

# COMPARISON THE EFFECT OF ONE SESSION SUBMAXIMAL EXERCISE ON PLASMA LEVELS OF IL6 AND TNF- A IN OBESE AND NON-OBESE WOMEN

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## Abstract

**BACKGROUND:** Cytokines are a group of low-molecular-weight regulatory proteins that produced by cells in response to stimulation. In fact, they increase in response to immune system during exercise. Also, many cytokines such as IL-6 and TNF $\alpha$  are secreted from adipose tissue in obese people. So the aim of this study was to investigate the effect of one session submaximal exercise on plasma levels of IL6 and TNF $\alpha$  in obese and non-obese women.

**METHODS:** Sixteen healthy women aged 20-30 years old participated in the study. Subjects were classified into obese (n = 8) and nonobese (n = 8) groups who performed submaximal exercise program (50-65% HRM) for 30 minutes. Blood samples were taken for cytokines measurement, before and after exercise. Data were analyzed with SPSS15. The effect of exercise on mentioned variables was evaluated using t-test and covariance test.

**RESULTS:** Level of IL-6 increased significantly in two studied groups after 30 minutes submaximal exercise (P < 0.05). Levels of TNF $\alpha$  increased significantly in obese subjects but not in non-obese subjects. There were no significant changes in the levels of IL-6 and TNF $\alpha$  after 30 minutes submaximal exercise between two studied groups (P > 0.05).

**CONCLUSION:** After submaximal exercise, plasma level of IL6 and TNF $\alpha$  may increase and adipose tissue is the main source of circulating IL6 and TNF $\alpha$ .

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**Keywords:** Submaximal Exercise, IL6, TNF $\alpha$ , Obese, Women.

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## Introduction

Cytokines are a group of low-molecular-weight regulatory proteins in the body that secreted by leucocytes and a variety of other cells such as the vascular endothelium in response to a number of inducing stimulus.<sup>1,2</sup>

They are classified in different groups, including; the interleukins (IL), tumor necrosis factors (TNFs), interferon, growth factors, colony stimulating factors (CSFs), and cell adhesion molecules.

Each family of cytokines contributes to species aspects of acute inflammation. Cytokines may be further characterized as either Pro- or anti-inflammatory, based loosely on their predominant action. At the onset of inflammation there is an up-regulation of the pro inflammatory cytokines.<sup>2</sup>

Proinflammatory cytokines (signaling proteins of immune cells), such as TNF $\alpha$  and IL-6, have a pivotal role in coordinating the body's response to inflammation.<sup>3</sup> TNF $\alpha$  effectively induces a local inflammatory response and helps to control infections.<sup>1</sup> IL-6 causes lymphocyte activation and antibody production. IL-6 and TNF $\alpha$ , along with IL-1, synergistically control infection by regulating the production of acute-phase proteins and by raising body temperature.<sup>1-4</sup>

It should be attention; another component of the immune system response to exercise is cytokines.<sup>5, 6</sup> Cytokines serve in a network to help regulate signaling of innate and specific immune responses. Traditionally, cytokine responses to exercise, in particular IL-6 and TNF $\alpha$ , have been interpreted as

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an immune mediated host defense.<sup>6</sup> Plasma-IL-6 increases with exercise that is related to exercise intensity, duration, the mass of muscle recruited, and one's endurance capacity.<sup>1</sup>

Recent studies clearly demonstrated that muscle contractions without any muscle damage induce a marked elevation in plasma IL-6.<sup>1-3</sup> Most studies have reported that exercise does not induce an increase in plasma levels of TNF $\alpha$  and it seems that exercise induces a very strong anti-inflammatory cytokine response, with the appearance of IL-6 in the circulation being by far the most marked and its appearance preceding that of other cytokines.<sup>1</sup>

On the other hand, many cytokines are secreted from adipose tissue in obese people.<sup>1-7</sup> There is much evidence that suggest cytokines can modulate metabolism and it should be attention, body adipose tissue may account for about 20-30% of IL-6 concentration during basal conditions that can be regulated by physical activity. In fact exercise may play an important role on adipose tissue.<sup>7-10,14</sup>

So, the aim of this study was to investigate the effect of one session submaximal exercise on plasma levels of IL6 and TNF $\alpha$  in obese and non-obese women, however this proposal hasn't been investigated in former issues.

