Journal of Biodiversity and Environmental Sciences (JBES)
ISSN: 2220-6663 (Print) 2222-3045 (Online)
Vol. 4, No. 2, p. 165-170, 2014
http://www.innspub.net

RESEARCH PAPER OPEN ACCESS

Effect of individualized weight loss program on fasting Interleukin 6 levels in obese adult subjects

Eizadi Mojtaba*, Samarikhalaj Hamidreza, Kiani Fatemeh, Dooaly Hossein

Department of Physical Education and Sport Sciences, Saveh Branch, Islamic Azad University, Saveh, Iran

Article published on February 08, 2014

Key words: IL-6, Obesity, Exercise, Body weight.

Abstract

Inflammation is hypothesized to play a central role in obesity and its related diseases; although the molecular mechanisms for this are less understood. Twenty-four healthy adult obese men were enrolled for this study through local advertising. The objective of study was to investigation of serum interleukin-6 response to long term exercise training in mentioned subjects that divided to exercise or control group. Subjects in exercise group were completed three months aerobic training and control subject did not participate in exercise program. Pre and post training of anthropometrical markers and fasting serum IL-6 were measured in two groups. Paired samples T test was used to determine significant difference between per and post values. Serum IL-6 levels were significantly increased in exercise group (from 2.77±0.24 to 3.36±0.41 pg/ml $p<0.0001$) and did not change in control group. All anthropometrical markers decreased after exercise program in exercise group ($p \leq 0.05$). In conclusion, serum IL-6 response to exercise training is appears to be independent of weight status.

***Corresponding Author:** Eizadi Mojtaba ✉ izadimojtaba2006@yahoo.com

Introduction

Throughout life numerous factors affect the body weight and fat mass. Some of these factors are caused by the body's internal mechanisms and others are a function of environmental conditions. In the meantime, in addition to genetics hormonal factors in particular, hormones affecting energy homeostasis, energy balance, fat and carbohydrate metabolism and daily physical activity levels are of particular importance in the phenomenon of obesity or the amount of subcutaneous fat in human. The role of inflammatory and anti-inflammatory cytokines mainly secreted from adipose tissue should not be overlooked. Among inflammatory cytokines, IL-6 is identified as an inflammatory cytokine (Ferrucci *et al.*, 2005). Concentration of plasma TNF-alpha and IL-6 is significantly higher in obese people than in people with normal weight (Ying *et al.*, 2008). Numerous studies support increased IL-6 in individuals with insulin resistance syndrome (Pickup *et al.*, 1997; Grau *et al.*, 1996). It is known that high plasma concentrations of IL-6 are associated with decreased muscle mass or reduced muscle mobility (Ferrucci *et al.*, 1999; Visser *et al.*, 2002). Increase in IL-6 strongly predicts mortality and deteriorated function in the elderly (Reuben *et al.*, 2002). Increase in IL-6 is associated with increased rate of skeletal muscle catabolism (Charles *et al.*, 2008). In human and animal models injected IL-6 increases gluconeogenesis and thereby increases blood glucose (Hyperglycemia) and ultimately increases blood insulin (Hyperinsulinemia) (Stith, 1994). Similar metabolic responses have also been observed after subcutaneous injection of IL-6 in humans (Tsigos *et al.*, 1997). Epidemiological evidence indicates the role of increased IL-6 as an inflammatory marker in pathogenesis of chronic heart failure (Rauchhaus *et al.*, 2000; Larsen *et al.*, 2002). IL-6 can have an inhibitory effect on the activity of T regulatory cells (Pasare *et al.*, 2003).

Scientific studies suggest that the combination of exercise and reduced calorie intake associated with weight loss decreases IL-6 mRNA (Brown *et al.*, 2000). Also a 6-month weight loss program in the form of diet and exercise by Momzolio (2003) on obese patients reduced the levels of plasma IL-6 in conjunction with reduced insulin resistance and BMI (Monzillo *et al.*, 2003). On the other hand, some studies suggest that exercise has anti-inflammatory effects at circulating levels (Gielen *et al.*, 2003). These researchers found that aerobic exercise reduced expression of IL-6 and other inflammatory cytokines in skeletal muscles but not at their systemic levels (Gielen *et al.*, 2003). Given the contradictory findings in this field, this study aims to evaluate the effect of an aerobic training program on serum levels of IL-6 in obese men.

Method and subjects

This research was sponsored by the Islamic Azad University with the general aim studying the response of IL-6 inflammatory cytokines to the short and long-term aerobic exercise in obese men. The study was conducted on obese men aged 30 to 45 years with a BMI greater than 30 kg/m. The sampling method was convenience sampling, as the sample includes 30 male obese adults, who are later randomly placed in two groups; control group (three months without participating in any exercise program) and experimental group (participating in a three-month training program) after measurement of anthropometric indices.

