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Moderate exercise test is not associated with recovery response of IL-1ß in smokers

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Key words: Smoking, exercise, interleukin-1 beta.

Abstract

Relationship between cigarette smoking and increased morbidity and mortality has already been reported in previous studies. Fifteen healthy untrained smoker males and fifteen non-smokers matched for age, gender, height, and BMI were recruited for this study by accessible sampling. Fasting blood samples were collected of all participants for measuring and comparing serum IL-1b between smoker and non-smokers at baseline. Then, all smokers were completed an exercise test for 35 min running on smooth surface without slope at 75% of maximal heart rate. Blood sampling were repeated immediately and 60 min after stopping the test in order to determine acute and recovery response of IL-1ß to exercise in smokers. Statistical analysis was performed using an independent paired t-test. At baseline there were no differences in the age, serum IL-1b, body weight and other anthropometrical indexes between the two groups. No significant differences were found in acute and recovery serum IL-1b by exercise test with compared to baseline in smokers. This study indicates that moderate exercise test is not associated with acute or recovery response of IL-1b in smoker men. Future studies should examine the potential role of short-term exercise systemic inflammation in this population.

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Introduction

Recent studies demonstrate that cardiovascular diseases contain a component of inflammation and have even been referred to as an inflammatory disease (Libby *et al.,* 2002; Ross, 1999). In addition, there is considerable evidence that some inflammation cytokines such as TNF-α and IL-1b play a important roles in the pathogenesis of inflammatory disorders, and recent studies have linked certain polymorphisms in TNF-a or IL-1b with altered risks of coronary artery disease (Francis *et al.,* 1999; Oda *et al.,* 2007; Sbarsi *et al.,* 2007).

It has been previously reported that cigarette smoking has been implicated in the activation of a complex inflammatory cascade resulting in the production of a variety of potent cytokines and chemokines, which in turn contribute to development of atherosclerotic plaques (Silvia *et al.,* 2011). Among cytokines, IL-1ß is a proinflammatory cytokine that plays important roles in inflammation. However, the role of this cytokine under physiological conditions is not fully understood. Review of research findings show that IL-1ß plays an important role in lipid metabolism by regulating insulin levels and lipase activity under physiological conditions (Matsuki *et al.,* 2003).

On the other hand, data from some recent observational studies indicate that smoking is associated with changes in the expression of cytokines (Hart *et al.,* 2008; Hou *et al.,* 2009) emphasizing that short-term exposure to cigarette smoke in vivo is sufficient to increase IL-1ß and/or TNF-a (Castro *et al.,* 2004; Barbieri *et al.,* 2007). In this area, Results from several investigations suggest that the levels of IL-1b and TNF-a in the serum of smoker subjects are elevated compared with non-smokers and that simultaneous inhibition of IL-1b and TNF-a-signalling pathways prevents smoking-induced endothelial dysfunction (Silvia *et al.,* 2011).

So that, most of researchers have focused on the inflammatory risk factors of smoking in recent years.

Meanwhile, the role of sport as an important factor in preventing or reducing smoking-related risk factors of systemic inflammation and vital organs has attracted health sciences researchers, though findings on cytokine response, particularly IL-1β are limited to the types of physical activity in smokers. However, findings regarding the response of inflammatory cytokine IL-1β to exercise are more or less contradictory in other healthy populations, so that some have reported the beneficial effects of exercise (Gomez-Merino *et al.*, 2007) and others have reported the lack of IL-1β response to exercise (Chida *et al.*, 2006).

On the other hand, recovery response of serum IL-1ß to short-time or one session exercise in smoker or other population has received limited attention. Therefore, this study aimed to assess recovery response of serum IL-1ß to one session moderate running test in smoker men.

Material and methods

Subjects

This study investigated the delayed circulating IL-1ß response (1 hour) to relatively prolonged running exercise in a group of smoker men. Fifteen healthy untrained smoker males and fifteen non-smokers matched for age, gender, height, and BMI were recruited for this study by accessible sampling. This semi-experimental study was conducted as part of ancillary study and was approved by Research Council and Ethics Committee of Islamic Azad University, Iran. After the nature of the study was explained in detail, informed consent was obtained from all participants.

