Decreased Plasma Adiponectin Levels in Young Obese Males

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Plasma adiponectin levels are reduced in middle-aged obesity and in patients with type 2 diabetes and coronary artery disease. The purpose of this study was to investigate the effects of early-aged obesity on plasma adiponectin level. Twenty-six male college students (19.2 ± 1.1 years, obese group: $n = 15$, [body mass index > 25 , percent body fat $> 25\%$], non-obese group: $n = 11$) participated in the present study. We measured anthropometric parameters and plasma adiponectin and leptin level. Plasma adiponectin levels in the obese group were significantly lower than those in the non-obese group (obese: 4.7 ± 2.0 $\mu\text{g/ml}$, non-obese: 6.8 ± 2.2 $\mu\text{g/ml}$, $p < 0.05$). On the other hand, plasma leptin levels in the obese group were significantly higher than those in the non-obese group (obese: 8.4 ± 3.2 ng/ml , non-obese: 2.6 ± 2.1 ng/ml , $p < 0.001$). Plasma adiponectin levels were significantly correlated with body weight ($r = -0.415$, $p < 0.05$) and percent body fat ($r = -0.412$, $p < 0.05$). Stepwise multiple regression analysis revealed that percent body fat was a significant independent predictor of plasma adiponectin level ($r = 0.406$, $p < 0.05$). These results show that obesity is associated with reduced plasma adiponectin even in young subjects. *J Atheroscler Thromb*, 2003; 10: 234–238.

Key words: Adiponectin, Leptin, Early aged obesity, Body fat

Introduction

Obesity is defined as an accumulation of excess body fat, and is one of the risk factors for lifestyle-related diseases such as type 2 diabetes, hypertension, and coronary artery disease (CAD) (1). Adipose tissue has long been misconstrued as a mere tissue of fat storage. In recent studies, however, it was reported that the character of regional fat is heterogeneous with respect to lipid and glucose metabolism (2), and adipose tissue secretes a variety of biologically active molecules (adipocytokine), including leptin (3), tumor necrosis factor- α (TNF- α) (4),

plasminogen activator inhibitor-1 (PAI-1) (5) and adiponectin (6). By secreting adipocytokines, adipose tissue plays active roles in energy homeostasis and other physiological functions (7, 8).

Functions of adiponectin include reducing TNF- α -induced macrophage attachment to endothelial cells, and suppressing the secretion of TNF- α from human monocyte-macrophages (6). These functions of adiponectin may protect against vascular injury as an early event in the atherosclerotic process (9). Furthermore, reduction in plasma levels of adiponectin is related to the development of insulin resistance (10). In fact, plasma adiponectin levels are decreased in patients with type 2 diabetes and CAD (9, 11, 12). Moreover, plasma adiponectin levels are lower in middle-aged obese than in non-obese subjects (6). Thus, reduced adiponectin in obesity plays an important role in the development of insulin resistance and vascular disorders.

Lifestyle-related disease is induced by excessive eat-

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ing or salt intake, lack of exercise, and smoking history from an early age. Therefore, early lifestyle might affect plasma adiponectin levels. Importantly, an inverse association between adiponectin and obesity was reported among middle-aged subjects (6, 11, 12). It is important to examine whether such a relation is present in young people, because young obese subjects may be exposed to potentially atherosclerotic conditions longer than older subjects. Only one study by Kazumi *et al.* (13) reported the adiponectin concentration in young people. Therefore, in the present study, we investigated the relation between early aged obesity and plasma adiponectin levels in young obese and non-obese subjects.

Methods

Subjects

Twenty-six sedentary male subjects (mean [$\pm$ S.D.] age, 19.2 ± 1.1 years) participated in this study. In advance, we measured blood pressure, plasma levels of insulin, triglyceride, total-cholesterol, HDL-cholesterol, and fasting blood sugar to confirm that no patients with diabetes, hyperlipidemia or hypertension participated in this study. None of the subjects had a history of smoking.

In this study obesity was defined as a body mass index (BMI) greater than 25 according to the Japan Society for the Study of Obesity (2000), and with it the subjects were separated into two groups (obese group: $n=15$, non-obese group: $n=11$) (Table 1). Written informed consent was obtained from each individual.

Biochemical and anthropometric measurements

Plasma adiponectin levels were determined by an enzyme-linked immunosorbent assay (ELISA) system as described previously (6). Plasma leptin levels were measured with a radioimmunoassay kit (Human Leptin RIA Kit, Cosmic Co. Ltd, Tokyo, Japan). Body composition including percent body fat, fat mass, percent body muscle and muscle mass was measured by the bioelectrical impedance method (Muscle- α , Art Heaven 9 Co. Ltd, Kyoto, Japan).

Statistical analysis

Values were presented as means $\pm$ SD. Difference between groups was examined by the unpaired Student's *t* test. Linear relations among variables were tested using Pearson's correlation coefficients. Stepwise multiple regression analysis was performed that included body weight, BMI, percent body fat, body fat mass and muscle volume as independent variables and plasma adiponectin and leptin level as dependent variables, respectively. *P* values < 0.05 were considered significant.