The subjects are non-smokers and have no history of controlled diet nor have they participated in regular physical activity during at least in the last 6 months. Apart from obesity, all participants are in good health, and those with a history of chronic diseases such as cancer, respiratory or gastrointestinal disease and diabetes and other metabolic and motor disorders are barred from participation in the study. Not having participated in regular exercise and diet for at least 6 months of represent the inclusion criteria.

First, body composition and body composition

parameters such as weight, body mass index, body fat percent, waist and hip circumference were measured. All the subjects appeared in hematology lab in fasting state and blood samples were taken from them to measure and compare baseline values of the intended variables between experimental and control groups. The experimental group then participated in a three-month training program including 3 sessions of 40 to 60 minutes per week. Every training session starts with proper warm-up (10 to 15 minutes). The main program mostly includes running on a fixed surface, on the treadmill and exercise on a stationary bike with the intensity of 60 to 80 percent of maximum heart rate and a proper cool-down at the end. Intensity in the first sessions is at the minimum and the intensity gradually increases. Through this three-month program the control group had no physical activity in excess of their daily activities. Finally, two days after the end of the third phase (the three months of training), subjects in the experimental and control groups attended the lab again in fasting state and blood samples were taken in the same manner as the previous stage.

Data analysis

Statistical analysis was used by Independent t-test was used to compare all variables at baseline and paired sample Test for determine significant values between pre and post training in exercise group as well as control groups.

Results

Anthropometrical characteristics of the participants at baseline are presented in Table 1. All values are given as mean and standard deviation.

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

Variables	Exercise group baseline	Control group baseline
Age (year)	35.33 ± 3.1	36.3 ± 4.1
Height (cm)	176.7 ± 4.4	175.6 ± 3.6
Weight (kg)	101 ± 13.6	102 ± 9.8
Abdominal circumference (cm)	108 ± 9.6	109 ± 7.7
Hip circumference (cm)	107 ± 8	109 ± 6.9
WHO	1.01 ± 0.02	1.01 ± 0.11
Body mass index (kg/m^2)	32.34 ± 3.3	33.08 ± 3.1
Body Fat (%)	31.78 ± 3.12	31.22 ± 4.1

Significant differences were not found in body weight, body mass index, body fat percentage and other anthropometrical markers between two groups at baseline ($p \geq 0.05$).

Table 2. Significant values in anthropometrical and serum IL-6 between pre and post training in exercise group. Data by Paired samples Test.

		Paired Differences				t	Sig. (2-tailed)
		Mean	Std. Deviation	95% Confidence Interval of the Difference Lower	Upper		
Pair 1	Weight (post) - Weigh (post)	4.29167	4.72161	1.29170	7.29163	3.149	.009
Pair 2	Abdominal (pre) - Abdominal (pos	4.41667	3.60450	2.12648	6.70686	4.245	.001
Pair 3	Hip (pre) - Hip post	2.91667	1.97523	1.66167	4.17166	5.115	.000
Pair 4	WHO (pre) - WHO post	.01500	.02111	.00159	.02841	2.462	.032
Pair 5	BMI (pre) - BMI (post)	1.33333	1.72328	.23841	2.42825	2.680	.021
Pair 6	%fat 9pre) - %Fat (post)	3.40000	3.17862	1.38040	5.41960	3.705	.003
Pair 7	IL-6 (pretest) - IL-6 (post test)	-10.717	15.600	-20.628	-.805	-2.38	.037

Interleukin 6 levels in the control and exercise group's subjects were same at baseline (8.63 ± 2.74 in exercise versus 9.11 ± 2.1 in control, pg/ml. $p \geq 0.05$). Aerobic exercise program resulted significant increase in serum IL-6 in exercise group when compared to baseline ($p = 0.037$, Fig 1). In contrast, body weight, body mass index and other anthropometrical markers decreased significantly by exercise training in exercise group ($p \geq 0.05$). Table 2 shows significant values in anthropometrical and serum IL-6 between pre and post training in exercise group.

Discussion

Although some recent studies support the reduction of serum or plasma levels after prolonged exercise, in this study, three months of aerobic exercise led to a significant increase in serum levels of this inflammatory cytokine. Increased IL-6 in response to the training program was observed while body weight and body fat percentage significantly decreased. However, Kern *et al* report a significant increase of IL-6 mRNA along with increased levels of adipose tissue and its subsequent reduction following weight loss (Kern *et al*., 1995).

