Effect of 8 Weeks Endurance Training on Plasma Lipocalin-2 in Overweight and Obese Men

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ABSTRACT

Lipocalin-2 has been known as adipocyte-driven acute phase protein that is positively correlated with potential effects in obesity and inflammation. The reactions of this protein in progressive exercise have not yet been evaluated. Therefore the purpose of this study was to examine the effects of 8 weeks endurance training on plasma lipocalin2 in overweight and obese young men. Sixty healthy young men (aged 28.93 ± 1.65 years, height 1.71 ± 5.37 cm, BMI 28.49 ± 1.49 kg/m², mean ± SD) participated as subjects in this study. The subjects were randomly assigned to endurance training group (n=30) or control group (n=30). Endurance training group underwent an 8-week intervention, with a frequency of 3 d/wk at an intensity corresponding to 65 – 80% maximum heart rate for 30 – 45 min. The results showed that body fat percent, WHR, BMI, were decreased (P<0.05), in the training group compared with control group. Maximum oxygen consumption, on the other hand, increases significant (P<0.05) in the training group compared with the control group. Plasma lipocalin-2, LDL-c, TG, TC and HOMA-IR decreased (P<0.05) and HDL-c increased (P<0.05). No significant changes in hs-CRP were found after 8 weeks endurance training. Conclusion, it seems that 8 weeks endurance training induced change in adipose tissue, decrease plasma lipocalin2, but this improvement was not accompanied by decreased hs-CRP in overweight and obese men.

INTRODUCTION

In developed word obesity and associated metabolic and cardiovascular complication is a major public health problem and one of the major contributors to premature death. Obesity also is the most common risk factor for insulin resistance, type2 diabetes mellitus and cardiovascular disorders. Studies have demonstrated close associations between obesity and increased circulating levels of proinflammatory molecules, including acute-phase proteins, cytokines, adipokines, and chemokines [12,15]. In obese state this proinflammatory factors are produced predominantly from in enlarged adipocytes and activated macrophages in adipose tissue and liver. Many of this proinflammatory factors such as interleukin-6 (IL-6) tumor necrosis factor-a (TNF-a) and hs-CRP can directly induce glucose intolerance and insulin resistance by antagonizing insulin’s metabolic actions at peripheral tissues, especially in liver and skeletal muscle [6]. Lipocalin2 also known as neutrophil gelatinase associated lipocalin, sidrocalin and 24p3, is another member of the lipocalin family recently reported to have possible metabolic roles [7]. Lipocalin 2 is expressed in many tissue, including neutrophils, macrophage, kidney, liver, lung, thymus, small intestine mammary tissue as well as adipocytes and is known to play a role in inflammation. It also has been implicated in apoptosis and innate immunity [14,16]. As an adipokine, circulating Lcn2 level has been reported to be increase in obese humans [14], and laboratory animals [16], than lean controls. It also has been showing that the plasma level of Lcn2 has a significant association with body mass index (BMI), fasting glucose and hyperinsulinaemia [14,2,16,11]. Lcn2 has been recognized as an adipocyte drive acute phase protein that is positively correlated with potential effect in obesity inflammation and insulin resistance in mice and humans [2,14]. It also has been showing that circulating levels of this adipokin has a strong direct correlation with hs-CRP as an acute phase protein [13].

One of the best strategies for preventing obesity and its associated inflammation is participation in regular physical activity [10]. On the other hand, exercise has been shown to have beneficial effects on obesity, type2 diabetes and the metabolic syndrome. Although the change in adipokine levels might be an important clue for understanding the beneficial effects of exercise, data on exercise-induced changes of Lcn2 is still unclear.
Recently, Damirchi (2011) reported that Lcn2 increased after single bout graded exercise in obese and normal weight men [4], in an only available study, isn’t reported that any change in Lcn2 level in obese women after 12 weeks moderate exercise training [2]. The magnitude of the changes in plasma adipokins levels depends on the type, duration and intensity of exercise [10]. The physiological and biochemical responses to resistance exercise are different from those exhibited in response to endurance training [9]. No previous study has investigated the effects of endurance exercise on Lcn2 concentration in overweight and obese men. Therefore the present study was designed to determine the effects of endurance training (ET) on Lcn2.

MATERIAL AND METHODS

Subjects:
Sixty healthy and university students aged (aged 28.93 ± 1.65 years, mean±SD) enrolled in this study. The inclusion criteria were men who had body mass index (BMI) ≥26 kg/m² did not engage in regular exercise training at the time of their enrolment. Student who were afflicted with heart diseases, hypertension, pulmonary diseases and diabetes, who needed orthopedic treatment, and who had neurological limitations to physical exercise were excluded. 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 instruction outlining the experimental procedure, and written informed consent was obtained. All the subjects completed the 3-day diet recall forms and were instructed to maintain their normal physical activity and dietary habits throughout the study. The subjects were randomly assigned to one of the endurance group (n=30) and control group (n=30).

