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EFFECT OF 12 WEEKS HIGH INTENSITY AEROBIC EXERCISE ON SERUM OXIDIZED LDL-C IN OBESE MIDDLE AGED MEN

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ABSTRACT
MOGHADASI, M.; HEIDARNIA, E.; NEMATOLLAHZADEH, M.; TORKFAR, A.; ARVIN, H. Effect of 12 weeks high intensity aerobic exercise on serum oxidized LDL-c in obese middle aged men. Brazilian Journal of Biomotricity. v. 5, n. 4, p. 263-270, 2011. Exercise significantly influences the progression of atherosclerosis. Oxidized LDL-c (ox-LDL-c), as a stimulator of oxidative stress, facilitates monocyte-related atherogenesis. We investigated the effect of 12 weeks high intensity aerobic exercise on serum oxidized LDL-c in obese middle aged men. Sixteen sedentary obese middle-aged men (aged: 41.18±6.1 years; ±SD) volunteered to participate in this study. The subjects were randomly assigned to training group (n=8) or control group (n=8). The training group performed endurance training 4 days a week for 12 weeks at an intensity corresponding to 75-80% individual maximum oxygen consumption for 45 min. High intensity aerobic exercise did not significantly alter serum ox-LDL-c, total cholesterol (TC) and low-density lipoprotein (LDL-c), while serum high-density lipoprotein (HDL-c) and triglyceride (TG) were significantly increased and decreased respectively (P<0.05). There were significant positive correlations between LDL-c and TC with ox-LDL-c (P<0.05) and a significant negative correlation between HDL-c and TG (P<0.05). We conclude that serum ox-LDL was not affected by high intensity aerobic exercise.

Key words: Exercise, ox-LDL-c, Obese male.
INTRODUCTION

The oxidation conversion of low-density lipoprotein (LDL-c) to oxidized low-density lipoprotein (ox-LDL-c) is now considered to be a key event in the biological process that initiates and accelerates the development of the early lesion, the fatty streak (STEINBERG, 1997). Experimental studies have shown that native LDL-c become atherogenic when it is converted to ox-LDL-c and that ox-LDL-c is more atherogenic than native LDL-c (STEINBERG, 1997; HEINECKE, 1998). Ox-LDL-c is found in monocyte-derived macrophages in atherosclerotic lesions, but not in normal arteries (YLA-HERTTUALA, 1998). The uptake of LDL-c into macrophages does not occur by way of the classic Brown/Goldstein LDL-c receptor (BROWN and GOLDSTEIN, 1983). Numerous studies have established that LDL-c, the major carrier of blood cholesterol, must first be converted to ox-LDL-c so that it can be recognized by scavenger or ox-LDL-c receptors on monocyte-derived macrophages (STEINBERG, 1997; HEINECKE, 1998). The binding of ox-LDL-c to macrophages is a necessary step by which ox-LDL-c induced cholesterol accumulation in macrophages, and thus transforms the macrophages into lipid-laden foam cells (CHISOLM et al., 1999). Holvoet and colleagues were the first to clearly demonstrate that patients with coronary artery disease had significantly elevated plasma levels of ox-LDL-c. Hulthe and fagerberg demonstrated the relationship between subclinical atherosclerosis and circulating ox-LDL-c levels by showing that ox-LDL-c levels were related to intima-media thickness and plaque occurrence in the carotid and femoral arteries. Sigurdardottir et al. found elevated levels of ox-LDL-c in patients with metabolic syndrome. In addition they found that elevated ox-LDL-c levels in metabolic syndrome patients were associated with small LDL-c particle size (SIGURDARDOTTIR et al., 2002). Elevated levels of circulating ox-LDL-c, also, were found in patients with impaired glucose tolerance (KOPPRASH et al., 2002) and in patients with over hypothyroidism (DUNTAS et al., 2002).

