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Effect of Exercise on Circulating Adipokine Levels in Obese Young Women

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Abstract. We studied the effect of exercise on circulating adipokine, high sensitivity C-reactive protein (hs-CRP), and metabolic parameters in obese young women. Ninety-six healthy Japanese young female students aged 18–23 years were studied. The longitudinal intervention study of a 7-month exercise training program (30–60 min/day, 60–70% HR-reserve, 200–400 kcal, 4–5 days/week) was performed in eight obese female students (BMI ≥25 kg/m^2). Eight control female students (mean BMI = 22 kg/m^2) were included in the follow-up study. Body weight, body mass index (BMI), percentage of body fat (%Fat), body fat mass, lean body mass, health-promoting lifestyle profile-scale (L-scale), Vo_2max (maximal oxygen uptake), hs-CRP, lipids, insulin homeostasis model assessment (HOMA-R), fasting levels for circulating adiponectin, leptin, and TNF-α, were measured before and after the exercise program. In obese subjects, body weight, BMI, %Fat, body fat mass, lean body mass, hs-CRP, leptin, and TNF-α were significantly higher, and L-scale and adiponectin were lower than those in control subjects. In obese subjects, exercise decreased body weight, BMI, %Fat, body fat mass, lean body mass, hs-CRP, leptin, and TNF-α, and increased L-scale, Vo_2max, HDL-cho, and adiponectin. It was concluded that changes in circulating adipokine levels are involved in the improvement of the metabolic state by exercise and may be useful markers for evaluation and prescription of exercise.

Key words: Obese young women, Exercise, Adiponectin, Leptin, TNF-α

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ADIPOSE tissue is not merely a fat storage depot, but has been recognized as an endocrine organ capable of producing biologically active proteins termed "adipokines". Adipokine include adiponectin, leptin, tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), which may be related to the development of obesity-mediated adverse effects on glucose and lipid metabolism [1, 2]. Adiponectin, also known as Acrp 30 [3], is decreased in obesity [4], and low adiponectin concentration is associated with insulin resistance [5]. Adiponectin has been reported to improve insulin sensitivity in obese diabetic patients [6]. It has been shown that significant resistance to leptin action is associated with the pathophysiology of type 2 diabetes [7]. TNF-α is elevated in obesity and contributes to insulin resistance, possibly through down-regulation of GLUT4 and inhibition of insulin receptor function and signaling [8]. IL-6 secreted by fat cells induces hepatic synthesis of C-reactive protein (CRP), and both molecules are associated with obesity and cardiovascular disease [9].

Several studies exploring the effects of exercise on circulating adiponectin levels have resulted in inconsistent findings [10–15]. It has been shown that basal adiponectin concentration was not altered after long-term exercise [10–14]. In contrast, Kriketos *et al.* [15] recently reported that fasting adiponectin levels increased by 260% above baseline values after 2–3 bouts of low to moderate intensity exercise. Although Hara *et al.* [13] performed a study on young obese men, no reports have been available on adiponectin concentra-

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tions in obese young women during prolonged and moderate intensity exercise.

Studies of the effects of regular exercise in adults showed that physical training resulted in decreased leptin concentrations [16, 17]. It has been reported that regular exercise decreased TNF-α levels, and may contribute to the improvement in glucose metabolism [18].

In order to study the effect of exercise in obese young women, we attempted to determine the metabolic parameters and circulating levels of adipokines, including adiponectin, leptin, and TNF-α before and after a single bout of prolonged and moderate intensity exercise in obese young women.

Materials and Methods

Subjects

Ninety-six healthy Japanese young female students of Gumma Paz College, aged 18–23 years, participated in this study. Obesity was defined as body mass index (BMI) greater than 25 kg/m^2, according to the Japan Society for the Study of Obesity. Eight obese young women (BMI ≥25 kg/m^2) participated in the exercise program, and eight control subjects (mean BMI = 22 kg/m^2) participated in the follow-up study.

Criteria for participation in the present study included 1) no past history of cardiovascular disease, 2) no use of prescribed medicine, 3) no history of smoking, and 4) no regular exercise. This study was approved by the Gumma Paz College Ethics Committee, and each subject gave their written informed consent.

