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Relationship between serum adiponectin level and lipid composition in each lipoprotein fraction in adolescent children

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Abstract

The association of lipid composition in each lipoprotein fraction with adiponectin level in relation to body fatness was investigated. The subjects were 283 children (144 boys and 139 girls) aged 11.6 years (S.D. 1.5). Cholesterol (C) and triglyceride (TG) levels in each lipoprotein fraction were measured by a combination of agarose gel electrophoresis and differential staining. Adiponectin level was not significantly different between girls and boys. In simple regression analyses, an association of adiponectin level with lipoprotein lipid profile was shown only in girls, and not in boys at all. In girls, very low-density lipoprotein (VLDL)-C, low-density lipoprotein (LDL)-C, VLDL-TG and LDL-TG were negatively correlated with adiponectin level, and high-density lipoprotein (HDL)-C and HDL-C/TG ratio were positively correlated. Multiple regression analyses including adiponectin level and body mass index (BMI) as predictors for the lipoprotein lipid profile demonstrated that adiponectin level was a significant independent predictor of VLDL-TG, LDL-C, LDL-TG, HDL-C and HDL-C/TG ratio. In conclusion, adiponectin level correlates with lipoprotein lipid profile independent of body fatness in adolescent girls.

Keywords: Adiponectin; Lipoprotein; Lipid composition; Children; Body fatness

1. Introduction

Adipose tissue has recently been shown to secrete bioactive proteins, called adipocytokines, that may regulate glucose, lipid metabolism and vascular function [1–3]. Adiponectin is an adipocytokine produced exclusively by adipocytes. This protein has potential anti-diabetic, anti-atherosclerotic and anti-inflammatory properties [4]. However, unlike other adipocytokines, serum adiponectin level is decreased in obese and diabetic subjects. The mechanisms of the physiological functions of adiponectin have not been sufficiently determined. Recent studies in the adiponectin knockout mouse [5] and in subjects with a genetic background of diabetes [6] suggest that adiponectin's biological effects may be independent of fat mass and insulin resistance.

Several clinical studies showed that adiponectin level was negatively correlated with serum triglycerides and small dense low-density lipoprotein and positively correlated with high-density lipoprotein [7,8]. These relationships were independent of intra-abdominal fat and degree of insulin resistance [9,10]. Moreover, a cross-sectional and intervention trial suggested that changes in adiponectin level after weight loss directly regulate improvements of lipid metabolism and that this effect is independent of fat mass, weight loss and insulin sensitivity [11].

However, the association between adiponectin level and each lipoprotein with respect to its lipid composition has not been investigated. Each lipoprotein fraction is composed of subclasses that vary in size, composition and atherogenicity [12]. These subclasses are differentially associated with body fatness, which have been found to be associated with the large triglyceride (TG)-rich very low-density lipoprotein (VLDL), small dense high-density lipoprotein (HDL) and small dense

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low-density lipoprotein (LDL) [13]. The lipid levels and composition of each lipoprotein subclass may be important in atherosclerosis. The aims of this study were to examine the association of lipid composition in each lipoprotein fraction with adiponectin level, and to analyze these associations in relation to body fatness.

2. Materials and methods

The subjects were 283 children (144 males and 139 females) aged 11.6 years (S.D. 1.5), who participated in school health checks in 2002. Two schools were randomly selected. Standing height and body weight were measured and body mass index (BMI) (kg/m^2) was obtained. Skinfolds were measured at the triceps and the subscapula using a skinfold caliper. The percent body fat (BF%) and fat mass (kg) were obtained by a bioelectrical impedance method using an Impimeter III (Sekisui Co., Tokyo, Japan). Blood sampling was performed in the morning after 12 h fast. Total cholesterol (TC) and TG levels were measured by enzymatic methods. All children were free from disease except for hyperlipidemia and obesity. Informed consent was obtained from the children and their parents prior to participation in this study.