Exercise training:
The participant’s of endurance training group underwent three exercise training sessions per week for 8 weeks. The training exercise consisted of a 10-minute warm-up period, as well as muscle stretches. It’s also consisted of walking and running at 65-80% of maximal heart rate (HR$_{max}$) for 30-45 min per day, 3 days per week, for 8 weeks. The programme started with 30 min running for the first few sessions, and this was then changed to 45 min per session until the end of training. Each training session finished with a cool down. The exercise intensity was controlled by the authors, using a hear rate monitor, who ensured that it was between 65 and 80% of HR$_{max}$ throughout the trial.

Measurements: (Anthropometric and body composition measurements):
Height and body weight were measured, and body mass index (BMI; kg/m²) was calculated from height and weight of each subject. Waist circumference was determined by obtaining the minimum circumference (narrowest part of the torso, above the umbilicus) and the maximum hip circumference (cm) (ACSM) [1]. Subcutaneous body fat was measured at 3 sites (chest, abdominal, and thigh) with a Lafayette caliper. Body fat percent was calculated from the formula developed by Jackson and Pollock [8]. VO$_{2max}$ was determined by Rockport One-Mile fitness walking test. In this test, an individual walked 1 mile (1.6 km) as fast as possible on a track surface. Total time was recorded and HR was obtained in the final minute (ACSM) [1]. VO$_{2max}$ was calculated by following formula:

\[
\text{VO}_{2\text{max}} = [139.68 - (0.388 \times \text{age (year)})] - [0.077 \times \text{body mass (pb)}] - [3.265 \times \text{time (min)}] - [0.156 \times \text{HR}].
\]

Biochemical analysis:
Fasted, resting morning blood samples (10ml) were taken at the same time before and after 8 weeks intervention.
All subjects fasted at least for 12 hours and a fasting blood sample was obtained by venipuncture. The plasma Lipocalin2 level was measured in duplicate using an enzyme-linked immunosorbert assay (ELISA) kits (Uscn Life Science Inc, Wuhan, China). hs-CRP levels were determined in duplicate via An enzyme-linked immunosorbert assay (ELISA) kits(Diagnostics Brochem Canada, Inc). Plasma glucose was determined by the enzymatic colorimetric method (Pars Azmon, Tehran, Iran) the serum insulin level was measured by a radioimmunossay (RIA). And the insulin resistance index was calculated according to the homeostasis model assessment (HOMA-IR) which correlates well with the euglycemic hyperinsulimemic clamp in people with diabetes [5].
Serum cholesterol triglycerides, HDL-c and LDL-c were assayed with automated techniques.

Statistical Analysis:
Statistical analyses were performed with SPSS program (version 16, SPSS, Inc., Chicago, IL). Values were expressed as mean ± standard deviation (SD). Independent t-test and paired t-test were used to evaluate changes in variables. General linear regression analysis and Pearson’s correlation were performed to calculate a
correlation between variables in response to training. P-values less than 0.05 were considered statistically significant.

Results:
Anthropometric, physiological and metabolic characteristics of subjects are shown in Table 1. The results showed that body weight, body mass index (BMI), body fat percent and WHR decreased (P<0.05) after endurance training. Maximum oxygen consumption, on the other hand, increases significant (P<0.05) in the training group compared with the control group. Plasma lipocalin-2, LDL-c, TG, TC and HOMA-IR decreased (P<0.05) and HDL-c increased (P<0.05) after 8 weeks endurance training (Table 1). For hs-CRP, there was no significant difference between endurance training group and control group after 8 weeks exercise. Pearson's correlation demonstrated a positive relationship between plasma lipocalin-2 levels at baseline (P<0.05) with body fat percent, WHR and BMI. No significant relationship between plasma Lcn2 with biochemical variables were found in the endurance group after 8 weeks intervention.