Results

Plasma leptin level and correlation with body composition

Table 1 shows the results of biochemical and anthropometric measurements in the obese and non-obese groups. Mean plasma leptin levels in the obese group were significantly higher than that in the non-obese group (Fig 1). Plasma leptin levels were significantly correlated with body weight ($r = 0.811$, $p < 0.001$), percent body fat ($r = 0.878$, $p < 0.001$) (Fig. 2), body fat mass ($r = 0.881$, $p < 0.001$), BMI ($r = 0.871$, $p < 0.001$), and muscle volume ($r = 0.524$, $p < 0.01$). Stepwise multiple regression analysis revealed that body fat mass was independently correlated with plasma leptin level ($r^2 = 0.805$, $p < 0.001$).

Plasma adiponectin level and correlation with body composition

Plasma adiponectin levels in the obese group were significantly lower than that in the non-obese group (Fig. 1). Moreover, plasma adiponectin levels were negatively but significantly correlated with body weight ($r = -0.415$, $p < 0.05$), percent body fat ($r = -0.412$, $p < 0.05$) and body fat mass ($r = -0.416$, $p < 0.05$) (Fig. 2). No significant correlation was observed between plasma adiponectin level and BMI ($r = -0.360$) or muscle volume ($r = -0.346$). Stepwise multiple regression analysis revealed that percent body fat was independently correlated with plasma adiponectin level ($r^2 = 0.165$, $p < 0.05$). No significant cor-

Table 1. Physical characteristics and adipocytokine levels of subjects.

		obese ($n = 15$)		non-obese ($n = 11$)		<i>P</i> value
		Mean	S.D.	Mean	S.D.	
Age	years	19.5	1.0	18.8	1.2	N.S.
Height	cm	172.6	6.9	171.8	5.0	N.S.
Weight	kg	93.0	13.8	64.6	5.0	<0.001
BMI	kg/m ²	31.2	4.1	22.0	2.3	<0.001
% body fat	%	28.7	3.3	13.7	3.5	<0.001
Body fat mass	kg	27.0	6.8	9.0	2.7	<0.001
Muscle volume	kg	30.3	5.6	25.4	2.7	0.010
Adiponectin	μ g/ml	4.7	2.0	6.5	2.2	0.033
Leptin	ng/ml	8.4	3.2	2.6	2.1	<0.001

P value are analyzed using unpaired *t* test.

Fig. 1. Plasma levels of adiponectin and leptin in obese (●: $n = 15$) and non-obese (○: $n = 11$) subjects.

*: $p < 0.05$, **: $p < 0.001$

Fig. 2. **A:** Correlations between plasma level of adiponectin and body weight ($r = -0.415$, $p < 0.05$) and %body fat ($r = -0.412$, $p < 0.05$) in obese and non-obese subjects. **B:** Correlations between plasma level of leptin and body weight ($r = 0.811$, $p < 0.001$) and %body fat ($r = 0.878$, $p < 0.001$) in obese and non-obese subjects.

relation was observed between plasma adiponectin and leptin.

Discussion

In this study, in young subjects, plasma adiponectin levels were significantly reduced in obese subjects compared with non-obese subjects, although no subjects had diabetes, hyperlipidemia or hypertension. Previous studies about adiponectin investigated middle-aged subjects with hyperinsulinemia or CAD, and obesity (9, 11, 12), reported these subjects showed low plasma adiponectin levels. However, there have been few studies about plasma level of adiponectin in young subjects. Since young obese males have low adiponectin levels, obesity is one of the risk factors to reduce the plasma adiponectin levels in young subjects.

It was reported that plasma adiponectin levels in middle-aged obese subjects were lower than that in non-obese subjects, although adiponectin is secreted only from adipose tissue (6). The mechanism of reduction about plasma adiponectin levels in patients with obesity has not been clearly determined. However, in middle-aged subjects, the increase of plasma adiponectin levels accompanied a reduction of body weight by gastric surgery (14, 15) or dietary therapy (11, 16). On the other hand, there was no significant change in plasma adiponectin levels with exercise training that did not alter body mass (15). In the present study, plasma adiponectin levels were negatively correlated with percent body fat and body fat mass, and percent body fat was the only independent variable on stepwise multiple regression analysis. Thus, body composition may be one of the important factors adjusting plasma adiponectin levels.

In a previous study, plasma levels of leptin in young subjects were correlated with %body fat (17). Moreover, body fat mass, calculated insulin resistance (HOMA-ratio) and triglyceride were significant determinants of leptin concentration by multiple regression analysis (18). In the present study, plasma leptin levels were increased in obese subjects, and were positively correlated with body fat mass. Leptin also affected insulin sensitivity and development of hypertension (19–21), and plasma leptin levels were decreased by weight reduction (22, 23). Obese subjects showed low adiponectin levels and high leptin levels compared with non-obese subjects in the present study.

It was unclear if these cytokines will affect the development of diabetes and atherosclerosis in the future. However, Hotta *et al.* (10) reported that plasma adiponectin levels were reduced in parallel with the progression of insulin resistance in rhesus monkeys. It was also reported that plasma adiponectin levels were decreased in obesity and in patients with diabetes in middle-aged sub-

jects (6, 11, 12). Therefore, a long standing low adiponectin level from an early age may cause insulin sensitivity and atherosclerosis. Further investigations will be needed about the effects of combinations of exercise training and dietary therapy to plasma levels of adiponectin and leptin in young obese subjects.

In conclusion, plasma adiponectin levels were already reduced in young male obese subjects, and were correlated with body fat. The present findings suggest that obesity in young people causes an atherogenic adipocytokine profile similar to that in middle-aged subjects. This observation has a potential importance for the prevention of atherosclerosis.

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