Cholesterol (C) and TG levels in each lipoprotein fraction were measured by a combination of agarose gel electrophoresis and differential staining reported by Kido et al. [14]. Sample application (1 μl), electrophoresis (400 V, 15 min), staining, drying and densitometric scanning (570 nm) were performed automatically using a Rapid Electrophoresis System (REP, Helena Laboratories, Beaumont, TX, USA). It was reported in adults that the lipid contents in each lipoprotein obtained by the REP method were highly correlated with those of ultracentrifugation method [14]. We also confirmed the validation of the method in children (data not shown). Serum adiponectin level was measured by ELISA as reported by Arita et al. [15].

2.1. Statistical analysis

All data were expressed as mean ± S.D. Differences in mean values were analyzed by Mann–Whitney *U*-test. The correlation coefficients between two variables were determined by simple regression analysis. Multiple regression analyses were carried out to determine variables (BMI and adiponectin) explaining the lipid composition of each lipoprotein fraction. A *p*-value less than 0.05 was considered to indicate statistical significance. All statistical analyses were conducted using the statistical package STATVIEW (ver. 4.5; Abacus Concepts, Berkeley, CA, USA).

3. Results

The characteristics of the subjects and C and TG levels in each lipoprotein fraction are shown in Table 1. In the present subjects, we found 12 children (4.2%; 8 males and 4 females) with BMI over 25 kg/m^2, and no child with glycosuria. According to the criteria of normal serum lipid levels for Japanese children [16], 11 children (3.9%; 4 males and 7 females) had hypercholesterolemia (>220 mg/dl), 73 (25.8%; 32 males and 41 females) had borderline TC level (190–220 mg/dl) and 43 (15.2%; 16 males and 27 females) had hypertriglyceridemia (>140 mg/dl). Girls had higher levels of VLDL-TG ($p = 0.0253$), LDL-TG ($p < 0.0001$) and LDL-C ($p = 0.0228$) than boys. VLDL-C/TG ratio and LDL-C/TG ratio were significantly lower in girls than in boys ($p = 0.0193$ and 0.0099, respectively). Adiponectin level was higher in girls than in boys, although the difference was not statistically significant ($p = 0.0511$).

In simple regression analysis (Table 2), adiponectin level was negatively associated with BMI and fat mass in boys, and with BMI and the sum of skinfold thicknesses (subscapular and triceps) in girls. An association of adiponectin level with lipoprotein lipid profile was shown only in girls, and not in boys at all. In girls, as well as in boys, adiponectin level had no correlation with TC level. However, VLDL-C ($r = -0.213, p = 0.0122$) and LDL-C ($r = -0.191, p = 0.0246$) were negatively correlated with adiponectin level, and HDL-C was positively correlated ($r = 0.216$, $p = 0.0108$). On the other hand, adiponectin level showed a negative correlation with serum TG level ($r = -0.229$, $p = 0.007$), as well as with VLDL-TG ($r = -0.230$, $p = 0.0065$) and LDL-TG ($r = -0.169, p = 0.0473$) in girls. HDL-C/TG ratio correlated positively with adiponectin level ($r = 0.174$, $p = 0.0408$) in girls.

Multiple regression analyses including adiponectin level and BMI as predictors for the lipoprotein lipid profile were performed in girls (Table 3). In these models, adiponectin level was a significant independent predictor of VLDL-TG, LDL-C, LDL-TG, HDL-C and HDL-C/TG ratio.

4. Discussion

The present study demonstrated that in girls, serum adiponectin level may modulate lipoprotein lipid levels and composition, and is independent of BMI, although BMI was negatively correlated with adiponectin level.

Increased adipocytokines released from omental tissue may play an important role in lipid metabolism in visceral obesity. Experimental data suggest that TNF-alpha decreases the expression of LPL and stimulates adipose tissue lipolysis, thereby potentially delaying catabolism of VLDL and increasing the hepatic supply of NEFAs and hepatic secretion of VLDL [17]. IL-6 also inhibits LPL expression and increases hepatic triglyceride synthesis [18]. However, in a human study on the relationships between adipocytokines and markers of triglyceride-rich lipoprotein metabolism, a low adiponectin level was highly predictive of increased plasma apoB-48, apoC-III, remnant-like particle cholesterol and TG levels, and increased IL-6, TNF-alpha and resistin