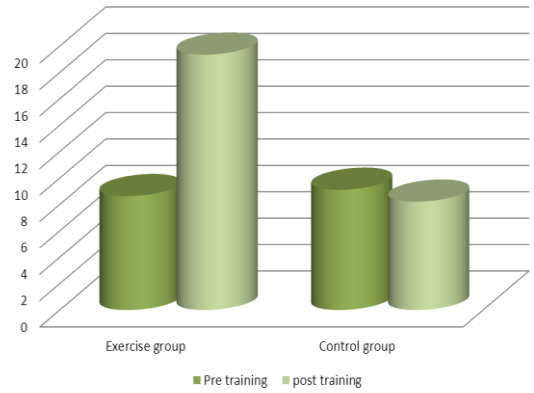

Fig. 1. The changes pattern of serum IL-6 at baseline and by exercise program interventions in two groups.

Also in a recent study regular physical activity involving 5 times a week for 8 weeks significantly increased IL-6 in diabetic and non-diabetic rats (Bonyadi *et al*., 2009). The effect of exercise on IL-6 depends on intensity and duration of exercise and muscle volume (Pedersen *et al*., 2001). IL-6 produced by muscle contraction is increased in short intense exercise (Luheshi *et al*., 1999; Moldoveanu *et al*., 2000).

However, in a recent study, despite a significant reduction in body weight due to 12 weeks of exercise on obese subjects, no significant change was observed in the serum levels of IL-6 (De Luis *et al*., 2007). However, according to their findings in another study, researchers found that aerobic exercise reduced expression IL-6 in skeletal muscles but not at their systemic levels (Gielen *et al*., 2003).

In another study consisting of 6 months of exercise training 4 to 6 cycling bouts of 10 minutes carried out during the day, although it did not change significantly the levels of systemic IL-6 or TNF-α or IL-1b it significantly decreased the levels of these inflammatory markers in their skeletal muscles. There is also the possibility that the response of IL-6 as an inflammatory cytokine to 3 months of exercise in obese subjects in the present study also follows this pattern. Moreover, in another study, Peterson *et al.* citing their findings concluded that increased levels IL-6 due to muscular activity seems to have anti-inflammatory effects (Pedersen, 2006). In this context, researchers argue that the reason why some of the pre-inflammatory cytokines do not change substantially through the exercise shows that those cytokines that are significantly changed by exercise are different from cytokines that are changed by infection(Pedersen, 2006).

Unlike some of the said findings, this study showed that three months of aerobic exercise significantly increased serum levels of IL-6. Confirming the findings of this study, the literature states that IL-6 significantly increases in the absence of post-exercise muscle damage (Pedersen *et al*., 2003; Febbraio *et al*., 2002). Scientific sources have also revealed that the concentration IL-6 increases in response to exercise extensively appropriate to the intensity and duration of exercise and the muscle mass involved (Pedersen *et al*., 2000; Pedersen *et al*.,

2003; Febbraio *et al*., 2002) Another scientific source reports that even moderate-intensity exercise significantly impact secretion of IL-6 from active muscles (Fischer *et al*., 2004; Pedersen *et al*., 2004).These data point out that IL-6 has an inhibitory effect on TNF-α and IL-1b during exercise (Fischer *et al*., 2004; Pedersen *et al*., 2004).

References

Bonyadi M, Badalzadeh R, Mohammadi M, Poozesh S, Salehi I. 2009. The effect of regular training on plasma cytokines response in healthy and diabetic rats. Saudi Medical Journal **30(11),** 1390-4.

Brown M, Sinacore DR, Binder EF, Kohrt WM. 2000. Physical and performance measures for the identification of mild to moderate frailty. Journals of Gerontology Series A: Biological Sciences and Medical Sciences **55,** 350–355.

Charles P, Lambert, Nicole R, Wright, Brian N, Finck, Dennis T, Villareal. 2008. Exercise but not diet-induced weight loss decreases skeletal muscle inflammatory gene expression in frail obese elderly persons. Journal of Applied Physiology **105,** 473–478.

De Luis DA, Aller R, Izaola O, Gonzalez Sagrado M, Bellioo D, Conde R. 2007. Effects of a low-fat versus a low-carbohydrate diet on adipocytokines in obese adults. Hormone Research **67(6),** 296-300.

Febbraio MA, Pedersen BK. 2002. Muscle-derived interleukin-6: mechanisms for activation and possible biological roles. Federation of American Societies for Experimental Biology **16,** 1335-1347.

Ferrucci L, Harris TB, Guralnik JM, Tracy RP, CortiMC, Cohen HJ. 1999. Serum IL-6 level and the development of disability in older persons (see comments). Journal of the American Geriatrics Society **47,** 639–646

Ferrucci L, Penninx BW, Volpato S, Harris TB, Bandeen-Roche K, Balfour J. 2002. Change in muscle strength explains accelerated decline of physical function in older women with high interleukin-6 serum levels. Journal of the American Geriatrics Society **50,** 1947–1954.

