Effectiveness of an Eight Weeks Aerobic Exercise in Improvement of Body Composition and Modulation of hsCRP, Fibrinogen and Resistin in Middle Aged Men

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Abstract: Fibrinogen, CRP and resistin are three novel cardiovascular risk factors. The aim of this study was to examine the effects of an eight weeks aerobic exercise program on concentrations of these factors in healthy and overweight middle aged men. Thirty inactive middle aged men whom their BMI was between 25 and 30 randomly assigned into experimental and control groups (each group 15 subjects). Subjects of the experimental group accomplished eight weeks (three sessions per week) aerobic exercise with intensity of 50 to 70 percent of their maximum heart rate. Before and after trainings weight, body fat percent, fibrinogen, CRP and resistin levels of subjects were determined. Obtained data were analyzed using independent samples T test. After trainings results showed a significant reduction of weight, BMI, body fat percent, fibrinogen and CRP and significant elevation of resistin in the experimental group (P<0.05). Overall, eight weeks regular aerobic exercise through reduction of weight, body fat, fibrinogen and CRP and elevation of resistin cause reduction of risk of atherosclerosis and improvement of antioxidant system in overweight middle aged men.

Key-Words: aerobic training, weight loss, fibrinogen, CRP, resistin.

Introduction

Low-mobility lifestyle is a problem facing both developed and developing countries. One of the side effects of this problem is increased burden of cardiovascular diseases and premature mortality [1]. In most cases, premature coronary artery disease has a direct relationship with the number and intensity of atherosclerosis risk factors [2]. Epidemiologically, the risk factor is a characteristic of an individual or a population, which enters their life and increases the risk of the disease. It could be an acquired behavior like smoking, a hereditary quality like hyperlipidemia, or a laboratory marker such as C-reactive protein (CRP) and cholesterol. Risk factors must be diagnosed before the onset of the disease [3].

Since hypercholesterolemia, diabetes, smoking, obesity, hypertension and low-mobility lifestyle are among factors contributing to atherosclerosis, it was believed that by the end of the 20th century, it would be possible to limit coronary diseases by controlling these factors, especially hypertension and hypercholesterolemia. However, other factors intervened [4]. For example, it was observed that half of the heart attacks occur to the people without hyperlipidemia [3].
women, reported 77% of the future cardiovascular diseases among women with low levels of low density lipoprotein (LDL) [5]. Furthermore, according to a study conducted on 120000 patients suffering from coronary artery disease, 19% of men and 15% of women showed no symptom of hyperlipidemia, hypertension, diabetes and smoking, and that over 50% of the subject showed only one of these symptoms [6]. The animal-related, clinical and epidemiological research conducted within 10 to 15 years showed that inflammation and its cellular and molecular mechanisms play an important role in atherogenesis processes. Three important inflammatory markers are CRP, fibrinogen and resistin, which cause tissue damage and infection and atherosclerosis development [7,8,9].

CRP is an acute phase protein whose increase results in an increase in the possibility of the coronary artery diseases by 2 to five times. CRP increases in the people with high fat, and has a direct relationship with the insulin sensitivity and type two diabetes mellitus [3]. CRP causes the development of atherosclerosis through the following mechanisms: 1) by binding to the phospholipids of damaged cells and increasing the consumption of these cells by macrophages; 2) by activating endothelial cells for the gene expression of adhesive molecules; 3) by reducing the gene expression of endothelial nitric oxide synthase [10,11,12].

Fibrinogen is the 340-kDa glycoprotein consisting of three polypeptide chains, Aα, Bβ and γ. This molecule is synthesized like CRP under the induction of interleukin-6 (IL-6) by hepatic cells. Its half-life is 3 to five days and plays an important role in the platelet aggregation, endothelial injury, clot formation processes, blood viscosity, and red blood cells aggregation. In the case of increased IL-6 plasma levels, the fibrinogen and CRP levels also increase [13].

