

Research paper

The Effect of Running Exercise on Some Novel Atherosclerosis Risk Factors in Middle Aged Men

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Abstract

Background: Resistin, fibrinogen, C-reactive protein (CRP) are three novel cardiovascular risk factors. The aim of this study was to evaluate the effects of an eight-week aerobic exercise program on concentrations of these factors in overweight and healthy middle-aged men.

Methods: Thirty inactive middle-aged men with BMI between 25 and 30 were randomly assigned into experimental and control groups (each group=15 participants). Participants of the experimental group did eight-week (three sessions per week) aerobic exercise with intensity of 50-70% of their maximum heart rate. Body fat percentage, weight, fibrinogen, CRP and resistin levels of participants were recorded before and after training. Obtained data were analyzed using independent sample t-test.

Results: After training, the results showed a significant reduction of weight ($P=0/000$), BMI ($P=0/000$), body fat percentage ($P=0/002$), fibrinogen ($P=0/000$) and CRP ($P=0/000$) as well as a significant elevation of resistin ($P=0/000$) in experimental group ($P\leq 0.05$).

Conclusion: Overall, eight-week regular aerobic training declined atherosclerosis risk through reduction of weight, body fat, fibrinogen and CRP.

Key-Words: Exercise, Weight loss, Fibrinogen, C-reactive protein, Resistin.

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Introduction

Low-mobility lifestyle is a problem encountering both developing and developed countries. One of the side effects of this problem is increased burden of cardiovascular diseases and premature mortality (1). The 10-15-year epidemiological studies have demonstrated that inflammation and its cellular and molecular mechanisms play an important role in atherogenic processes. The C-reactive protein (CRP), fibrinogen and resistin are three important inflammatory markers, leading to tissue damage and infection in addition to atherosclerosis development (2, 3). The CRP develops atherosclerosis through following mechanisms: 1) activating endothelial cells for the gene expression of adhesive molecules 2) binding to the phospholipids of damaged cells and increasing the consumption of these cells by macrophages, and 3) decreasing the gene expression of endothelial nitric oxide synthase. Fibrinogen plays an important role in the platelet aggregation, endothelial injury, clot formation processes, blood viscosity and red blood cells aggregation (2). Resistin impairs glucose and lipid metabolisms, stimulates proinflammatory cytokines and elevates lipid deposition in vessels via increasing the gene CD36 expression in macrophages and forming foam cells in vascular walls (3).

Church et al. (2002) studied the relationship between CRP and cardio respiratory fitness and found that these two variables were negatively related (4). Jones et al. (2010) evaluated the effect of eight-month aerobic exercise on the level of resistin and other risk factors in overweight teenagers and reported reduction of resistin after exercise (5). Kushnick et al. (2003) have shown that 12-month power exercise does not significantly change level of fibrinogen, triglyceride (TG) and total cholesterol (TC) in male and female students (6). Considering high prevalence of atherosclerosis in Iranian middle-aged men and importance of fibrinogen, CRP and resistin in pathogenesis of atherosclerosis, the purpose of this study was to evaluate the effect of eight-week aerobic exercise program on the level of the above-mentioned factors in overweight male non-athletes.

Materials and Methods

The participants of this applied study were 30 healthy, sedentary and overweight ($25 < \text{BMI} < 30$) middle-aged men divided randomly into two control (N=15) and experimental (N=15) groups. The training program consisting of eight-week aerobic training (three sessions per week) was conducted on participants with 50-70% maximum heart rate. The maximum heart rate of each subject was measured using the formula of 220 minus age (7). Using Heart Rate Control (Polar), the heart rate of the participants was controlled. Each session included ten-minute warm-up with joint rotations as well as jumping and stretching movements. Each training session consisted of 10-minute warm-up, 10-25-minute running exercise and 10-minute cool down.

