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Serum interleukin-1beta and lipid profile responses to aerobic training in obese men

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Abstract

Obesity is known to be associated with systemic inflammation. To investigate serum IL-1B and lipid profile responses to aerobic exercise program. A total thirty four sedentary adult obese men aged 38-43 years were selected to participate in study and divided to exercise and control group by randomly. The participants of exercise group were completed an aerobic exercise program for 3 months (3 days/weekly) and control group were banned of exercise in this period. Pre and post exercise training of serum IL-1β, lipid profile markers and anthropometrical indexes were measured in two groups. Statistical analysis was performed by independent and paired T test ($p \leq 0.05$). No significant differences were found in anthropometrical and biochemical parameters between 2 groups at baseline. Despite of a significant decrease in all anthropometrical parameters, but serum IL-1β concentration did not change significantly after aerobic program when compared to baseline data. Triglyceride concentration was decreased significantly with exercise training whereas concentrations of TC, HDL cholesterol, and LDL cholesterol did not change. Based on these data, it seems that if aerobic exercise does not improve lipid profile blood lipid levels in obese subjects it does not cause any change in the levels IL-1B an inflammatory cytokine.

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Introduction

According to the population studies, it has been indicated that aging is associated with an increase in the chronic systemic inflammation (Grimble, 2003). On the other hand, obesity induces chronic inflammation and, thus, may further contribute to the age-related increase in the production of inflammatory cytokines (Trayhurn *et al.,* 2004; Charles *et al.,* 2008). Additionally, it is reported that obese persons have increased levels of intramuscular cytokines (Saghizadeh *et al.,* 1996). Among them, Interleukin-1 beta, proinflammatory cytokine, plays important roles in inflammation (Matsuki *et al.,* 2003). However, the role of this cytokine under physiological conditions has not drawn much attention. It was found 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). It has been previously reported a positive association between IL-1β gene polymorphism and obesity, suggesting functional effects on fat mass, fat metabolism and body mass (Manica-Cattani *et al.,* 2010). It has been demonstrated that this inflammation cytokine plays an important role in lipid metabolism by regulating insulin levels and lipase activity under physiological conditions (Matsuki *et al.,* 2003). In this area, a recent study reported that Serum IL-1β is significantly higher in obese men when compared with none-obese subjects (Eizadi *et al.,* 2011).

Regular physical activity is known as a non-pharmacological treatment of metabolic disorders and based on the "anti-inflammatory" effects of exercise, it has been also proposed for improving the "chronic low-grade inflammation" in obesity and related diseases. The mechanisms by which physical inactivity might influence IL-1β are unclear. Recently, several reports have identified exercise-induced reductions (Larsen *et al.,* 2001; LeMaitre *et al.,* 2004) or unchanged levels (Nicklas *et al.,* 2004; White et al., 2006) of plasma/serum inflammatory cytokines. It was observed that the single bout of acute exercise increased the release of IL-1β by the LPS-stimulated macrophages from obese rats, in both sedentary and trained animals, but these researchers have pointed out that this cytokine did not change by exercise training for long time (Martin-Cordero *et al.,* 2009). Recent epidemiological studies and clinical interventions have reported contradictory findings related to dietary or exercise interventions and the resulting alterations in serum cytokines. In this study, we aimed to evaluate serum IL-1β and lipid profile responses to aerobic exercise training in sedentary obese men.

Material and methods

The Study Protocol was approved by the Ethics Committee of Islamic Azad University, Islamshahr Branch. Subjects were thirty four sedentary obese men matched for age (38-43 year) and BMI (30-33 kg/m^2) that participated in the study by voluntarily. Participants were divided into exercise and control groups by randomly. Informed consent was obtained from each subject after full explanation of the purpose, nature and risk of all procedures used. Participants were included if they had not been involved in regular physical activity/diet in the previous 6 months. Exclusion criteria for the study group were: Diagnosed type 2 diabetes, having history of known hyperlipidemia, hypertension, coronary artery disease, cerebrovascular disease, and peripheral artery disease, using medicine or hormone preparations that affect the carbohydrate and lipid metabolism.

Pre and post exercise training blood sampling and anthropometrical measurements were performed of all participants.

All anthropometric measurements were made by the same trained general physician and under the supervision of the same pediatrician following standard protocols. The weight and height of the participants were measured by the same person when the participant had thin clothes on and was wearing no shoes by using the standard hospital

scales. Waist circumference (WC) was measured with a non-elastic tape at a point midway between the lower border of the rib cage and the iliac crest at the end of normal expiration. Also, Waist to hip circumference ratio (WHO) was calculated through dividing the abdominal circumference by hip circumference. BMI was calculated as weight (in kilograms) divided by the square of height (in meters). Body composition monitor (BF508-Omron made in Finland) with a precision error of less than 100 g was used to measure body fat percentage and visceral fat of the subjects.