Anthropometric measurement

Before and after the training program, all subjects underwent anthropometric measurements (body weight, BMI and body composition). Body fat mass was measured by the bioelectrical impedance method [19]. The validity of segmental bioelectrical impedance analysis has been demonstrated in obese women [20].

Exercise performance test

Participants underwent a cycle ergometer (Conbi-aerobic 75XLII, Tokyo, Japan) ramp exercise test (20 watt · min^{-1}) to determine Vo_2max after 3 min rest on the ergometer and a 3 min 0 watt warm-up. Vo_2max was measured with AE-300S Aero-monitor (Minato Medical Science Inc., Japan). The electrocardiogram and heart rate were continuously monitored with a Life-scope 8 (Nihon Koden, Tokyo, Japan) throughout the ramp exercise test. Perceived exertion was rated every minute using the Borg scale. Validation of attainment of Vo_2max satisfied two of the following four criteria (American College of Sports Medicine): 1) an oxygen uptake plateau despite increasing exercise intensity (≤150 ml · min^{-1}), 2) respiratory exchange ratio ≥1.10, 3) maximal heart rate within 10 beats · min^{-1} of the age-predicted maximal value, and 4) Borg scale = 10.

Blood sampling and biochemical measurements

Blood samples were drawn from the median cubital after a 12 h overnight fast. The blood samples were distributed to individual tubes, and each sample was taken after centrifugation at 3,000 rpm for 15 min. All samples were immediately frozen at –80°C and stored until measurement. Assays for total-cholesterol (T-cho), triglyceride (TG), high-density lipoprotein cholesterol (HDL-cho), hs-CRP and glucose were performed in a commercial laboratory (Mitsubishi BCL, Tokyo, Japan). Adiponectin was measured by ELISA [4], using a human adiponectin ELISA kit (Otsuka Pharmaceutical, Tokyo, Japan). Leptin and insulin were determined by RIA (Cosmic Corp., Tokyo, Japan). TNF-α was measured by ELISA (Biosource International, Camarillo, CA, USA).

Insulin resistance in the fasting state was examined by homeostasis model assessment (HOMA-R) using the following formula: fasting plasma glucose (mg · dl^{-1}) × fasting plasma insulin (μU · dl^{-1}) 405^{-1} [21].

Lifestyle management

Since Gumma Paz College of Nursing is a boarding school, all students are required to live in the college dormitories. Students have meals that provide an average of 1925 kcal/day. The study was started at the beginning of the college term in August 2004. Health-promoting lifestyle profile-scale (L-scale) was assessed using Breslow and Enstrom's health-promoting lifestyle profile [22], which has been used in several recent investigations of health-promoting behavior in African-American and European-American adults [23].

Exercise training

The obese subjects performed endurance exercises more than 30 min four to five times per week. The exercise regimen combined fast slope walking, slope jogging, dumbbells, stretching, leg cycling, and jumping rope with the preferred exercise for each subject. The exercise program was performed for 7 months. Exercise intensity was set at the 60–70% HR-reserve, because the aim of this program was to improve the fat metabolism. During exercise, participants had a wristwatch type heart rate monitor (WAH-55, WATEX, Gunma, Japan) at the target heart rate corresponding to the 60–70% HR-reserve in a previous exercise performance test.

The estimated energy consumption was 400–500 kcal. While the subjects participated in training, the authors carried out medical checkups to confirm that all subjects were in good health. If a reduction of daily training activity was noted, subjects were advised to increase their daily training activity.

Statistical analyses

All values are expressed as mean ± SD. The effects of training on each variable were evaluated by Student's paired *t*-test. Correlation between plasma adiponectin level and other parameters was determined by Pearson's correlation. All statistical analyses were performed using SPSS version 8.0.

Results

The correlation coefficients of adiponectin and metabolic parameters in 96 healthy young women at the beginning of the study are shown in Table 1. Adiponectin levels exhibited a significant negative correlation with body weight ($r = –0.32$, $p<0.05$), BMI ($r = –0.26$, $p<0.05$), %Fat ($r = –0.33$, $p<0.05$) and leptin ($r = –0.28$, $p<0.05$), and a significant positive correlation with L-scale ($r = 0.33$, $p<0.05$), Vo_2max ($r = 0.34$, $p<0.05$), and HDL-cho ($r = 0.35$, $p<0.05$).