Resistin is a cysteine rich peptide hormone which has 108 amino acids. In the obese patients with diabetes, the level of this hormone is high. In human beings, this hormone is mainly made in fat and inflammatory cells and is directly related to CRP levels and atherosclerosis risk [8,14]. Resistin raises atherosclerosis risk by impairing glucose and lipid metabolisms. It also increases the vulnerability of atherosclerosis plaques by stimulating proinflammatory cytokines [15]. Resistin cause lipid deposition by increasing the gene CD36 expression in macrophages and forming foam cells in the vascular walls [16]. Church et al (2002) studied the relationship between CRP and cardio respiratory fitness and found that these two variables are negatively related [17]. Little research has been done on the effect of exercise on the resistin level. Jones et al (2010) studied the effect of eight months of aerobic exercise on the levels of resistin, adiponectin, glucose, insulin, total cholesterol (TC), LDL, high density lipoprotein (HDL), triglyceride (TG), leptin, active ghrelin, and peptide YY (PYY) in overweight teenagers and reported the desired effects of this exercise. They claimed that eight months of regular aerobic exercise can reduce resistin levels [18]. Kushnick et al (2003) showed that 12 months of power exercise does not significantly change levels of fibrinogen, TG and TC in male and female students [19]. Borer (2001) examined the effect of 15 weeks (three days per week) of exercise on fibrinogen levels in menopausal women and reported a significant increase in
this inflammatory marker after the exercise [20].

Considering limited findings, and since the positive effect of aerobic exercise on the prevention of cardiovascular diseases and insulin resistance has been proven, and that exercise can be used as a therapeutic approach for the treatment of diabetes and atherosclerosis, research on the effect of regular aerobic exercise on resistin levels can produce new and interesting results. On the other hand, there has been no research on the long-term effect of aerobic exercise on resistin, fibrinogen and CRP levels in middle-aged Iranian men with overweight. Considering the importance of cardiovascular health, especially in middle age, the purpose of this study was to examine the effect of eight weeks of aerobic exercise on the levels of the above-mentioned factors in healthy, sedentary men with overweight.

Methods

The subjects of this applied research were 30 middle-aged men, healthy, sedentary with overweight, who were divided randomly into two groups: control and experimental (each consisting of 15 members). All the subjects had body mass index (BMI) levels between 25 and 30 and their mean body fat percentages were above 15%. The exercise program consisted of eight weeks of aerobic exercise (three sessions per week) with 50% to 70% maximum heart rate of the subjects. The maximum heart rate of each subject was measured using the formula: 220 minus age of the subject. Using the heart rate control watch (Polar), the heart rate of the subjects was controlled. Each session included ten minutes of warm-up with joint rotations, stretching and jumping movements. The main part of the exercise, taking ten minutes in the first session, rising to 25 minutes in the last session, was followed with ten minutes of cooling down along with stretching activities and light jogging.

Before and after the exercises, the percent of body fat and fibrinogen, resistin and CRP levels of the subjects were measured. The body fat percentage of the subjects was measured using the Dale Wagner three point formula. Before blood was taken from the subjects in the beginning of the exercises, they were recommended to avoid any intense physical activity as well as eating and smoking for 12 hours before the exercise. They were allowed to drink water. Blood samples were taken from the left brachial veins of the subjects and was placed in the tubes containing sodium citrate and sent to the laboratory for analysis, where they were kept at the temperature minus 20 degrees. Fibrinogen levels were measured using a special kit. Serum resistin was also measured using Human Resistin Elisa Kit, and Sandwich Elisa method. The method used for measuring CRP was strengthened immunoturbidimetric for measuring two points with a photometer. In this method, the CRP existing in the sample of the subject forms a complex with the antibody of the sensitized polyclonal against human CRP coded on the latex particles and creates opacity. The amount of opacity created is related to the amount of CRP existing in the sample of the subject. The kit used was made by the Iranian Pars Azmoun Company. The kit has been designed to measure CRP within 0.1 to 20 milligrams per liter and the minimum CRP it can measure is 0.1 milligram per liter.

The statistical operations using SPSS.15. Software conducted on the data included descriptive statistics (measuring standard
deviation and mean) and inferential statistics. One sample Colmogorov Smirnov test was used to measure the normality of the distribution of the data. After it was made sure that the distribution of all the data was normal, paired samples T test was used to compare intragroup results and independent samples T test was used to examine the intergroup results. Pearson's correlation coefficient was used to determine the relation between dependent variables (weight, BMI, percentage of body fat, fibrinogen, resistin, CRP). The meaningfulness level was P<0.05.