On the other hand, antioxidant molecules prevent and/or inhibit these harmful reactions (EREL, 2004; YOUNG and WOODSIDE, 2001). Antioxidants increase during exercise (YOUNG and WOODSIDE, 2001), thus the beneficial effects of exercise are generated through an antioxidant defense mechanism (CLARKSON and THOMPSON, 2000). In contrast, exercise-induced oxidative stress has also been reported (HARTMANN et al., 1994).

Previous studies indicated that acute high intensity exercise generates an imbalance between reactive oxygen species (ROS) and antioxidant defense, resulting in an oxidative stressful environment in the body (JI, 1999; URSO and CLARKSON, 2003). Conversely, regular moderate-intensity exercise hinders LDL oxidation by enhancing antioxidant release or production (WANG et al., 2000). The effect of regular high intensity aerobic exercise on LDL-c oxidation remains unclear. We hypothesize that the effect of exercise training on ox-LDL-c depends on the mode and type of exercise, e.g. regular exercise regimens versus acute exercise. Thus the aim of this study was to determine the effect of 12 weeks high intensity aerobic exercise on serum ox-LDL-c levels in obese middle aged men.

MATERIALS AND METHODS

Subjects

Sixteen sedentary obese middle-aged men with a mean (±SD) body mass index of 31.5 ± 3.9 kg/m², volunteered to participate in a 12 weeks training study. All the subjects were asked to complete a personal health and medical history questionnaire, which served as a
screening tool. The subjects were given both verbal and written instructions outlining the experimental procedure, and written informed consent was obtained. The study was approved by the University of Guilan Ethics Committee.

**Study design**

A two-group, randomized, repeated measures, controlled trial was employed. During their first visit, the subjects were medically screened and had their anthropometric profiles measured. At the second visit, the subjects underwent a progressive diagnostic treadmill test to exhaustion (modified Bruce protocol) to evaluate their VO$_{2\text{max}}$. At the third visit, fasting blood samples were collected. Then, the subjects were randomly assigned to control group (n=8) or training group (n=8). The training groups performed endurance training 4 days a week for 12 weeks at an intensity corresponding to 75-80% individual maximum oxygen consumption for 45 min and control group were instructed not to change their physical activity and diet. All the measurements were repeated 48h after the last session of training.

**Exercise training**

The 12 weeks exercise training program included 4 training sessions per week on treadmill in the physiological laboratory of The University of Guilan. The intensity of exercise was customized for each subject based on the relationship between heart rate and oxygen uptake measured at baseline. During the 12 weeks intervention, the subjects were trained for 45 min per session at a heart rate corresponding to 75-80% of the maximal oxygen uptake measured at baseline. Each participant was equipped with a heart rate monitor (Polar, FS3c, Finland) to ensure accuracy of the exercise level.

**Measurements**

**Anthropometric and body composition measurements**

Height and weight were measured, and body mass index (BMI) was calculated by dividing weight (kg) by height (m$^2$). Waist circumference was determined by obtaining the minimum circumference (narrowest part of the torso, above the umbilicus) and the maximum hip circumference while standing with their heels together. The waist to hip ratio (WHR) was calculated by dividing waist by hip circumference (cm) (ACSM, 2005). Fat mass and lean body mass were assessed by bioelectrical impedance analysis using a Body Composition Analyzer (Biospace, Inbody 3.0, Jawn, Korea).

**Measurement of VO$_{2\text{max}}$**

VO$_{2\text{max}}$ was determined during graded exercise testing using modified Bruce protocol (ACSM, 2005). Each subject performed a graded treadmill exercise test to estimate VO$_{2\text{max}}$ by indirect calorimetry. A pulmonary gas exchange system (Cosmed, Quark b$^2$, Germany) was used to evaluate the participants' VO$_{2\text{max}}$. Oxygen uptake (VO$_2$) was measured continuously via breath by breath analysis with the use of a computerized system. To ascertain that VO$_{2\text{max}}$ had been attained, standard criteria had to be met (ACSM, 2005).