### Materials and Methods

This semi-experimental study conducted in Khorasgan Azad University. Sixteen healthy women aged 20-30 years old participated in the study. Subjects were classified into obese (n = 8) and non-obese (n = 8) group. Obesity was defined as having 35 < body fat percent < 45 and normalweight was 23 < body fat percent < 25.

**Risk stratification;** A risk stratification form about participants' medical history, family history of disease, height and weight and current medications was completed by all subjects following initial informed consent. It should be notice, that weight, waist to hip ratio(WHR), Body Mass Index(BMI) and body fat percent were measured with Body Composition Analyzer 3.0 (Biospace Company, Korea).

In addition, Fasting Blood Sugar, Total Serum Cholesterol, Low-density Lipoprotein, Cholesterol, and High-density Lipoprotein were measured and all subjects were reported to be non-smoker.

Subjects arrived in the laboratory after an overnight fast to participate in the study. They were instructed to abstain from alcohol, caffeine, and strenuous exercise for 24h prior to testing.

Blood samples were taken 15 minutes prior exercise program and immediately after it.

At the beginning, subjects rested on the chair and blood samples (pre-exercise) were drawn from antecubital vein. Then they began exercise program and heart rate were continuously monitored throughout the exercise.

**Exercise program;** Initially, subjects warm-up for ten minute by performing stretching, jogging and training. After that, they running on the treadmill with 50-65% of maximal heart rate (age-220) for 20 min and then at the end of exercise program, subjects performed cool down by walking and stretching training for 10 min.

**Cytokines measurement;** For cytokines measurement (Interleukin-6 and TNF $\alpha$ ), 5-ml blood was drawn into a glass tube and were centrifuged at the room temperature, separated and frozen at -70c and stored until subsequent analysis. IL-6 and TNF $\alpha$  were analyzed by commercially available enzyme linked immunosorbent assay (ELISA kits, Bender systems, Australia).

At the end of the program all data were collected and analyzed with SPSS15 and the effects of exercise training were evaluated. For comparing the mean of variables outcome between two groups covariance test was used.

### Results

We studied sixteen healthy women between 20-30 years old. At baseline mean and standard deviation of some physical and metabolic characteristics such as weight, fat percent, WHR and BMI of all subjects are described in table 1.

Table 2 illustrates the changes of variables in

**Table 1.** Basline physical and metabolic characteristics of studied population in obese and non-obese groups

	Obese group	Non-obese group
Weight (Kg)	54.7 ± 91.0	56.23 ± 4.37
Fat percentage	43.70 ± 3.09	33.82 ± 2.46
BMI ( kg/m <sup>2</sup> )	34.39 ± 1.5	24.06 ± 1.52
WHR	1.0 ± 0.02	0.94 ± 0.04

**Table 2.** Mean and standard deviation of variables in obese and non-obese groups before and after 30 minutes submaximal exercise

Variable	Group	Mean $\pm$ SD		T	Sig
		Pre test	Post test		
Interlukin 6 ((pg/ml))	Obese	2.75 $\pm$ 0.56	0.53 $\pm$ 3.45	2.73	0.02
	Non obese	3.17 $\pm$ 0.53	3.58 $\pm$ 0.48	2.39	0.04
TNF $\alpha$ (pg/ml)	Obese	5.87 $\pm$ 0.60	7.53 $\pm$ 1.24	3.98	0.005
	Non obese	6.08 $\pm$ 1.15	6.90 $\pm$ 1.68	1.02	0.34

response to exercise in both groups using t-test.

The level of IL-6 increases significantly in two groups after 30 minutes submaximal exercise. The level of TNF $\alpha$  increased significantly in obese subjects but not in non-obese ones.

Also, in comparing two groups with covariance test, there were no significant changes in levels of IL-6 and TNF $\alpha$  after 30 minutes sub maximal exercise (Table 3).