Results

The subjects were homogeneous in terms of age, height, weight, BMI and percentage of body fat (See Table 1). The results of the independent T test showed that in the experimental group, weight, BMI and percentage of body fat have been reduced significantly. In addition, the amount of CRP and fibrinogen of plasma showed a significant reduction while the amount of resistin of the serum showed a significant elevation. None of the said variables in the control group showed a significant change (p<0.05) (See Table 2).

The independent T test showed that the reduction of weight, BMI and percentage of body fat in the subjects of the experimental group was significantly higher than those at the control group. Moreover, the reduction of CRP and fibrinogen and elevation of resistin in the subjects of the experimental group was significantly higher than those in the subjects of the control group (P<0.05) (See Table 2).

Discussion

One of the advantages of this study is the new findings it offers about middle aged Iranian men. Another advantage of the study is the higher number of the subjects participating in the experimental and control groups of the study, compared to similar studies [18,24].

The results of the study showed a significant reduction in plasma fibrinogen levels in the experimental group after doing aerobic exercises. Furukawa et al (2008) studied the effect of 12 weeks of walking on the fibrinogen levels of women aged 32 to 57 and reported that this factor brought no significant change after the exercises [25]. In a cross sectional study, Myint et al (2008), reported a reverse relationship between regular physical activities and fibrinogen levels [26].

Previous studies showed that the age and sex of the subjects and type and duration of the exercises were effective in the response of fibrinogen to regular exercise. There are several mechanisms that can explain the reduction of fibrinogen in the subjects of this study. Fibrinogen is positively correlated with stress, obesity and LDL and negatively correlated with HDL. Therefore, an increase in HDL and a reduction in LDL, stress and fat due to aerobic exercise can reduce fibrinogen [27]. Moreover, regular aerobic exercise can reduce fibrinogen concentration in blood by reducing catecholamine stimulation, increasing blood flow in muscles and increasing the volume of blood [25]. The reduction of fat, which was observed in the subjects, can reduce IL-6 produced in the fat tissue and since IL-6 is a fibrinogen synthesis, its reduction results in a reduction of fibrinogen [25,28]. Generally, too much fat cause inflammation in the body, which stimulates the increase of blood fibrinogen. Accordingly, the reduction of fat (which was observed in the subjects of this study), can reduce inflammatory processes and fibrinogen concentration in blood [25]. The
reduction of fractional synthesis rate (FRS) as a consequence of long exercise is a yet another mechanism for reducing fibrinogen levels [29].

In this study, the amount of serum CRP in the subjects of the experimental group showed a significant reduction; it also showed a significant difference with the results from the control group. This finding was similar to that of Hamedinia et al (2009). They reported a significant reduction of CRP levels and the number of white blood cells (WBC) in twenty healthy and sedentary middle-aged men [30].

Lakka et al (2005) studied the effect of physical exercises on CRP levels in healthy and sedentary men and women. The subjects pedaled on the bicycle for 20 weeks (three days per week with an intensity of 55 to 75% Vo2max). The results showed a significant reduction in the CRP level [31]. Stouneberg (2008) studied the effect of 17 weeks of semi-marathon exercise on the CRP level of 42 men of 26 to 30 years of age. There was no significant change in the CRP and IL-6 concentration, but the Vo2max increased and fat decreased [32]. Daray (2009) studied the effect of endurance and concurrent exercise (endurance + resistance) on the CRP level. The results showed a significant reduction in the CRP level of the concurrent exercise group [33]. Heffernan et al (2009) studied cardio inflammatory response to resistance exercise among white and black men. The results showed a significant decrease in the CRP level of the black men [34].