The subjects were advised to avoid any physical activity or exercise 48 hours before the blood sampling. Blood samples were taken following an overnight 12-hour fast. Blood samples were obtained in order to measuring serum IL-1β, Triglyceride (TG), total cholesterol (TC), HDL-cholesterol and LDL- cholesterol in each subject. 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.
Triglyceride, total cholesterol, HDL-cholesterol was measured directly with enzymatic methods (Randox direct kits) using Kobas Mira auto-analyzer made in Germany.

The participants of exercise group were completed an aerobic exercise program for 3 months (3 days/weekly) and control group were banned of exercise in this period. Exercise training program lasted 3 months (3 days/wk) 60 to 80 percent of maximum 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 and stationary cycling. Initially, subjects exercised at low intensity and the intensity of exercise was gradually increased to 80% of peak heart rate in next sessions. The intensity of the activity of any person was controlled using the Polar heart rate tester (made in the US).

Statistical analysis

All values are given as mean and standard deviation. We used the SPSS for Windows software (version 15:00; SPSS) for statistical analysis. After assessment of the normal distribution by the Kolmogorov-Smirnov test, Independent t-test was used to compare the means of variables between two groups. Comparisons within groups were performed by paired Student's t test. The differences between the groups were considered to be significant at a p-value of ≤ 0.05.

Results

Anthropometric and metabolic characteristics of the study participants' of two groups are shown in Table 1. All values are given as mean and standard deviation. The analysis of baseline data (pre-test) showed no differences in the age, body weight and other anthropometrical indexes between the two groups. Also, No significant difference in serum IL-1β or lipid profile (TG, TC, HDL, LDL) were found between the exercise and control at baseline. With aerobic exercise training, subjects in exercise group lost fat mass seen as a decrease in percent body fat, Body weight, BMI and visceral fat ($p < 0.05$). Waist circumference was reduced in the exercise subjects, but not in control subjects ($p = 0.021$). Serum IL-1β did not change significantly after aerobic program when compared to baseline values ($p = 0.213$). Serum TG levels were significantly decreased in response to aerobic exercise program when compared with baseline levels in exercise group ($P = 0.023$). Despite the decrease in triglyceride, other markers of lipid profile such as TC, HDL cholesterol and LDL cholesterol did not change by exercise program in exercise group ($p \geq 0.05$). All variables in control group remained without change.

Table 1. Mean and standard deviation of anthropometrical and biochemical variables in baseline and after intervention.

Variables	Exercise group		Control group	
	Pretest	post-test	Pretest	post-test
Age (years)	40 ± 3	40 ± 3	39 ± 4	39 ± 4
Weight (kg)	100 ± 11.5	94.5 ± 10.3	101 ± 9.8	102 ± 10.3
Height (cm)	177.5 ± 9.6	177.5 ± 9.6	176.3 ± 6.5	176.3 ± 6.5
Abdominal circumference (cm)	108 ± 12.3	102 ± 9.6	107 ± 7.9	108 ± 8.2
Hip circumference (cm)	107 ± 9.5	103 ± 9.8	108 ± 11.3	108.3 ± 9.2
Abdominal to hip ratio	1.01 ± 0.21	0.99 ± 0.11	1.01 ± 0.23	1 ± 0.19
Body fat (%)	33.2 ± 5.3	28.1 ± 6.2	32.7 ± 3.2	32.9 ± 5.3
Body mass index (kg/m²)	31.74 ± 3.2	30 ± 4.3	32.49 ± 2.4	32.8 ± 3.3
Visceral fat	14.3 ± 3.2	12.2 ± 3.3	14.5 ± 4.2	14.6 ± 3.2
TG (mg/dl)	167 ± 33	116 ± 32	171 ± 29	175 ± 41
TC (mg/dl)	183 ± 41	188 ± 33	187 ± 33	181 ± 29
LDL (mg/dl)	111 ± 23	118 ± 31	116 ± 29	121 ± 33
HDL (mg/dl)	42.6 ± 6.8	44.2 ± 5.6	43.1 ± 4.3	43.3 ± 5.3
Serum IL-1β (pg/ml)	2.63 ± 0.53	2.78 ± 0.41	2.68 ± 0.36	2.71 ± 0.41

Discussion

Our study findings showed that aerobic exercise program for three months resulted in decrease in body weight, body mass index and fat mass in exercise subjects. Main finding of present study was no significant change in serum IL-1β by exercise program compared to baseline values. On the other hand, there was no change in total cholesterol, HDL and LDL cholesterol in exercise group at the end of the 3-month exercise program. Regarding these findings, Fasting triglyceride concentration decreased significantly in response to aerobic program.