The characteristics of obese group and control group at the beginning of the study are shown in Table 2. In obese subjects, body weight ($p<0.01$), BMI ($p<0.01$), %Fat ($p<0.05$), body fat mass ($p<0.05$), lean body mass ($p<0.05$), hs-CRP ($p<0.01$), leptin ($p<0.01$), and TNF-α ($p<0.01$) were significantly higher, and L-scale ($p<0.01$), and adiponectin ($p<0.01$) were lower than those in control subjects.

Effects of exercise training program on metabolic

Table 1. Correlation coefficients of adiponectin and metabolic parameters in 96 healthy young women at the beginning of the study

Body weight	–0.32	*
BMI	–0.26	*
%Fat	–0.33	*
Body fat mass	–0.35	
L-scale	0.33	*
Vo_2max	0.34	*
T-cho	–0.11	
TG	–0.21	
HDL-cho	0.35	*
hs-CRP	–0.21	
FPG	–0.11	
Insulin	–0.22	
HOMA-R	–0.22	
Leptin	–0.28	*
TNF-α	–0.12	

BMI: Body mass index, %Fat: Percentage of body fat, L-scale: Lifestyle profile-scale, T-cho: Total cholesterol, TG: Triglyceride, HDL-cho: HDL cholesterol, hs-CRP: high sensitivity C-reactive protein, FPG: Fasting plasma glucose, HOMA-R: Homeostasis model assessment, TNF-α: Tumor necrosis factor-α
* $p<0.05$

Table 2. Characteristics of obese group and control group at the beginning of the study

Characteristics	Obese (n = 8)	Control (n = 8)	Significance (p)
Age (years)	18.0 ± 1.0	18.0 ± 1.5	NS
Body weight (kg)	72.5 ± 6.9	55.0 ± 2.3	<0.01
BMI (kg/m^2)	29.5 ± 2.7	21.9 ± 3.2	<0.01
%Fat (%)	29.8 ± 0.9	22.5 ± 8.9	<0.05
Body fat mass (kg)	21.7 ± 2.1	12.2 ± 6.5	<0.05
Lean body mass (kg)	51.0 ± 4.9	42.5 ± 4.9	<0.05
L-scale (point)	3.5 ± 1.2	6.0 ± 1.2	<0.01
Vo_2max (ml/kg/min)	28.8 ± 10.2	32.0 ± 11.2	NS
T-cho (mg/dl)	187.8 ± 25.4	140.5 ± 15.5	NS
TG (mg/dl)	126.9 ± 22.9	82.6 ± 13.5	NS
HDL-cho (mg/dl)	44.1 ± 10.2	66.3 ± 12.1	NS
hs-CRP (mg/l)	0.15 ± 0.01	0.05 ± 0.02	<0.01
FPG (mg/dl)	95.6 ± 8.6	87.6 ± 10.5	NS
Insulin (μU/ml)	4.9 ± 1.1	4.3 ± 1.2	NS
HOMA-R	1.3 ± 0.2	0.93 ± 0.7	NS
Leptin (ng/mL)	16.4 ± 4.6	6.7 ± 1.2	<0.01
Adiponectin (μg/mL)	2.4 ± 1.3	8.3 ± 1.5	<0.01
TNF-α (pg/mL)	7.6 ± 2.3	2.3 ± 0.9	<0.01

Data are means ± SD. NS: not significant

parameters and adipokines are shown in Table 3. In obese subjects, exercise decreased body weight ($p<0.05$), BMI ($p<0.05$), %Fat ($p<0.05$), body fat mass ($p<0.05$), lean body mass ($p<0.05$), hs-CRP ($p<0.05$), leptin ($p<0.05$) and TNF-α ($p<0.01$), and increased L-scale ($p<0.05$), Vo_2max ($p<0.05$), HDL-cho ($p<0.05$) and adiponectin ($p<0.01$). As shown in Fig. 1, the exercise increased adiponectin level by 42.8%, decreased leptin level by 25%, and TNF-α level by 36.8%. In control subjects, exercise decreased %Fat ($p<0.05$) and body fat mass ($p<0.05$), and increased Vo_2max ($p<0.05$). Other parameters did not change significantly after exercise in control subjects.