Inclusion criteria

Inclusion criteria to study for smoker group were smoking history of At least 10 cigarettes a day for 5 years. Participants were non-athletes and non-alcoholics. Neither the control or diabetic subjects had participated in regular exercise for the preceding 6 months, nor did all subjects have stable body weight. Subjects were reported to be not currently taking supplements of any kind, and having no major

health problems (i.e., diabetes, cardiovascular disease, etc.).

Anthropometrical measurements

In first stage, all anthropometrical markers were measured in two group subjects. Anthropometric measurements (body height and weight, waist and hip circumference) were performed with the subjects wearing light underwear and without shoes. Abdominal circumference was measured in the most condensed part using a non-elastic cloth meter. Body weight was measured in duplicate in the morning following a 12-h fast. Body mass index (BMI) was calculated as weight (kg) divided by squared height (m).

Biochemical analysis and exercise test

Then, subjects were asked to attend Hematology Lab between the hours of 8 to 9 am. All blood samples were taken following an overnight 12-hour fast. Blood samples were obtained in order to measuring serum IL-1ß and its comparison between smoker and non-smoker groups. Blood samples were centrifuged for 10 minutes by 3000 rpm speed for serum separation. Serum IL-1ß 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. After blood sampling, all subjects of smoker group were completed a moderate intensity running test for 35 min on smooth surface without slope at 75% of maximal heart rate. Test conditions were the same for all subjects. Blood sampling were repeated immediately and 60 min after stopping the test in order to determine acute and recovery response of IL-1ß to exercise.

Statistical analysis

The statistical significance of divergences between the means in the two groups were evaluated using an independent sample T-test in the case of normal distribution of data sets, and using the Kolmogorov-Smirnov's test when at least in one of the data sets the normal distribution was excluded. Student's t-tests for paired samples were performed to determine significance of changes in variables by exercise test in smoker subjects. Significance was accepted at $P < 0.05$.

Results

Baseline anthropometric and metabolic characteristics of the study participants in the smoker and non-smoker groups are shown in Table 1. Data were expressed as individual values or the mean ± SD. Based on baseline data, significant differences were not found in all anthropometrical indexes such as body weight, body mass index and body fat percentage between two groups ($p \geq 0.05$). There were no significant differences in serum IL-1β level between smoker and non-smoker group at baseline ($p \geq 0.05$).

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

Variable	Age (years)	Height (cm)	Weight (kg)	Abdominal circumference (cm)	BF (%)	BMI (kg/m2)	Serum IL-1B (pg/ml)
Smoker	35 (5.3)	176 (7.2)	92 (6.7)	97 (6.8)	28.9 (3.11)	29.7 (3.3)	6.71 (2.3)
Non-smoker	34 (4.6)	174 (6.3)	91 (5.9)	96 (5.9)	29.1 (3.9)	30.1 (2.7)	6.38 (2.1)

Abbreviations: BMI, body mass index; AC, BF, Body fat percentage SD, standard deviation.

Data of serum IL-1β after exercise test showed that serum level of IL-1β did not change immediately post-exercise (from 6.71 ± 2.3 to 6.3 ± 1.8 pg/ml, $p > 0.05$). On the other hand, we observed no acute response in serum IL-1β after exercise. In addition, serum level of IL-1β remained without change at 60 min of recovery compared to pre-exercise (from 6.71 ± 2.3 to 5.9 ± 2.1 pg/ml, $p > 0.05$) (Fig. 1).

Discussion

In present study, we measured serum interleukin1 beta at baseline, immediately prost-exercise (acute

response) and 60 min recovery (recovery response) after a relatively moderate exercise in healthy adult smoker males. Main finding of this study was no significant change in serum level of this inflammation cytokine at acute or recovery response compared to baseline.