Before and after training, the body fat percentage as well as fibrinogen, resistin and CRP levels of participants were measured. The body fat percentage of the participants was measured using the Jackson and Pollock's skinfold thickness formula (8). In the beginning of training, before taking blood from participants, it was recommended them to avoid doing any intense physical activity, eating and smoking for 12 hours before training. They were allowed to drink water. Blood samples were taken from left brachial veins of the participants, placed in the tubes containing sodium citrate and sent to the laboratory for analysis. Fibrinogen level was measured using a special kit (Sigma Chemical Co, USA). Moreover, serum resistin was measured using Human Resistin Elisa Kit (Ray Bio Human) and Sandwich Elisa method. The enhanced immunoturbidimetric method was applied to measure CRP. The used kit was made by Iranian Pars Azmoun Company (9, 10).

Kolmogorov-Smirnov test was used to measure normal distribution of data. Paired sample t-test was utilized to compare intragroup results, and independent sample t-test was used to assess intergroup results in SPSS 22.

Results

The participants were homogeneous in terms of age, height, weight, BMI and body fat percentage (See Table 1). The results of paired t-test indicated that in experimental group, the weight, BMI and body fat percentage reduced significantly ($P \leq 0/05$). In addition, the amount of CRP and fibrinogen of plasma showed a significant reduction while the amount of serum resistin had significant elevation ($P \leq 0/05$). None of the said variables in the control group showed a significant change ($P > 0/05$) (Table 2). There were significant differences between groups in all dependent variables ($P \leq 0/05$) (Table 2).

Tables

Table 1- Descriptive and anthropometric characteristics of groups and their differences

Variables	Exercise Group	Control Group	P-Value
Age (y)	45/73 ± 7/08	46/13 ± 1/51	0/87
Height (m)	1/74 ± 0/05	1/74 ± 0/05	0/93
Weight (kg)	84/78 ± 6/46	82/78 ± 6/62	0/41
BMI (kg/m^2)	27/85 ± 1/89	27/2 ± 1/2	0/27
BFP (%)	18/33 ± 2/51	18/88 ± 2/96	0/59

BFP: Body Fat Percent

Table 2- Changes of dependent variables in response to two-month aerobic training

Variables	Exercise Group			Control Group			P value [#]
	Pre-test	Post test	P-value [*]	Pre-test	Post test	P-value [*]	
Weight (kg)	84/78±6/46	83/77±6/49	0/000	82/78±6/62	82/91±6/68	0/14	0/000
BMI (kg/m^2)	27/85±1/89	27/52±1/85	0/000	27/2±1/2	27/24±1/21	0/15	0/000
BFP (%)	18/33±2/51	17/87±2/43	0/000	18/88±2/96	18/94±2/91	0/63	0/002
hsCRP (mg/l)	2/54±0/41	2/21±0/33	0/000	2/2±0/4	2/2±0/39	0/47	0/000
Fibrinogen (mg/dl)	334/06±28/81	310/33±26/26	0/000	328/4±29/18	329/93±28/7	0/12	0/000
Resistin (pg/ml)	6/08±0/48	8/47±0/72	0/000	6/28±0/42	6/26±0/42	0/13	0/000

* P-value based on paired samples T-test

P-value based on independent samples T-test (differences of groups based on post-test minus pre-test)

Discussion

The results of the study showed a significant reduction in plasma fibrinogen level in the experimental group after doing aerobic training. Ghanbari-Niaki et al. (2015) demonstrated that circuit resistance training might cause fibrinogen and plasma viscosity reduction (11). Laswati et al. (2018) have shown that low-intensity resistance training has no effects on CRP and fibrinogen (12). Mongirdien et al. (2015) noted that long-term physical activity might reduce fibrinogen level in chronic heart failure patients (13).

Previous studies have suggested that the age and gender of participants as well as type and duration of training are effective in the response of fibrinogen to regular training. Several mechanisms can explain the reduction of fibrinogen in participants of the current study. Regular aerobic training can decline fibrinogen concentration in blood by reducing catecholamine stimulation, increasing blood flow in muscles and enhancing volume of blood. The reduction of body fat percentage, observing in participants can decrease interleukin-6 (IL-6) produced in fat tissue as well as since IL-6 is a fibrinogen synthesis, its reduction results in a reduction of fibrinogen (14, 15). Totally, eating too much fat causes inflammation in the body, stimulating blood fibrinogen to increase. Hence, the decrease of fat (observed in the participants of the present study) can decline inflammatory processes in addition to fibrinogen concentration in blood (14, 15). In the ongoing study, the amount of serum CRP in experimental group indicated a significant reduction. Costello et al. (2018) have demonstrated that chronic training has no effects on IL6 and CRP in active men (16). A study reveals that the Pilates training decreases CRP concentrations in elderly individuals (17). Tangvarasittichai et al. (2009) have reported that eight-week moderate intensity training diminishes CRP level in patients with type 2 diabetes (18). In another study, Lakka et al. (2005) evaluated the effect of physical training on CRP level