### Discussion

This study provided information about increases of plasma concentration of IL6 in both obese and non-obese women after the 30 minutes submaximal exercise. These results are in agreement with several investigations. Timmons et al. demonstrated an increase in serum level of IL6 among young adult men after 60 minutes strenuous exercise and concluded that the level of increase in IL6 after exercise is typically dependant on the intensity of exercise.<sup>6</sup> Also Peterson et al. suggested that moderate exercise has major effects on muscle-derived IL-6 and it increases the level of plasma-IL-6.<sup>1</sup>

In addition, Cosio-Lima et al. reported an increase in the level of IL6 in old non diabetic and young health groups after submaximal incremental treadmill test. It should be noted that release of plasma IL6 is related to exercise intensity, duration, the mass of involved skeletal muscle and endurance capacity of individuals.<sup>11</sup>

Furthermore, You et al. mentioned that strenuous acute exercise often increases cytokine production (IL6 and TNF $\alpha$ ) due to muscle tissue injury.<sup>8,9</sup>

Fischer et al. suggested that obesity was associated

with elevated magnitude of IL6 that is similar with the findings of our study.<sup>7</sup> Peterson and colleagues indicated that IL-6 stimulates lipolysis as well as fat oxidation.

Another factors which investigated in our study, were TNF $\alpha$ . In our data, TNF $\alpha$  significantly increased in obesity group but not in normal group during the study.

Brian et al. revealed that TNF $\alpha$  level didn't change after exercise in men which is in line with our results.<sup>6</sup>

This result maybe for the reason that TNF $\alpha$  generally increases only with high intensity, long duration exercise that engage a large muscle mass. On the other hand, some studies indicated physiological concentrations of IL-6 inhibit the production of the proinflammatory cytokine TNF $\alpha$ .<sup>1</sup>

Another studies suggested that production of TNF $\alpha$  enhanced after exercise task that is likely to be related to an inflammatory response to exercise.<sup>4-11</sup> The physiological mechanism of IL6 and TNF $\alpha$  elevation in response to exercise has not been fully revealed. Several similarities exist between high intensity exercises and immune reactions inflammatory processes such as mobilization and action of leukocytes, induction of acute phase response, increases in proinflammatory cytokine production, cellular infiltration and tissue damage.<sup>4</sup>

The results indicated that in response to submaximal exercise, plasma IL6 increases from basal level, mainly due to a major release of contracting skeletal muscle.<sup>4</sup> On the other hand, exercise induced muscle injury has been attended to be primary stimulus for the IL6 response. Recent studies suggest that exercised muscle stimulates with complex intra

**Table 3.** Comparing obese and non-obese groups after 30 minutes submaximal exercise using covariance test

Variable	Mean square	F	P
Interlukin 6 (pg/ml)	0.005	0.02	0.88
TNF $\alpha$ ((pg/ml))	0.782	0.333	0.57

muscular signaling and release IL6, independently of muscle damage. Subsequently, muscle damage per se induces a repair response, including macrophage entrance into the muscle, causing further IL6 production. This injury persuaded IL6 response is delayed and smaller than the IL6 production related to muscle contraction.<sup>8-12</sup>

On the other hand, obesity is associated with a number of metabolic complications including changes in the plasma lipid profile, such as increase in free fatty acids that consequently result in the activation of proinflammatory genes.<sup>8-14</sup>

It should be noted, under normal physiological conditions, proinflammatory cytokines induce lipolysis after acute aerobic exercise. As adipose tissue is a serious organ that produces and exudes proinflammatory cytokines and their soluble receptors and lipolysis occurs in adipose tissue, it is reasonable to consider that the loss of body fat with exercise could be one method that links changes in inflammation and lipolysis.<sup>8, 9, 13</sup>

In sum, we concluded that after submaximal exercise, plasma level of IL6 and TNF $\alpha$  may increase that could be in response to muscle injury after continuous contractions or adipose tissue. That adipose tissue is a significant source of circulating IL6 and TNF $\alpha$  and these cytokines and their receptors are highly revealed in individual with more fat.

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### Conflict of Interests

Authors have no conflict of interests.

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