Anti-inflammatory Effect of Aerobic Training on Asthma Patients

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ABSTRACT
The production of the inflammatory cytokine tumor necrosis factor alpha (TNF-α) is increased in lungs and circulating of patients with chronic obstructive pulmonary disease (COPD) or asthma. The aim of present study was to assess the effect of an aerobic training program on serum TNF-α in asthma patients. For this purpose, twenty four non-trained, non-smoker adult men with mild to moderate asthma aged 35 – 45 years and height 171 – 178 cm were randomly divided into exercise (3 months, 3 time weekly) and control group. Pre and post training TNF-α level and anthropometrical were measured of all patients in two groups. The comparisons between the measurements of the parametric parameters were determined by paired and unpaired samples t test. Aerobic training results in a significant decreased in serum TNF-α in exercise group (p = 0.001), but not in the control group (p = 0.63) (Table 2). Compared to pre-training, anthropometrical markers decreased significantly after exercise program (p ≤ 0.05). In conclusion, we can say, aerobic training program is associated with a anti-inflammatory property in asthma patients.

Keywords: Asthma, Aerobic training, Spirometry, Inflammation, Body weight

INTRODUCTION
Asthma is the disease of respiratory tract with an allergic origin. Physiologically, asthma is associated with the narrowing of the airways of the respiratory tract. From a clinical perspective, asthma is associated with sudden attacks of shortness of breath, coughing and wheezing [1]. There are continuous studies on the establishment of medical treatments and other strategies to reduce the prevalence of asthma. In this regard, there are numerous studies on identification of proteins, hormones and inflammatory factors affecting the prevalence of asthma. Several metabolic and hormonal factors are involved in the presence of asthma. Understanding the interactions between these factors and their patterns of changes in training programs will provide the grounds for most recent research to provide appropriate methods for the treatment of this devastating disease.

Systemic inflammation plays an important role in allergic and respiratory diseases. It has been introduced as an important factor affecting the relationship between respiratory impairment and cardiovascular disease. Impaired respiratory function with systemic inflammation caused by some plasma proteins has been previously reported [2, 3]. The release of some mediators from mast cells in the smooth muscles of the respiratory pathways plays an important role in the pathogenesis of respiratory pathways over-response or narrowing of the bronchus in asthmatic patients [4].

Among the hormonal factors and inflammatory peptide mediators secreted by the endocrine organs, tumor necrosis factor alpha (TNF-α) is a cytokine with inflammatory features. TNF-α is secreted by some proinflammatory cells such as macrophages and mast cells. TNF-α is known as a cause of inflammatory responses and regulation of the immune system [5]. Increased secretion of tumor necrosis alpha is associated with increased clinical symptoms of asthma and inflammation of the respiratory pathways [6]. It is believed that TNF-α is involved in the lack of systematic inflammatory responses of respiratory pathways in asthmatic patients, because there are reports on the increased levels of this inflammatory protein or its over-expression in the respiratory pathways in asthmatic patients [7, 8].
Physical activity and chemotherapy lead to beneficial effects on physiological parameters in asthmatic patients [9]. Although there are limited studies on inflammatory mediator response to a variety of sports activities in asthmatic patients, there is not a general consensus on the cytokine response to physical activity in other healthy and diseased populations. The findings are somewhat contradictory and inconsistent. Some findings show the beneficial effects [10, 11], some reveal the lack of response [12], while some reported an increase in TNF-α level following physical activity [13]. Due to discrepancies in the previous findings as well as due to limited studies on asthmatic patients, the present study aimed to determine the effect of aerobic training on the levels of TNF-α as an inflammatory cytokine in asthmatic patients.

**METHOD AND SUBJECTS**

**Patients:** This study was aimed to determine the effect of three month aerobic training on serum TNF-α in asthma patients. Patients included twenty four non-trained men with mild to moderate asthma aged 35 – 45 years and height 171 – 178 cm that recruited through an accessible sampling in study and randomly divided into exercise (three months aerobic training) and control (no training) groups. The ethics approval was taken from Islamic Azad University of Iran ethical committee. Each participant received written and verbal explanations about the nature of the study before signing an informed consent form.

**Inclusion and exclusion criteria:** Asthma diagnosis and its severity were determined by FEV1/FVC. All patients were non-trained and non-smokers. All participants reported being weight stable (±1kg) for 6 months prior to the study and engaged in physical activity less than once per month. Potential participants were excluded from the study if they reported smoking or had a history of heart disease, stroke, diabetes and other chronic disease. In addition, exclusion criteria included inability to exercise and supplementations that alter carbohydrate-fat metabolism.

**Anthropometrics, Spirometrical and Biological Markers:** Body weight, height, waist circumference and body fat (%) measurements were obtained by standard methods. Body weight was measured in duplicate in the morning following a 12-h fast. Height of the barefoot subjects was measured to the nearest 0.1 cm. Body mass index (BMI) was calculated as weight (kg) divided by squared height (m).