**Biochemical analyses**

Fasting blood samples were collected at rest (before training) and after training. All the
subjects fasted at least for 12 hours and a fasting blood sample was obtained by venipuncture. The serum ox-LDL-c level was measured in duplicate using an enzyme-linked immunosorbent assay (ELISA) kits (Mercodia, Upssala, Sweden). The assay sensitivity was 1 mU/l and its intra assay coefficient of variation was 8.5%. Fasting serum total cholesterol (TC), triglycerides (TG) and high-density lipoprotein (HDL-c) concentrations were measured by an enzymatic colorimetric method (Pars Azmun, Tehran, Iran). LDL-c concentration was calculated with the Friedwald formula.

Statistical analysis

Results were expressed as the mean ± SD and distributions of all variables were assessed for normality. Paired-samples t-test and independent-samples t-test was used to evaluate change in variables. Pearson correlation was performed to calculate a correlation. The level of significance in all statistical analyses was set at P ≤ 0.05. Data analyses were performed using SPSS software for windows (version 13, SPSS, Inc., Chicago, IL).

RESULTS

The physical characteristics and demographic data for all subjects are presented in Table 1. Before the study (pre-test), the training and control groups had similar BMI, fitness levels (VO2max) serum TC, TG, LDL-c, HDL-c and ox-LDL-c. At the end of the study, body weight, BMI, body fat percent, WHR and TC decreased and VO2max and HDL-c increased in the training group in compared to the control group (P<0.05). For ox-LDL-c, LDL-c and TG, there was no significant difference between the training group and the control group (Table 2). In addition, there were significant positive correlations between LDL-c and ox-LDL-c (r=0.58, P<0.05) and TC and ox-LDL-c (r=0.64, P<0.01) and a significant negative correlation between HDL-c and TG (r=0.6, P<0.01).

Table 1 - Pre-test physical characteristics and demographic data

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control (mean±SD)</th>
<th>Training (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43.2±6.1</td>
<td>39.1±5.7</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>90.47 ± 13.9</td>
<td>87.86 ± 8.5</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>32.03 ± 5.3</td>
<td>30.96 ± 2.1</td>
</tr>
<tr>
<td>Lean body mass (kg)</td>
<td>58.27 ± 4.3</td>
<td>58.73 ± 6.1</td>
</tr>
<tr>
<td>Body fat mass (kg)</td>
<td>29.62 ± 9.5</td>
<td>25.98 ± 3.7</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>31.41 ± 5.5</td>
<td>29.56 ± 3.1</td>
</tr>
<tr>
<td>WHR</td>
<td>0.99 ± 0.08</td>
<td>0.96 ± 0.03</td>
</tr>
<tr>
<td>VO2max (ml.kg⁻¹.min⁻¹)</td>
<td>31.88 ± 5.6</td>
<td>32.05 ± 3.6</td>
</tr>
</tbody>
</table>

No significant differences were observed at the baseline.
Table 2 - Effect of high intensity aerobic exercise on the outcome variables after 12 weeks (mean±SD)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Training</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-test</td>
<td>Post-test</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>90.47±13.9</td>
<td>87.86±8.5</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
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<tr>
<td>WHR</td>
<td>0.99±0.08</td>
<td>0.96±0.03</td>
</tr>
<tr>
<td>VO₂max (ml.kg⁻¹.min⁻¹)</td>
<td>31.88±5.6</td>
<td>32.05±3.6</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td>169.3±42.5</td>
<td>200.3±36.7</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>170.1±118.4</td>
<td>255.5±68.7</td>
</tr>
<tr>
<td>HDL-c (mg/dl)</td>
<td>41.5±9.14</td>
<td>34.6±8.3</td>
</tr>
<tr>
<td>LDL-c (mg/dl)</td>
<td>99.7±39.7</td>
<td>120.3±36.1</td>
</tr>
<tr>
<td>ox-LDL-c (U/l)</td>
<td>5.01±1.3</td>
<td>4.5±1.3</td>
</tr>
</tbody>
</table>

a P<0.05, pre-test vs. post-test values.
b P<0.05 for between-group differences.