Fischer CP, Hiscock N, Basu S. 2004. Supplementation with vitamins C and E inhibits the release of interleukin-6 from contracting human skeletal muscle. Journal of Physiology **558,** 633-645.

Gielen S, Adams V, Mobius-Winkler S, Linke A, Erbs S, Yu J, Kempf W. 2003. Anti-inflammatory effects of exercise training in the skeletal muscle of patients with chronic heart failure. Journal of the American College of Cardiology **42,** 861–868.

Grau AJ, Buggle F, Becher H, Werle E, HackeW. 1996. The association of leukocyte count, fibrinogen and C- reactive protein with vascular risk factors and ischemic vascular diseases. Thrombosis Research **82,** 245-55.

Kern PA, Saghizadeh M, Ong JM. 1995. The expression of tumor necrosis factor in human adipose tissue. Regulation by obesity, weight loss, and relationship to lipoprotein lipase. Journal of Clinical Investigation **95,** 2111-19.

Larsen AI, Lindal S, Aukrust P, Toft I, Aarsland T, Dickstein K. 2002. Effect of exercise training on skeletal muscle fibre characteristics in men with chronic heart failure. Correlation between skeletal muscle alterations, cytokines and exercise capacity, International Journal of Cardiology **83(1),** 25-32.

Luheshi GN, Gardner JD, Rushforth DA, Loudon AS, Rothwell NJ. 1999. Leptin actions on food intake and body temperature are mediated by IL-1. Proceedings of the National Academy of Sciences of the United States **96,** 7047-7052.

Moldoveanu AI, Shephard RJ, Shek PN. 2000. Exercise elevates plasma levels but not gene expression of IL-1beta, IL-6, and TNF-alpha in blood mononuclear cells. Journal of Physiology **89,** 1499-1504.

Monzillo LU, Hamdy O, Horton ES, Ledbury S, Mullooly C. 2003. Effect of lifestyle modification on adipokine levels in obese subjects with insulin resistance. Obesity Research **11(9),** 1048-54.

Pasare C. and Medzhitov R. 2003. Toll pathway-dependent blockade of CD4+CD25+ T cell-mediated suppression by dendritic cells. Science **299,** 1033-1036.

Pedersen BK, Hoffman-Goetz L. 2000. Exercise and the immune system: regulation, integration and adaption. Physiological Reviews **80,** 1055-1081.

Pedersen BK, Steensberg A, Fischer C. 2003. Searching for the exercise factor - is IL-6 a candidate. Journal of Muscle Research and Cell Motility **24,** 113-119.

Pedersen BK, Steensberg A, Schjerling P. 2001. Muscle- derived interleukin-6: possible biological effects. Journal of Physiology **536,** 329-337.

Pedersen BK. 2006. The anti-inflammatory effect of exercise: its role in diabetes and cardiovascular disease control. Essays in Biochemistry **42,** 105–117.

Pedersen M, Steensberg A, Keller C. 2004. Does the aging skeletal muscle maintain its endocrine function? Exercise Immunology Review **10,** 42-55.

Pickup JC, Mattock MB, Chusney GD, Burt D. 1997. NIDDMas a disease of the innate immune system: association of acute-phase reactants and interleukin-6 with metabolic syndrome X. Diabetologia **40,** 1286-92.

Rauchhaus M, Doehner W, Francis DP. 2000. Plasma cytokine parameters and mortality in patients with chronic heart failure, Circulation **102(25),** 3060–67.

Reuben DB, Cheh AI, Harris TB, Ferrucci L, Rowe JW, Tracy RP, Seeman TE. 2002. Peripheral blood markers of inflammation predict mortality and functional decline in high-functioning community-dwelling older persons. Journal of the American Geriatrics Society **50,** 638–644.

Stith R. 1994. Endocrine and carbohydrate responses to interleukin-6 in vivo. Circulatory Shock **44,** 210-15.

Tsigos C, Papanicolaou DA, Kyrou I, Defensor R, Mitsiadis CS, Chrousos GP. 1997. Dose-dependent effects of recombinant human interleukin-6 on glucose regulation. Journal of Clinical Endocrinology & Metabolism **82,** 4167- 70.

Visser M, Pahor M, Taaffe DR, Goodpaster BH, Simonsick EM, Newman AB. 2002. Relationship of interleukin-6 and tumor necrosis factor-alpha with muscle mass and muscle strength in elderly men and women: the Health ABC Study. Journals of Gerontology Series A: Biological Sciences and Medical Sciences **57,** 326–332.

Ying BW, Song XB, Fan H, Wang LL, Li YS, Cheng Z. 2008. Plasma ghrelin levels and weight loss in Chinese Uygur patients with chronic obstructive pulmonary disease. Journal of International Medical Research **36(6),** 1371-7.