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Serum Interleukin 6 before and Immediately after a Moderate Exercise in Asthma Patients

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ABSTRACT: Recent observation suggests the presence of systemic inflammation in asthma or other respiratory disease. The purpose of this investigation was to examine the influence of one exercise test on serum Interleukin-6 (IL-6) in asthma patients. Asthma severity diagnosed by spirometry test. For this purpose, sixteen untrained adult men with chronic asthma were completed a relatively long time exercise test involved 45 min running with moderate intensity on smooth surface without slope. Blood samples were obtained before and immediately after exercise test in order to measure serum IL-6. Data were evaluated using, paired T tests. Exercise test resulted significant decrease in serum IL-6 in studied patients (from 7.98 ± 4.94 to 6.18 ± 3.65 Pg/ml, p = 0.011). We concluded that one session long time running with moderate intensity is associated with inflammatory property in asthma patients.

Keywords: Interleukin-6, Asthma, Exercise, Respiratory function

INTRODUCTION

It has been clearly identified that respiratory dysfunction is strongly associated with cardiovascular risk factors, arthrosclerosis, cardiovascular diseases, and mortality. However, pathophysiological mechanisms undertaking this relationship are still unknown [1]. Chronic obstructive pulmonary disease and asthma are defined as airway chronic inflammatory disease. Evident also exist regarding the fact that systemic inflammation is involved in their pathogenesis [2]. Asthma has become increasingly prevalent in developing countries during the past three decades. Studies in developing countries have also shown the increasing outbreak of this disease. Again, adequate evidences support the mutual relationship between asthma and obesity [3,4].

Some scientific resources have supported asthma as an inflammatory disease. They have implied the presence of systemic inflammation in asthma [5]. On the other hand, disruption in inflammatory mediators (especially, inflammatory cytokines' increase) provides the scene for the outbreak of the disease in susceptible individuals and its intensification in patients suffering from asthma. The relationship between cytokines and the increase of Interleukin-6 levels – as an inflammatory cytokine – has been frequently reported in allergic condition (6]. In fact, IL-6 is one of the inflammatory indices with increasing levels in asthma patients [7]; especially, in asthma attacks [8].

IL-6 secretion increase from alveolar macrophage is observed in asthma patients [9]. Similarly, increasing IL-6 serum levels and expression in bronchial epithelial cells is also reported before [10]. The increase in its secretion – especially, by alveolar macrophages and mastocyte cells - induces the appearance of respiratory paths inflammation and bronchi's activity suppression in these patients [11].

Identifying asthma as an inflammatory disease gave rise to several studies regarding the determination of inflammation signs such as some cytokines (e.g. IL-6) in respiratory oaths inflammation. Besides, a variety of treatment methods have been presented for improving cytokines levels in these patients. The relationship between the role of medicinal treatment, exercises, and physical activity in inflammatory profile improvement in chronic patients such as asthma have been discussed frequently, although these studies have presented paradoxical results depending on the intervention components of the exercises. Nevertheless, some studies report the futility of short or long term exercises on these factors [12, 13]. Yet, few studies have been carried out on the role of short term or single-session sport tests on these cytokines or these cytokines' instant response to a single-sport session, on the other hand; especially, in asthma patients. Accordingly, the present study determines IL-6 instant response to a single session of running at an average rate in adult asthma patients.

MATERIAL AND METHOD

A. Human subjects and inclusion criteria: In this study, acute response of serum IL-6 to a long time exercise test was measured in asthma patients. The Study Protocol was approved by the Ethics Committee of Islamic Azad University, Iran. Participants were forty sedentary adult men with chronic asthma aged 41 ± 4 year and body weight 92 ± 10 kg. Inclusion criteria to study were as existing moderate asthma for at least 3 years. The diagnosis of asthma was made by spirometry test. Subjects were asked to refrain from tea, coffee, chocolates and caffeinated soft-drinks on 4 hours before Spirometry. 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.
All subjects were non-smokers. All participants had not participated in regular exercise/diet programs for the preceding 6 months. We also excluded people who had any self reported physician diagnosed chronic disease (arthritis, stroke, diabetes, hypertension, cancer, heart attack, chronic cough, or bronchitis). After the nature of the study was explained in detail, informed consent was obtained from all participants.

B. Anthropometrics Markers: All anthropometric measurements were made by the same trained general. Body weight was measured in duplicate in the morning following a 12-h fast. Height was measured with high precision with an error of ± 0.1 cm. Body mass index (BMI) was calculated by dividing body mass (kg) by height in meters squared (m^2). Abdominal obesity and hip circumference were determined in a standing position at the end of normal expiration and ratio between them (AHO) was calculated for each subjects. Percentage body fat was measured using body composition monitor (OMRON, Finland).

C. Biochemical Analysis: Venous blood samples were obtained before, immediately exercise test. Exercise test was 45 min running at 75(%) of maximal heart rate on smooth surface without slope. Serums were immediately separated and Concentrations of serum IL-6 were measured. All participants refrained from any severe physical activity 48 h before measurements. The sensitivity of the IL-6 assay was 0.92 Pg/mL. Intra and inter-assay coefficients of variation were 3.4 and 5.2%, respectively.

D. Data Collection: Statistical analysis was performed with the SPSS software version 16.0. The Kolmogorov-Smirnov test was applied to determine the variables with normal distribution. Pre- and post exercise serum IL-6 were compared using a paired-samples t-test. All statistical tests were performed and considered significant at a $P \leq 0.05$.