Discussion

The present study demonstrated that adiponectin levels were negatively correlated with body weight, BMI, %Fat and leptin, and positively correlated with L-scale, Vo_2max and HDL-cho in 96 healthy young women. The longitudinal intervention study of a 7-month moderate intensity exercise regimen resulted in a decrease in circulating leptin and TNF-α, and an increase in circulating adiponectin in 8 obese young women. Because obese subjects and control subjects had the same meals of approximately 1925 kcal/day, the changes of metabolic parameters observed in obese subjects were

Table 3. Effects of exercise training program on metabolic parameters and adipokines

Characteristics	Obese (n = 8)		p value	Control (n = 8)		p value
	Before	After		Before	After	
Body weight (kg)	72.5 ± 6.9	64.5 ± 4.1	<0.05	55.0 ± 2.3	53.2 ± 2.5	NS
BMI (kg/m^2)	29.5 ± 2.7	26.3 ± 5.1	<0.05	21.9 ± 3.2	21.8 ± 2.9	NS
%Fat (%)	29.8 ± 0.9	25.6 ± 4.6	<0.05	22.5 ± 8.9	18.5 ± 3.2	<0.05
Body fat mass (kg)	21.7 ± 2.1	16.5 ± 2.3	<0.05	12.4 ± 6.5	9.9 ± 4.2	<0.05
Lean body mass (kg)	50.3 ± 4.9	48.2 ± 8.5	<0.05	42.5 ± 4.9	43.5 ± 3.2	NS
L-scale (point)	3.5 ± 0.5	5.0 ± 0.5	<0.05	6.0 ± 1.2	7.0 ± 0.5	NS
Vo_2max/BW (ml/kg/min)	28.8 ± 2.5	32.5 ± 1.5	<0.05	32.0 ± 11.2	37.5 ± 2.2	<0.05
T-cho (mg/dl)	187.8 ± 25.4	174.2 ± 12.3	NS	140.5 ± 15.5	121.5 ± 12.2	NS
TG (mg/dl)	126.9 ± 22.9	112.6 ± 10.5	NS	82.6 ± 13.5	80.6 ± 10.2	NS
HDL-cho (mg/dl)	44.1 ± 10.2	55.0 ± 6.5	<0.05	66.3 ± 12.1	69.4 ± 4.5	NS
hs-CRP (mg/l)	0.15 ± 0.01	0.07 ± 0.03	<0.05	0.05 ± 0.02	0.06 ± 0.28	NS
FPG (mg/dL)	95.6 ± 8.6	90 ± 10.2	NS	87.6 ± 10.5	89.0 ± 1.5	NS
Insulin (μU/mL)	4.9 ± 1.1	4.5 ± 2.1	NS	4.3 ± 1.2	4.1 ± 2.5	NS
HOMA-R	1.3 ± 0.2	1.0 ± 0.8	NS	0.93 ± 0.7	0.88 ± 1.6	NS
Leptin (ng/mL)	16.4 ± 4.6	12.3 ± 5.4	<0.05	6.7 ± 1.2	6.5 ± 2.2	NS
Adiponectin (μg/mL)	2.4 ± 1.3	4.2 ± 1.2	<0.01	8.3 ± 1.5	8.2 ± 2.3	NS
TNF-α (pg/mL)	7.6 ± 2.3	4.8 ± 1.2	<0.01	2.3 ± 0.9	2.1 ± 1.4	NS

