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Anti-inflammatory effects of exercise training on Tumor necrosis factor-alpha in obese women

Mona Sarhadi[1*], Ali Khorjahani[1], Zabihallah Naghiloo[1], Ghanbari Shahpour[2]

[1]*Department of Physical Education and Sport Sciences, Takestan Branch, Islamic Azad University, Takestan, Iran*

[2]*Department of Physical Education and Sport Sciences, Saveh Branch, Islamic Azad University, Saveh, Iran*

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Abstract

In this study, In order to investigate whether 6 weeks aerobic training can lead to improve inflammation profile in obese men. Thirty healthy adult obese women ($30 \leq$ BMI ≤ 36) divided into exercise or control group by randomly. Aerobic exercise program lasted 6 weeks (3 times weekly). Pre and post training of blood samples were obtained of each participant of two groups after a overnight between 8:00 and 9:00 a.m. Measurements of anthropometry parameters were also performed before and the end of aerobic program. Student's t-tests for paired samples were performed to determine whether there were signigcant within-group changes in the outcomes. Aerobic training program resulted in significant decrease in weight, BMI, body fat percentage and serum TNF-a in exercise group but these markers remained without change in control group. These findings highlight the importance of anti-inflammatory property of exercise training particularly after weight loss in obese subjects.

***Corresponding Author:** Mona Sarhadi ✉ monasarhadi@yahoo.com

Introduction

Recent research indicates that abnormal levels a number of macrophage/ monocytes-derived cytokines such as Tumor necrosis factor (TNF-α) mediate a number of metabolic changes that are known as acute phase reactions (Parsa *et al.,* 2007). Tumor necrosis factor (TNF-α) is a member of a group of cytokines and is a cytokine involved in systemic inflammation that stimulate the acute phase reaction (Nadia *et al.,* 2012).

On the other hand, it has been widely accepted that obesity is now considered as a state of low grade chronic inflammation and is associated with an increasing prevalence the most common metabolic disorder in the world (Miyazaki, 2003; Tzanavari *et al.,* 2010). It is now clearly established that the production of TNF alpha, is noticeably enhanced in Obesity (Hotamisligil *et al.,* 1994). This inflammatory cytokine is a pleiotropic cytokine with diverse functions and occurs in many pathological diseases like cancer, cardiovascular disease or type II diabetes (Simona *et al.,* 2005).

These authors indicate a statistical significant association between elevated serum cytokine levels (especially TNF-alpha) and as well as exercise intolerance (Gielen *et al.,* 2003). Studies on healthy young population have assessed the interaction between TNF-α as an inflammatory markers, physical activity or cardiorespiratory fitness and fatness (Kelly *et al.,* 2004; Williams *et al.,* 2005; Ruiz *et al.,* 2007; Halle *et al.,* 2004; Platat *et al.,* 2006; Eizadi *et al.,* 2011).

It has been widely noted that exercise training improves the inflammatory profile in chronic disorder or obese pupulation by inhibition of cytokine-chemokine production, regulation of monocyte activation and adhesion, inhibition of inflammatory cell-growth signals and growth factor production (Adamopoulos *et al.,* 2002). Despite numerous studies regarding the effect of prolonged exercise on circulating cytokines such as TNF-α on obese and some chronic diseases with conflict findings (LeMaitre *et al.,* 2004; Xu *et al.,* 2002), few studies have prospectively examined the effect of acute exercise on this cytokine. On the other hand, it has been previously reported that the role of fatness in relation to fitness and inflammatory pathways may be especially prominent in women (Hamer, 2007). But, more Studies about TNF-α or the other cytokines in short or long term exercise training was performed on men and there are limited studies in this area on women. Therefore, this study was aimed to evaluate effect of single bout cycling test on this cytokine in healthy adult obese women.

Material and methods

Aim and subjects

The objective of this study was to evaluate effect of an aerobic exercise program (6 weeks, 3 times weekly) on serum TNF-α in adult obese women. For this purpose, thirty healthy adult obese women matched for age (38 ± 5 years of old) and BMI (30 ≤ BMI ≤ 36) participated in this study and divided into exercise or control group by randomly. All participants gave their informed written consent before participation in accordance with the ethical guidelines set by Islamic Azad University.

