 2011) while other papers has been reported lack of response to exercise training. Additionally, there has been little attention about its response to acute exercise in these patients. Therefore, in this study, we aimed to investigation effects an acute cycling test on serum level of this inflammatory cytokine in mild to moderate asthma patients.

Material and methods

Subjects

Participants included seventy none-trained adult men (age 39±6 yrs, body weight 95±11 Kg) with mild to moderate asthma. Asthma diagnosis and its severity were determined by FEV1/FVC. Each participant received written and verbal explanations about the nature of the study before signing an informed consent form. The measurements for weight, height, abdominal and hip circumference and blood pressure were first performed. Weight was measured in the morning, in fasting condition, standing, wearing light clothing and no shoes. Height was measured without shoes 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).

Inclusion or Exclusion criteria

Inclusion criteria to study for asthma group were as existing asthma for at least 2 years. The exclusion criteria were as follows: Patients with known history of acute or chronic respiratory infections which may interfere with lung function tests, neuromuscular disease, cardiopulmonary disease and those who had undergone chest surgery or other major operations. Participants had no evidence of coronary artery disease; tobacco use; participation in exercise/diet programs. Persons with a known diagnosis of

diabetes (defined as a physician's diagnosis or the regular use of diabetic medications) were excluded. After introduction and awareness of the subjects of the objectives of the study and once they had completed consent forms, the process of test implementation began. Participants were included if they had not been involved in regular physical activity in the previous 6 months.

Blood Samples and exercise protocol

The subjects were advised to avoid any physical activity or exercise 48 hours before the blood sampling. Blood samples were collected from brachial vein before and immediately after single bout cycling test according to YMCA protocol on

cycle ergometry (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 Blood samples were collected in order to measuring serum adiponectin and leptin. Serums were immediately separated and stored at -80° until the assays were performed. Serum IL-1β was determined by ELISA method (Enzyme-linked Immunosorbent Assay for quantitative detection of human IL-1β), using a Biovendor- Laboratorial kit made by Biovendor Company, Czech. The Intra-assay coefficient of variation and sensitivity of the method were 5.1% and 0.3 pg/mL, respectively.

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

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age (year)	17	32	49	39.41	5.821
Height (cm)	17	170	179	174.00	2.424
Weight (kg)	17	78	114	95.41	10.589
BMI 1	17	27	38	31.41	3.222
Body fat (%)	17	20	37	29.47	4.888
FVC (%)	17	75	100	89.35	9.165
FEV1 (%)	17	58	87	78.88	9.034
FEV1 to FVC (%)	17	63	73	70.06	2.657
IL-1B (pre-test)	17	1.1	8.9	3.594	2.3368
IL-1B (post-test)	17	1.1	6.4	3.471	1.9672
Valid N (listwise)	17				

Statistical analysis

Statistical analysis was performed with the SPSS software version 15.0. Normal distribution of data was analyzed by the Kolmogorov-Smirnov normality test. Student's paired 't' test was applied to compare the pre and post exercise values. A p-value of less than 0.05 was considered to be statistically significant.

Results

Anthropometric, spirometric and metabolic characteristics of the study participants are shown in Table 1. No significant differences were found in serum IL-1ß by cycling exercise with compared to baseline (p = 0.639, Fig. 1).

Discussion

The major finding of this investigation was no significant change of serum IL-1ß in response to single bout cycling in mild to moderate asthma. In present study, although we observed a reduction in serum levels of this cytokine, but this change was no significant of statistical perspective.

Accumulating evidence suggest that inflammation cytokine plays a role in various diseases, including autoimmune diseases such as rheumatoid arthritis, inflammatory bowel diseases, as well as in diseases associated with metabolic syndrome such as

atherosclerosis, chronic heart failure and type 2 diabetes (Maedler *et al.,* 2009). Marked evidence indicates that cytokines often possess overlapping biological activities, exert different effects at different concentrations, can synergize or antagonize the effects of other cytokines and regulated in a complex manner and function via cytokine cascade (Kunkel *et al.,* 2000). It is also important to note that cytokines and their receptors exhibit very high affinity for each other. Because of this high affinity, picomolar concentrations of cytokines can mediate a spectrum of biological effect (Mahajan *et al.,* 2006).
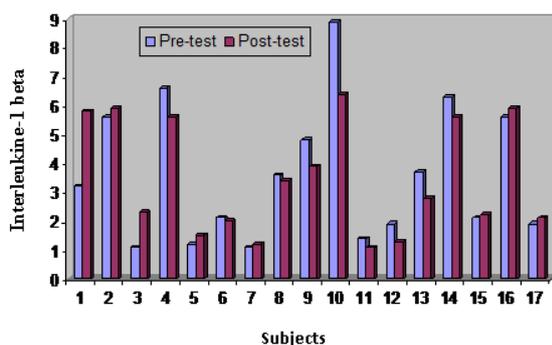
Fig. 1. Mean and standard deviation of serum IL-1B before and after cycling test in studied patients. No significant differences were found in serum IL-1B by cycling exercise with compared to baseline. Each number on the vertical axis represents one subject.

It has been previously reported that IL-1 is a critical mediator of the inflammatory process in various disease states, including asthma (Dinarello, 1998). Review of research evidence highlights the important role of IL-1ß in the pathophysiology of asthma (Whelan *et al.,* 2004). On the other hand, it is also important to note that apart from its contractile properties, airway smooth muscle (ASM) is capable of producing IL-1ß as well as a wide range of other inflammatory molecules that have been implicated in asthma (Shore *et al.,* 2002; Hakonarson *et al.,* 1999). In this regard, in the current study, it has been established that when administered to ASM cells, IL-1ß is capable of modulating the expression of hundreds of genes, of which a large number have been previously implicated in the pathobiology of asthma (Hakonarson *et al.,* 2001). These authors

noted that, the ASM also has synthetic functions, producing molecules that are involved in the development of the airway inflammatory response and induction of altered airway responsiveness in asthma (Whelan *et al.,* 2004).

The role of various exercise activities in asthma pathophysiology and disease control has gained considerable attention, although the specific mechanisms responsible for these observations are not obvious. It has been widely accepted that exercise can provoke an increase in airway resistance leading to exercise-induced asthma. It is also important to make a note here that regular exercise training and participation in sports are considered to be useful in asthma management (Orenstein, 1996). The benefits of physical activity and exercise training in these patients are related to the improvement of ventilatory capacity and lessening of asthma-related symptoms (Ram *et al.,* 2005). It has been previously reported that regular exercise training improves physical fitness and work capacity and decreases dyspnea, exercise-induced bronchospasm, peak expiratory flowvariability, and daily use of inhaled steroids (Ram *et al.,* 2005; Fanelli *et al.,* 2007).

Most studies on the effects of exercise on inflammatory mediators are longitudinal and their response to short-time or acute exercise has received limited attention. Our study finding showed no significant change in serum IL-1ß by on session cycling. No significant changes in this inflammatory cytokine in response to cycling test in this study may be attributed to Short duration or low intensity of exercise. There is also the possibility that the response of cytokines to single bout exercise to be a delayed response is not acute response. This hypothesis was supported by other authors. In this regard, one recent study showed that adiponectin as an anti-inflammatory cytokine was unchanged immediately after a 6.5 km rowing at the individual anaerobic threshold and significantly increased above pre-exercise values after 30 min of recovery (Jurimae *et al.,* 2006). In another study, maximal rowing exercise for thirty minute led to a decline in

leptin concentrations after 30 min recovery (Jurimae *et al.,* 2005).

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