Table 1: Anthropometric and metabolic characteristics of study subjects (mean ± SD).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pre-test</th>
<th>Post-test</th>
<th>Training (Endurance group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>81.30±6.76</td>
<td>81.29±6.40</td>
<td>83.65±7.04</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.49±10.45</td>
<td>28.30±10.43</td>
<td>28.67±1.50</td>
</tr>
<tr>
<td>%Body fat</td>
<td>23.56±1.53</td>
<td>23.36±1.65</td>
<td>23.66±2.22</td>
</tr>
<tr>
<td>WHR</td>
<td>90±0.3</td>
<td>90±0.3</td>
<td>93±0.2</td>
</tr>
<tr>
<td>VO₂max (mL.kg⁻¹.min⁻¹)</td>
<td>35.76±3.37</td>
<td>35.96±3.23</td>
<td>35.9±2.77</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>1.61±2.03</td>
<td>1.58±2.03</td>
<td>1.71±1.56</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>1.89±2.7</td>
<td>1.88±2.6</td>
<td>1.96±1.62</td>
</tr>
<tr>
<td>LDL-c</td>
<td>1.27±2.57</td>
<td>1.27±2.39</td>
<td>1.32±3.1</td>
</tr>
<tr>
<td>HDL-c</td>
<td>38.01±4.98</td>
<td>38.23±5.27</td>
<td>35.4±6.81</td>
</tr>
<tr>
<td>Lipocalin2 (ng/ml)</td>
<td>23.56±2.26</td>
<td>23.02±2.8</td>
<td>23.79±2.82</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>52.56±12.54</td>
<td>51.41±11.93</td>
<td>55.65±10.99</td>
</tr>
<tr>
<td>Hs-CRP</td>
<td>.83±.88</td>
<td>.86±.88</td>
<td>.78±.73</td>
</tr>
</tbody>
</table>

*a P<0.05 for between-group differences.
*b P<0.05, pretraining vs. posttraining values.

Discussion:
Lcn2 has been identified as a novel adipokine associated with obesity, type2 diabetes and the metabolic syndrome. The effects of endurance training on plasma Lcn2 are still unclear, thus this study aimed to investigate the effects of endurance training (ET) on Lcn2 in overweight and obese men. The results showed that Plasma Lipocalin-2 decreased (P<0.05, 11.2%) in response to 8 weeks endurance training compared to the control group. Although no previous study has investigated the effects of endurance exercise on Lcn2 concentration, Choi (2009) indicated that there was no significant change in the Lcn2 in obese women after 12 weeks moderate exercise training [2]. This discrepant result may be attributed to variation in the exercise protocols and differences in subject populations. The results showed that body weight; body mass index (BMI), body fat percent and WHR were decreased after endurance training, thus exercise-induced changes in body fat, especially visceral adipose tissue, may attribute to plasma Lipocalin2 decrease. On the other hand, there was the positive relationship between plasma lipocalin2 and body fat percent at baseline and after the training. The results are in agreement with previous reports showing that there was a significant positive relationship between plasma lcn2 levels with body mass, body fat percentage and WHR, suggesting that the increased fat mass might account for the elevated blood levels of this adipokine in obese individuals. Wang (2007), showed a higher concentration of Lcn2 in obesity and this adipokine is positively related to the BMI, Waist circumference and body fat percentage [14]. Choi et al demonstrated that a positive relationship between Lcn2 and body mass and Damirchi et al (2011) showed a positive relationship between Lcn2 level with waist circumference, fat mass and BMI [3, 4]. Body fat percent decreased 8.8% after 8 weeks endurance training, thus it seems that the endurance training could offer a sufficient stimulus for plasma Lcn2 decreases.

Lcn2 can be recognized as an inflammatory marker that increases after a progressive physiological stress in sedentary individual. Furthermore, increasing of Lcn2 secretion from fat cells may be stimulated by lipopolysaccharides that suggesting Lcn2 as an acute phase protein [14]. It is reported that a direct relation between the Lcn2 and hs-CRP levels and Lcn2 can be use by researchers and clinicians as the inflammatory index [2].results showing no significant relationship between Lcn2 and hs-CRP after 8 weeks endurance training. Suggesting that decrease of the other inflammatory markers might decrease Lcn2 concentration. Serum Lcn2 levels correlated with serum IL-6 and TNF-α concentration in this study. Additional research is needed to examine whether exercise induced change in IL-6 and TNF-α concentrations, decreases Lcn2. Summer et al and Yan (2009, 2007) indicated that appositive relationship between Lcn2 concentration and insulin resistance
However we found a significant related between Lcn2 and insulin resistance determined by HOMA-IR. Choi et al (2009) reported that HOMA-IR is not a very sophisticated measure of insulin resistance, although it has been used widely in clinical and epidemiological studies [2]. We did not measure IL-6 and TNF-α in the present study. If we could measure these inflammatory markers, we could carefully explain the decrease of plasma Lcn2 in response to 8 weeks exercise training in overweight and obese men.

Conclusions and Practical Application:
In conclusion, endurance training induced change in adipose tissue, decrease plasma lipocalin2 in overweight and obese men. These findings suggested that changes in adipokine lcn2 levels may be associated with the beneficial effect of exercise. Further studies are needed to elucidate the mechanisms responsible for the effects of exercise on adipokines.

REFERENCE