Respiratory function was measured by spirometry. Subjects were asked to refrain from tea, coffee, chocolates and caffeinated soft-drinks on the day of recording 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.

Venous blood samples were also collected before and at the end of exercise program for analysis serum TNF-α by ELIZA method in two groups.

**Training protocol:** Exercise training program duration was three months for three times per week (3 days/wk). Exercise intensity was 60-80 (%) of maximal heart rate. Each session started by 15 min of flexibility exercises, 30-40 min of aerobic exercise and 5-10 min of cool down activity. Aerobic exercises in each session included walking on a treadmill with no slope. The intensity of the activity of any person was controlled using the Polar heart rate tester (made in the US). Anthropometrical and blood samples were repeated after exercise program.

**Statistical analysis**

All data were tested for normal distribution by the Kolmogorov-Smirnov test. Data were analyzed by computer using the Statistical Package for Social Sciences (SPSS) for Windows, version 11.5. For the nonparametric variables; the median, along with the minimum and maximum values, were expressed in the descriptive tables. The comparisons between the measurements of the parametric parameters were determined by paired and unpaired samples t test. A p value less than 0.05 was considered statistically significant.

**RESULTS**

In this study, effect of three month aerobic training on serum TNF-α was investigated. The Spirometrical characteristics of the patients are shown in Table 1. Baseline level of serum TNF-α and anthropometric and characteristics of the study participants in exercise and control group are shown in Table 2. Based on independent T test, no significant difference was observed in all anthropometrical markers between two groups at baseline (p ≥ 0.05). There were no statistically significant differences between the exercise and control groups with regard to the Spirometrical markers (P ≥ 0.05). Serum TNF-α was also similar between two groups at baseline (p = 0.84).
Baseline and post training serum TNF-α levels and anthropometrical indexes of two groups are shown in Table 2. Data of paired T test showed that aerobic training results in a significant decreased in serum TNF-α in exercise group (p = 0.001, Fig 1), but not in the control group (p = 0.63) (Table 2). Compared to pre-training, anthropometrical markers decreased significantly after exercise program (p ≤ 0.05) but were not changed in control group (p ≥ 0.05, see Table 2).

**DISCUSSION**

Despite confirming the beneficial effects of exercise on pulmonary function and physiological parameters, health researchers have paid much attention to the role of physical activity in addition to chemotherapy.
in the improvement or decline in immune system inflammation in obese subjects and related illnesses including asthma. The major finding of the present study is significant reduction in the serum levels of TNF-α in response to a three-month training program. In other words, three months of aerobic exercise significantly decreased the serum levels of TNF-α compared to baseline levels in men with asthma. This finding supports the anti-inflammatory characteristics of long-term aerobic exercise in asthmatic patients.

TNF-α is one of the most effective cytokines which is mainly secreted by activated macrophages. It is also secreted by some other tissues [14]. Regarding the mechanisms by which TNF-α affects asthma, the researchers have suggested that mast cell mediators are associated with bronchospasm. TNF-α as a cytokine or mast cells mediator plays a potential role in over-response of the respiratory pathways [15, 16]. This inflammatory cytokine directly accelerates the release of histamine from human mast cells and participates in a positive autocrine ring increasing the release of cytokines from mast cells [17]. It is likely that TNF-α is involved in the relationship between the mast cells and smooth muscles. This feature is particularly important in the prevalence of over-response of respiratory pathways. Some researchers believe that TNF-α is probably involved in the lack of a systematic inflammatory response of respiratory pathway in asthmatic patients. The increased levels of this inflammatory protein or its over-expression in respiratory pathways have been reported in asthmatic patients [7, 8]. Some studies have also concluded that the intranasal administration of TNF-α by normal people leads to over-response of the respiratory pathways as well as increased neutrophil levels in the respiratory pathways [17]. The use of TNF-α increases over-response of the respiratory pathways in asthmatic patients [18]. Although the mechanisms responsible for these responses are not yet fully known, these findings support the direct impact of TNF-α on the smooth muscles of the respiratory pathways [19]. Although the exact mechanisms of the relationship between asthma and obesity is still not fully understood, some studies have found a causal relationship between them [20]. It seems that the malfunction and obesity-related pulmonary mechanisms lead to increased resistance of the respiratory tract. In other words, asthma is an inflammatory disease and research findings suggest obesity as a factor increasing inflammatory symptoms [21]. Although all asthmatic patients in the present study were not obese individuals, some of them were overweight or had high levels of BMI. On the other hand, the training program led to reduced weight and body fat in these patients. Based on this evidence and some previous studies, a significant reduction in the serum levels of TNF-α is probably rooted in reduced body fat level following the training program, because the adipose tissue and macrophages are the main sources secreting this cytokine [5]. According to literature, if the training program is associated with a significantly weight loss, it will lead to improved inflammatory profile in the study population [22].

REFERENCES