Inclusion and exclusion criteria

All subjects had a body mass index (BMI) of between 30 – 36 kg/m2. Participants were non-athletes and non-alcoholics. Participants had no evidence of coronary artery disease; tobacco use; participation in exercise/diet programs; or use of systemic steroids, diabetes treatments. We also excluded people who had any self reported physician diagnosed chronic disease (arthritis, stroke, hypertension, cancer, heart attack, chronic cough, or bronchitis). Neither the control nor experimental subjects had participated in regular exercise for the preceding 6 months, nor did all subjects have stable body weight.

Anthropometrical and blood pressure measurement

All anthropometric measurements were made by the same trained general physician and under the supervision of the same pediatrician following standard protocols. Body weight, height, waist circumference, % body fat and blood pressure measurements were obtained by standard methods as described elsewhere (21 of 356). Percentage of body fat was estimated by bioelectrical impedance method (Omron Body Fat Analyzer, Finland). Body weight was measured in duplicate in the morning following a 12-h fast. Obesity was measured by body mass index (BMI). Body mass index was measured for each individual by division of body weight (kg) by height (m2). Waist and hip circumferences were measured at the level of umbilicus and of trochanter major, respectively. Waist to hip circumference ratio was measured by dividing the abdominal circumference into that of the hip. All anthropometrical measurements were performed before and after exercise program 48 h following the last session exercise and under fasted condition in the morning.

Blood sampling and exercise program

Aerobic exercise program in exercise group lasted 6 weeks (3 times weekly) at intensity between 60-80% of maximal heart rate. Each session started by 5-10 min warm up, 30-45 min of aerobic exercise and 5–10 min of cool down activity. Aerobic exercises in each session included walking on a treadmill. The first sessions, subjects exercised at low intensity and the intensity of exercise was gradually increased in next sessions. In this 6-week period, control subjects were instructed to maintain their habitual activities. Resting blood samples were drawn at weeks 0 and 6 (48 hours after lasted exercise session). Venous blood samples were obtained at rest between 8:00 and 9:00 am from the antecubital vein. Blood was drawn after 12 h of fasting and 1 day of minimal physical activity. Blood was collected in test tubes containing EDTA, separated by centrifugation, frozen, and stored −80 °C until biochemical analysis was performed. Serum TNF-α was determined by ELISA method (Enzyme-linked Immunosorbent Assay for quantitative detection of human TNF-α total). The Intra-assay coefficient of variation and sensitivity of the method were 6% and 5.0 pg/mL for TNF-α.

Statistical analysis

All values are given as mean and standard deviation. Statistic analysis was done with SPSS 15.0 for Windows. After assessment of the normal distribution by the Kolmogorov-Smirnov test, within group changes were compared by the paired t-test for those variables. Also, Independent t-test was used to compare the means of variables between two groups at baseline. P value of <0.05 was accepted as significant.

Results

Baseline and post training of anthropometric and biochemical features of the study groups are shown in Table. Data were expressed as individual values or the mean ± SD for groups. At baseline there were no differences in the age, body weight and other anthropometrical indexes between the two groups. Based on data of independent method, we did not difference in serum TNF-α between two groups a baseline.

After exercise program, Anthropometrics markers such as body weight ($p = 0.000$), BMI ($p = 0.000$), body fat percentage ($p = 0.000$) and abdominal circumference ($p = 0.001$) decreased significantly in exercise group but not to control group when compared to baseline. Despite these changes, hip circumference ($p = 0.222$), visceral fat ($p = 0.163$) and abdominal/hip ratio ($p = 0.329$) did not change with exercise training in exercise group. Furthermore we observed a significant reduction in serum TNF-α after exercise intervention program ($p = 0.041$).

Discussion

Key findings of our study were that decreased significantly in serum TNF-a in response to exercise program in obese women. Obesity is known to be accompained with a chronic inflammatory response characterised by abnormal cytokine production and is associated with increased synthesis of acute-phase reactants and activation of inflammatory signaling pathways (Moschen *et al.,* 2010).

Table 1. Baseline and post training anthropometrical and clinical characteristics of two groups.