Data are means ± SD. NS: not significant

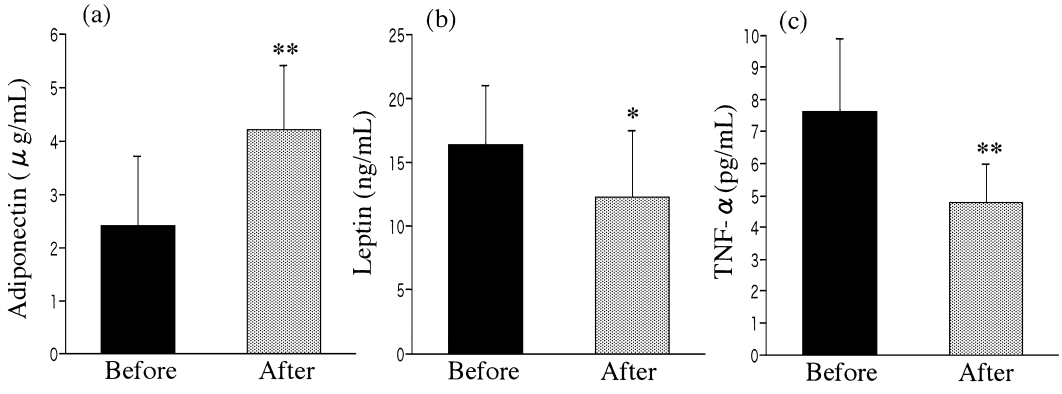

Fig. 1. Concentrations of adiponectin (a), leptin (b) and TNF-α (c) before and after the exercise program in obese young women. Each bar represents mean ± SD. * P<0.05 and ** P<0.01 compared with the concentrations before the exercise.

likely the results of the 7-month exercise program in the present study.

It is suggested that adiponectin may act as an anti-atherosclerotic factor not only through direct effects on vascular endothelial cells, but also through improving insulin resistance and lipid metabolism [24]. It has been reported that adiponectin levels are decreased in young and adolescent subjects who are obese [25–28]. The present results also demonstrated that circulating adiponectin levels were significantly decreased in the obese young women. Adiponectin levels have also been found to decline concurrently with progression of insulin resistance [29], and to decrease in middle-aged subjects who have obesity, cardiovascular risk factors, coronary artery disease or type 2 diabetes [30–32]. Although it is not clear whether long-standing low adiponectin levels from an early age has an adverse effect, it appears of great importance to elucidate the mechanisms underlying the low adiponectin levels not only in middle-aged subjects but also in young subjects to prevent lifestyle-related diseases. A few studies have been conducted on the relationship between adiponectin levels and aerobic exercise training [10, 11], and it was reported that the exercise training was not able to increase adiponectin levels in obese young men [13, 33]. However, the effect of aerobic exercise on adiponectin levels in obese young women is not known. Our present study demonstrated that prolonged and moderate intensity exercise increased adiponectin level by 42.8% in obese young women. Therefore, the effect of exercise on adiponectin levels in obesity may be different between male and female subjects. Adiponectin levels have been reported to be inversely correlated with central adipose tissue stores [34, 35] and positively correlated with subcutaneous adipose tissue [36]. Thus, it is possible that loss of visceral fat has resulted in increased adiponectin levels concomitante with body weight reduction in obese young women in the present study. The present results suggested that suppressing excess body fat tissue is important for preventing reduction of adiponectin levels in young women.

In the present study, exercise-induced body fat reduction was significantly correlated with other adipokine levels, such as leptin and TNF-α. Prolonged and moderate intensity exercise decreased leptin level by 25.0%, and decreased body weight, %Fat and body fat mass by 11%, 14.1% and 24.0%, respectively, in obese young women. This is in agreement with a number of studies which have shown the decrease in leptin levels in response to weight loss [37]. The present study demonstrated that prolonged and moderate intensity exercise decreased TNF-α level by 36.8% in obese young women. Fat cells produce and secrete TNF-α, which interacts with adiponectin to mutually inhibit each other's production in adipose tissue and function in skeletal muscle [38]. The present results further support the concept of the existence of an interrelationship between adipokine levels and body fat tissue.

Recently, hs-CRP has been reported to be a useful marker for atherosclerosis [9]. Prolonged and moderate intensity exercise may prevent atherosclerotic cardiovascular disease. In the present study, hs-CRP was increased in obese young women compared with control subjects, and hs-CRP was decreased after the exercise program. IL-6 is secreted by fat cells, and induces hepatic production of CRP [9]. Therefore, IL-6, which increases hepatic CRP production, might be increased in obese young women in the present study.

The present study has limitations when interpreting the results, since the number of the subjects studied was relatively small. It is therefore necessary to study the effect of prolonged and moderate intensity exercise on metabolic parameters in a larger number of obese subjects to confirm the present results.

In conclusion, the present study suggests that changes in circulating adipokine levels are involved in the improvement of the metabolic state by exercise and may be useful markers for evaluation and prescription of exercise in obese young women. Further studies are required to investigate the causal relationships between exercise and changes in adipokine levels in obese young women.

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