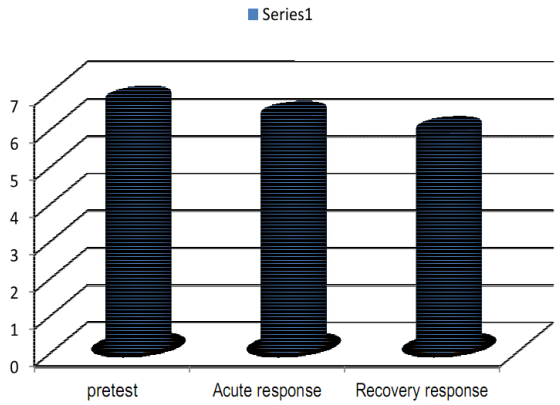

Fig.1. The changes pattern of serum IL-1ß in immediately post-exercise and 60 min of recovery compared to pre-exercise. The results showed that serum IL-1ß did not change immediately post-exercise and 60 min of recovery of exercise test in smoker men.

Interleukin-1 is known as a potent inflammatory cytokine that was discovered in the 1970s and was first described as lymphocyte-activating factor or leukocytic pyrogen (Gery *et al.,* 1972; Gery *et al.,* 1972). IL-1β is the best-studied cytokine of the IL-1 family (Krause *et al.,* 2012). It is also important to note 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). Although macrophages are the primary source of IL-1, but epidermal, epithelial, lymphoid and vascular tissues also synthesize IL-1. IL-1beta production and secretion have also been reported from pancreatic islets (Maedler *et al.,* 2009).

IL-1β, Apart from its physiologic role in host protection, is known to be important in a number of severe inflammatory diseases including the rare cryopyrin-associated periodic syndromes (CAPS) and other hereditary and polygenic autoinflammatory diseases and some previous studies have indicated most of these diseases can be completely controlled by anti-IL-1β treatment (Goldbach-Mansky *et al.,* 2006; Ozen *et al.,* 2011).

Despite extensive studies on the effects of smoking on cytokines and adipokines, the specific mechanisms responsible for these observations are less understood. Among them, most previous studies have noted higher circulating serum IL-1β in smoker than non-smoker subjects (Arnson *et al.,* 2010). Lack significant difference in serum CRP between smoker and non-smoker in present study is somewhat controversial, although its baseline levels were far higher in both studied smokers and non-smokers compared with healthy non-smokers reported in previous studies. However, the findings of this study are somewhat controversial and undermine many previous studies.

Because, Cigarette smoke was shown to increase the secretion of numerous pro-inflammatory cytokines such as TNF-alpha, IL-1, IL-6, IL-8 GM-CSF and to decrease the levels of anti-inflammatory cytokines such as IL-10 (Arnson *et al.,* 2010). In a previous study showed that In both smokers and non-smokers, secreted levels of IL-1beta increased from 0 to 5 min of in vitro smoke exposure with levels in smokers higher than in non-smokers (Ryder *et al.,* 2002). It has been previously reported that blocking IL-1 or TNF-a receptors protects against acute smoke-mediated increases in inflammatory cells present in bronchial lavage fluid (Churg *et al.,* 2009).

So far, several studies aiming at studying the response of inflammatory cytokines to exercise were carried out in healthy populations, patients, athletes, and non-athletes that have resulted in different answers, depending on the type of subjects or sportive protocols. Some have noted decrease (Gomez-Merino *et al.*, 2007), increase (Rowsey *et al.*, 2009), or no change (Chida *et al.*, 2006, Eizadi *et al.*, 2011) in the cytokine response to exercise. But among them, few studies existed regarding immediate or delayed response of IL-1β to single session exercise in smokers. It seems that the present study with the mentioned objectives is the first one in this area on smokers.

Regarding the impact of single session exercise on the level of IL-1β, running an exercise session has increased serum levels of IL-1β in obese mice (Martin-Cordero *et al.*, 2009), while the findings of this study showed that single session exercise as moderately severe running for 35 minutes is not associated with significant immediate or delayed response of IL-1β in smokers. Other studies have also reported increased levels of IL-1β immediately after exercise, although its levels was declined to baseline after 24 hours of recovery (Moldoveanu *et al.*, 2000). According to these findings, it can be concluded that a sportive activity with mentioned specifications has not anti-inflammatory effects on IL-1β levels in male smokers.

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