RESULTS

In present study, serum levels of IL-6 were compared between pre and immediately after a relatively long time running test in asthma patients. Table 1 presents the anthropometric and Spirometrical characteristics of studied subject. No collimations were found in serum IL-6 with each makers of spirometry ($p > 0.05$). Data of statistical analysis showed a significant decrease in serum IL-6 by exercise test (from 7.9 ± 4.9 to 6.18 ± 3.6 pg/ml, $p = 0.011$, Fig. 1).

able 1: Mean and standard deviation of anthropometrical and clinical features of studied patients

	Mean	Std. Deviation
Age (year)	41.25	4.123
Height (cm)	175.25	2.082
Weight (kg)	92.19	10.394
Abdominal (cm)	107.25	9.205
Hip (cm)	105.19	8.093
BMI (kg/m2)	29.9856	2.99945
Body fat (%)	29.169	3.4095
Visceral Fat	12.75	2.176
Forced vital capacity (%)	81.63	6.592
forced expiratory volume in 1 s (%)	77.69	6.300
FEV1 / FVc (%)	67.63	1.708
Interleukin 6 (pre)	7.981	4.9437
Interleukin 6 (post)	6.175	3.6490

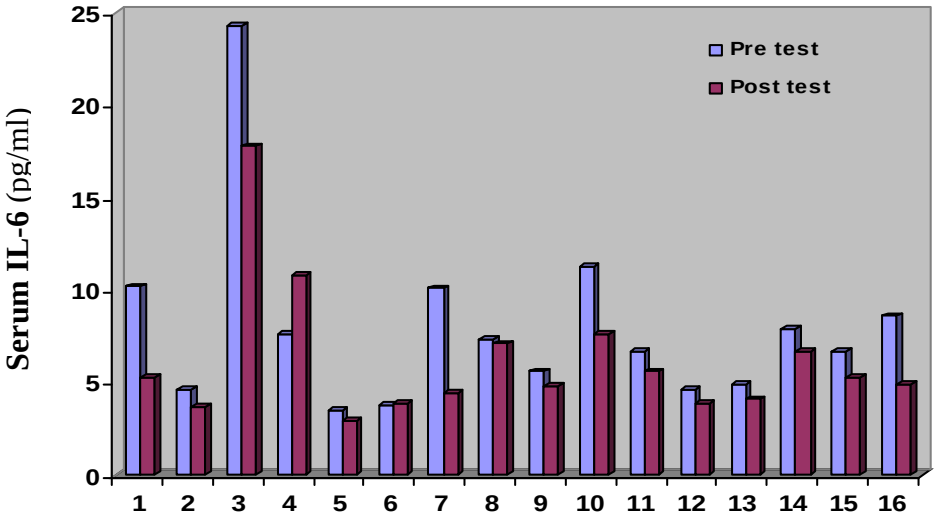

Fig 1: This fig shows the change of serum IL-6 in response to exercise test in each subjects. Exercise test resulted significant decrease in this cytokine in studied patients.

DISCUSSION

Exercise training together with medicinal treatment results in useful effects on the main physiological parameters in asthma patients [14]. Asthma is an airway disease with allergic origin. Physiologically, it appears with respiratory airway narrowness. Among the clinical symptoms of asthma include the sudden attacks of loosing breath, coughing, and wheezing [15]. Results concerning the instant response of peptide and hormonal mediators to short term exercises in asthma patients are limited. However, few studies have measured the effect of single-session sport tests on cytokines levels in asthma patients so far. Yet, based on the existing evidences in this study, it is concluded that a session of aerobic exercise in form of 45 running on a flat surface with a relatively average rate results in a significant decrease of IL-6 as an inflammatory cytokine.

This observation evidently contributes to the anti-inflammatory qualities of this sport test with an emphasis on IL-6. In asthma, inflammatory processes are affected by a complex network of cytokines and growth factors secreted not only by inflammatory cells but also by other tissues such as epithelial cells, fibroblasts, and smooth muscles' cells. Hence, the inflammation of respiratory paths mucus is accompanied by systemic acute or chronic inflammation [5].

It is also mentioned before that asthma patients have higher IL-6 levels as compared to healthy people [16,17]. Some studies have also reported that IL-6 levels only increased in response to inflammatory condition rather than having a pivotal role in these processes [18]. Recent findings have also contributed to not only the role of topical inflammation, but also systemic inflammation in asthma patients.

It has become crystal clear that systemic inflammation plays a critical role in allergic and respiratory diseases. Again, it can be among the factors connecting between respiratory and cardio-vascular diseases. That is, a decrease in respiratory function is reported with systemic inflammation resulted from some plasma proteins [19,20]. Researchers have also implied that IL-6 levels in asthma children are higher than healthy individuals especially, those with familial history of the disease [21]. Its significant increase in these patients and in particular at the time of asthma attacks have been frequently reported [22]. The outbreak of inflammation symptoms in respiratory paths through taking antigens is similar to the time when IL-6 levels increase [23]. Increasing eosinophils accumulation in lungs in response to IL-6 levels increase is also observed before [24,25]. At the same time, hindering IL-6 function via neutralizing or controlling its receptors in rats infected by asthma led to the reduction of eosinophils accumulation in lungs [26]. Although cytokines' instant response to exercise in asthma patients is barely studied, some other studies have examined these objectives in other healthy or infected samples. Yet, there are some studies that reported no changes in cytokines in response to a single-session exercise [27, 28, 29, 30].

On the other hand, some research have pointed that sport test improves cytokines' or inflammatory profile only when it takes 60min or calorie consumption level is at least between 600 and 800Kcal during the test [31]. For instance, in a study, 60min running with %70 VO2max intensity resulted in a significant decrease of leptin in male athletes [32]. Now, perhaps, the significant reduction of IL-6 in the present study can be attributed to the type of exercise plan with the least energy consumption required for improving cytokines. This is because, based on individuals' weight and the intensity and duration of the sport test, it seems that consumed energy in this test is over 600Kcal.

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