Variables	Control group		Exercise group	
	Pretest	post-test	Pretest	post-test
Age (year)	36.8 ± 6.5	36.8 ± 6.5	37.6 ± 5.4	37.6 ± 5.4
Height (cm)	161.4 ± 5.8	161.4 ± 5.8	160.7 ± 5.9	160.7 ± 5.9
Weight (kg)	83.02 ± 7.3	83.9 ± 6.5	82.01 ± 7.9	80.9 ± 8.6
Abdominal circumference (cm)	110.7 ± 9.8	111 ± 7.9	109.6 ± 8.6	108.7 ± 8.5
Hip circumference (cm)	114.2 ± 10.3	114.9 ± 11.5	113.4 ± 7.5	107.5±24
BMI (kg/m2)	31.87 ± 2.7	32.21 ± 3.2	31.78 ± 2.61	31.36 ± 2.89
Body fat (%)	44.8 ± 6.1	45.1 ± 4.3	45.26 ± 4.22	44.56 ± 4.06
Serum TNF-α (pg/dl)	36.5 ± 7.21	37.6 ± 6.3	35.29 ± 9.22	31.59 ± 7.14

According to the population studies, it has been indicated that inflammatory cytokine levels is increased in obese subject. It has been widely noted that adipose tissue and some other organs secretes a variety of bioactive mediators including adipocytokines such as adiponectin, leptin, resistin or classical cytokines such as the pro-inflammatory mediators tumour necrosis factor a (TNFa) and interleukin 6 (IL-6) (Hotamisligil, 2006; Tilg *et al.,* 2006). It is generally accepted that pro-inflammatory cytokines such as TNFa is produced by human adipose tissue dependent on the degree of obesity. This inflammatory cytokine produced by macrophages in response to inflammation, endotoxemia and cancer (Zahorska Markiewicz *et al.,* 2000) and plays a key role in the pathogenesis of peripheral insulin resistance in Obesity (Rajarajesyari et al., 2011). Recent evidence has shown that TNF is produced predominantly by activated macrophages and T lymphocytes as a 26 kDa protein, pro-TNF, which is expressed on the plasma membrane, where it can be cleaved in the extracellular domain by the matrix metalloproteinase (Bradley, 2008).

Although it is widely accepted that Diet-induced weight loss can be reduced levels of circulating cytokines, and the effect is greater with larger amounts of weight loss (Bastard *et al.,* 2000; Dandona *et al.,* 1998; Kopp *et al.,* 2005), the results regarding the effect of exercise training is limited.

A large body of evidence suggests that 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. While some but not all recent studies found 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; Charles *et al.,* 2008).

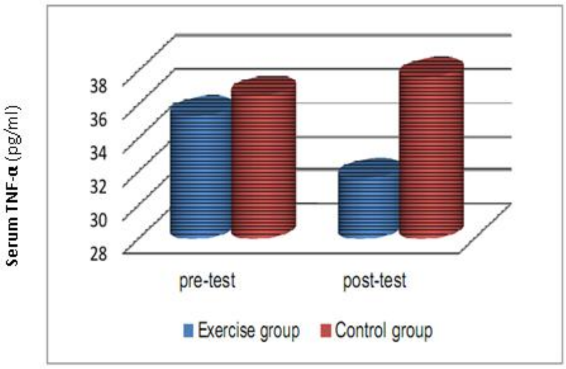

Fig. 1. Serum TNF-α before and after exercise program in two groups. Aerobic training program resulted in significant decrease in TNF-α in exercise group but not in control group.

These authors noted that aerobic training 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 (Greiwe *et al.,* 2001; Charles *et al.,* 2008). In support of the above findings, results of our study indicate that 6 weeks aerobic exercise improves circulating TNF-α levels. These data is provided by previous worker (Greiwe *et al.,* 2001). It is important to make a note here that decreased serum TNF-a was associated with reduced anthropometrical markers such body weight, body fad percentage and BMI. Therefore, According to our findings and based on some previous study, improved serum TNF-a Can be attributed to weight reduction or decreased fat percentage. Contrary to these results, some previous investigations indicated no changes in cytokines even in the presence of weight loss (Bruun *et al.,* 2006; Mingrone *et al.,* 2002).

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