in sedentary and healthy men and women. The results revealed a significant reduction in CRP level (19). Heffernan et al. (2009) studied cardio inflammatory response to resistance training among white and black men. They suggested that there was a significant decrease in CRP level of black men (20).

Obesity leads to chronic inflammation, and the discharge of pre-inflammatory cytokines from the adipose tissue enhances with weight gain including tumor necrosis factor-alpha (TNF- α) and its soluble receptors (TNFR2, TNFR1), IL-6 and leptin. These cytokines make liver cells discharge CRP (21). Some leptin receptors resemble cytokine ones, especially IL-6, which is receptor of gp120 family. By activating Janus Kinases, mitogen-activated protein kinase (MAPK), nuclear factor kappa (NF- κ) and p38, Leptin has pre-inflammatory effects. Hence, an enhancement of leptin increases CRP (22). In the current study, the leptin level was not determined, but other studies suggested that aerobic training declined leptin level leading to reduction of CRP (23).

The resistin level of the participants of the present study showed a significant increase at the end of the experiment. Wu et al. (2016) have reported that eight-week (five days per week) running training has no effect on resistin concentrations in elderly obese rats (24). Khanna et al. (2015) have shown that eleven-week (four days per week) circuit resistance training has no effects on resistin level of sedentary obese women (25). In another study, Shafiee et al. (2017) concluded that eight-week aerobic training and concurrent training had no effects on resistin level in obese women (26). Liu et al. (2017) declared that training might decline resistin level in impaired glucose tolerance patients (27).

The mechanisms of increased resistin in participants of the ongoing study were not exactly clear while a review of the conducted studies suggested a few possible mechanisms. Proinflammatory cytokines including TNF- α , IL-6 and interleukin-1 (IL-1) stimulate resistin gene expression in mononuclear cells of blood, and although there are inconsistent results about the effect of regular training on TNF- α level, the resistin increase can be attributed to these cytokines. Since resistin is directly linked to adiponectin, then the increase of adiponectin elevation according to exercise can enhance resistin (28,29). Resistin is also directly related to insulin like growth factor binding protein-I (IGFBP-I). In the current study, the most important mechanism indicating increased resistin after aerobic training was the role of this hormone in the anti-oxidant defense of the body for the resistin was negatively correlated with nitrotyrosine (NT). One of the important regulators of inflammation in the body is reactive nitrogen species are among important. Nitric oxide (NO) as a vascular substance discharged by endothelial cells produces peroxynitrite (ONOO-) in response to superoxide anion radical. Peroxynitrite as nitrating oxidant can oxidize many biomolecules. The NT generated in the tyrosine oxidation process is directly associated with the oxidant stress and is an index of oxidant damage owing to ONOO-. In response to inflammatory

stimulant, resistin acts as an antioxidant as well as a meaningful interaction has been discovered between polymorphism of a single nucleotide in the promoter of human resistin gene with an oxidant marker and insulin resistance. In blood, mononuclear cells generate resistin in response to low-grade inflammation, which can have antioxidant properties. Bo et al. (2005) found no significant relationship between CRP and NT, representing there was a complicated interaction between oxidant and inflammatory markers (30). Therefore, the reduced CRP and increased resistin in participants of the present study could be the result of the anti-inflammatory and anti-oxidant compatibility.

Overall, eight-week regular aerobic training decreases atherosclerosis risk through reduction of weight, body fat, fibrinogen and CRP as well as the resistin elevation after training may improve antioxidant system function.

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