Jones et al (2009) examined the effect of eight months of aerobic exercise on serum lipid levels, leptin, adiponectin, resistin, peptide YY and ghrelin in overweight youngsters. They reported a significant reduction of resistin [18]. Elloumi et al (2009) studied obese youngsters and reported that their subjects showed a significant reduction of resistin levels after two months of exercise [42]. Balducci et al (2010) reported a reduction of resistin in the patients with diabetes and overweight after 12 months of physical activity [41]. Kelly et al (2007) studied overweight children in an eight-week exercise program of 50 to 60 percent of Vo2max. Resistin levels showed an insignificant elevation [39]. Camera et al
(2010) showed that ten days of duration exercise increase resistin gene expression in sedentary young men [22].

Thus, none of the studies mentioned above had any resemblance to this study in terms of type, intensity, exercise period or subjects. Therefore, no comparison can be made between the findings of this study with those of others, even though it can be inferred that regular duration exercise with an average intensity can cause elevation of resistin levels.

The mechanisms of the resistin increase in the subjects of the study are not exactly clear, but a review of the studies conducted suggests a few possible mechanisms. Proinflammatory cytokines, including TNF-α, interleukin-1 (IL-1) and IL-6 stimulate resistin gene expression in mononuclear cells of blood [23] and since there are contradictory results about the effect of regular exercise on TNF-α level [38] resistin increase can be attributed to these cytokines. Since resistin is directly linked with adiponectin [23] adiponectin elevation pursuant to exercises [38] can increase resistin. Resistin is also directly related to insulin like growth factor binding protein-I (IGFBP-I) [43]. In this study, the most important mechanism explaining resistin elevation after aerobic exercise is the role of this hormone in the anti-oxidant defense of the body, since resistin is negatively correlated with nitrotyrosin (NT) [44]. Reactive nitrogen species are among important regulators of inflammation in the body. Nitric oxide (NO), which is a vascular substance, and is discharged by endothelial cells, produces peroxynitrite (ONOO-) in response to superoxide anion radical. Peroxynitrite is nitrating oxidant and is capable of oxidizing many biomolecules. NT, which is produced in the tyrosine oxidation process, is directly related to the oxidant stress and is an index of oxidant damage due to ONOO-. In response to inflammatory stimulant, resistin acts as an antioxidant, a meaningful interaction has been discovered between polymorphism of a single nucleotide in the promoter of human resistin gene and an oxidant marker and insulin resistance. Mononuclear cells of blood produce resistin in response to low grade inflammation, which can have antioxidant properties. Bo et al (2005) found no significant relationship between CRP and NT, which indicates that there is a complicated interaction between oxidant markers and inflammatory markers [44].

Thus the CRP reduction and resistin elevation of in the subjects of this study can be the result of the anti-inflammatory and anti-oxidant compatibility. Generally, it can be deduced that regular aerobic exercise coupled with weight loss by reducing adipocytes such as leptin and IL-6 reduces fibrinogen and CRP levels while it increases antioxidant defense of the body by stimulating the synthesis of resistin in mononuclear cells.

**Conclusion**

Generally, the results of the study showed that regular aerobic exercise not only causes weight loss and body fat reduction, but fibrinogen and CRP levels reduction and resistin elevation as well. These results in the reduction of heart attack risk and increase of antioxidant defense power of the body. Of course, more research is needed on the effect of long-term exercise on resistin levels.

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References

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Tables

Table 1: descriptive characteristics of the subjects and differences among them before trainings

<table>
<thead>
<tr>
<th>variables</th>
<th>Exercise group</th>
<th>Control group</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>45.73 ± 7.08</td>
<td>46.13 ± 1.51</td>
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<tr>
<td>Height</td>
<td>1.74 ± 0.05</td>
<td>1.74 ± 0.05</td>
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<td>Weight</td>
<td>84.78 ± 6.46</td>
<td>82.78 ± 6.62</td>
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<td>BMI</td>
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<tr>
<td>BFP*</td>
<td>18.33 ± 2.51</td>
<td>18.88 ± 2.96</td>
<td>0.59</td>
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</tbody>
</table>

* body fat percent

Table 2: changes of dependent variables in response to two months aerobic training

<table>
<thead>
<tr>
<th>Variables</th>
<th>Exercise group</th>
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<th>P value</th>
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<td>Pre test</td>
<td>Post test</td>
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<td>BMI</td>
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<td>hsCRP</td>
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<tr>
<td>resistin</td>
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<td>8.47±0.72</td>
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