It is also important to note that proinflammatory cytokines can cause insulin resistance in adipose tissue, skeletal muscle and liver by inhibiting insulin signal transduction. A significant body of research has demonstrated that the diseases related to metabolic syndrome are characterized by abnormal cytokine production, including elevated circulating IL-1β , increased acute phase proteins CRP (Koenig *et al.,* 2006) and activation of inflammatory signaling pathways (Wellen *et al.,* 2005).

In recent years, it has been demonstrated that expression of IL-1β is increased in adipose tissue of both obese rodents and humans (Juge-Aubry *et al.,* 2004). Accumulating evidence suggests a positive association between IL-1β and obesity, suggesting functional effects on fat mass, fat metabolism and body mass (Manica-Cattani *et al.,* 2010). However, whereas the involvement of other cytokines in obesity and related diseases is well documented, the potential role of IL-1β in the alteration of insulin signaling and metabolic effects is poorly documented. Interleukin-1Beta gene, part of a cluster of genes on chromosome 2 coding for a family of IL-1 proteins, has been shown to be an important modulator of inflammatory pathways, with potential involvement in the pathogenesis cardiovascular diseases (Maruyama *et al.,* 2003). Considering to the findings of previous studies on the role of IL-1B gene on adipose tissue regulation, investigators have explored potential interrelationships between obesity, IL-1β genotype (Um *et al.,* 2009; Markovic *et al.,* 2004). IL-1*β* expression is shown to be increased in islets from type 2 diabetic patients (Böni-Schnetzler *et al.,* 2008). It has been previously reported that IL-1*β* plays an important role in lipid metabolism by regulating insulin levels and lipase activity under physiological conditions (Matsuki *et al.,* 2003).

In present study, we observed that aerobic exercise program for long time could nit improve serum IL-

1β in non-trained obese men. But this exercise protocol resulted in significant decrease in anthropometrical indexes such as body weight and body fat percentage in studied subject. Of course, the mechanisms controlling inflammatory cytokines by various exercise modes are still not completely elucidated. Our results were supported by other authors. In the light of these observations, some researchers have pointed out that this cytokine did not change by exercise training for long time (Martin-Cordero *et al.,* 2009). The finding of another study showed that 12 weeks of moderate endurance increased IL-1β in eight healthy subjects (Baum *et al.,* 1999).

Serum levels of IL-1 β remaining unchanged after prolonged aerobic exercise is observed in the present study while the training program was associated with significant reduction in anthropometric indices. Moreover, in response to this exercise protocol the fasting levels none of the lipid profile markers except TG was affected. Other words the exercise program led to no significant change in TC - LDL and HDL in the subjects. Given the close relationship between levels of IL-1 β and the parameters of lipid profiles reported in some previous studies, it is possible that insignificant change of IL-1 β in response to aerobic exercise is due to he lipid profiles of the subjects remaining unchanged. On the other hand, it has been suggested that not only does adipose tissue release cytokines, but also skeletal muscles express cytokines that have direct autocrine and paracrine effects (Saghizadeh *et al.,* 1996). In this area, some previous study suggested that obese persons have increased levels of intramuscular cytokines (Saghizadeh *et al.,* 1996). Considering to the findings of previous studies, it is important to make a note here that exercise training may induce local anti-inflammatory effects in skeletal muscle that may not be reflected in the systemic circulation (Gielen *et al.,* 2003). To support this hypothesis, some researchers have pointed out that aerobic training for long time reduced TNF-α, IL-6, and IL-1 gene expression in skeletal muscles but had no effect on levels of these cytokines in the systemic circulation (Gielen *et al.,* 2003). The finding of a recent study showed that exercise training improves inflammation cytokines markers in muscle of elderly subjects (Greiwe *et al.,* 2001). In another study, regarding increased VO2peak in response to 6 months exercise training in patients with chronic heart failure, but serum levels of IL-1β and other cytokines such as TNF-α and Il-6 remained without change, whereas exercise training significantly reduced the local expression of TNF-α, IL-1β and IL-6 in the skeletal muscle of these patients (Gielen *et al.,* 2003).

Lack of a control group (normal weight group) is one of the limitations of this study. It is possible that baseline levels of inflammatory cytokines in the obese subjects, are not significantly different from the respective values in people with normal weight and that is why they have not been affected by the exercise protocol.

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