DISCUSSION

Increased oxidative stress and lipoprotein oxidation have been linked to atherosclerotic diseases including coronary artery disease (STEINBERG et al., 1989). It has been shown that there is a positive relationship between ox-LDL-c and cardiovascular mortality (YAGI, 1987). The aim of this study was to evaluate the effect of high intensity aerobic exercise on serum ox-LDL-c. Our results demonstrated that after 12 weeks exercise training, BMI, body fat percent and TC decreased but TC, LDL-c and ox-LDL-c have not significantly changed. Recent studies have reported that regular moderate physical activities decrease ox-LDL-c in patients with coronary artery disease (SRIMAHAHOTA et al., 2010), thought we did not find any significant change in serum ox-LDL-c in the training group. Afzalpour et al. also, demonstrated that serum ox-LDL-c was not affected by vigorous aerobic exercise. Additionally, previous studies indicated that regular moderate exercise suppresses ox-LDL-promoted platelet activation by enhancing nitric oxide release (as an antioxidant) of platelets (WANG et al., 2000). Our study demonstrated that the high intensity aerobic exercise had no effect on ox-LDL-c; thus it seems that the mode and type of exercise, especially intensity of exercise, are the effective parameters on LDL-c oxidation.

On the other hand, in agreement to Sturgeon et al. significant positive correlation was observed between ox-LDL-c with TC and LDL-c. Studies show that exercise induced decrease in LDL-c is associated with the decrease in ox-LDL-c (SHERN-BREWER et al., 1998). In our study, there was virtually no change in LDL-c after 12 weeks training. In exercisers, the oxidation of LDL-c in the plasma might itself account for some of the lipid-lowering effects of exercise and might actually be beneficial (SHERN-BREWER et al., 1998). LDL-c and ox-LDL have been shown to have adverse effects on endothelial cell function such as uncoupling of endothelial nitric-oxide synthase (eNOS) (BLAIR et al., 1999), increased ROS (COMINACINI et al., 2000), and transcriptional regulation of eNOS (RAMASAMY et al., 1998).
Aerobic exercise is believed to reduce the risk of cardiovascular disease partially through increasing serum levels of HDL-c and decreasing serum levels of TC, TG and LDL-c. Improving in blood lipid profile is related to the amount and intensity of the exercise (KODAMA et al., 2007; O’DONOVAN et al., 2005). O’Donovan et al. suggested that changes in coronary heart disease risk factors are influenced by exercise intensity and high-intensity training is more effective in improving cardiorespiratory fitness than moderate-intensity training of equal energy cost.

Durstine et al. reported that weekly energy expenditure greater than 1200 kcal/wk was frequently associated with elevations in HDL-C level. Our training induced approximately 2000 kcal/wk, thus it seems that our training has sufficient stimuli to increase HDL-c levels. Despres suggested that changes in triglyceride and HDL-C concentrations may dependent on substantial reductions in body fat mass. The decreasing body fat mass and BMI after 12 weeks training may respectful for decrease of TG and increase of the HDL-c respectively. In conclusion, ox-LDL-c no affected by the high intensity aerobic exercise training, suggesting that the moderate aerobic exercise training may effective for ox-LDL-c decreasing. However, additional research is needed to determine the effects of exercise intensity on ox-LDL-c levels.

PRACTICAL APPLICATION

The results showed that ox-LDL-c no affect ed by the high intensity aerobic exercise training, while these exercise training increase the HDL-c and decrease TC levels respectively. Thus it seems that high intensity aerobic exercise training is effective for improve cardiovascular risk factors in obese middle aged men, but oxidative stress parameters such as ox-LDL-c not affected by this protocol.

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