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Influence of serum leptin levels on future overweight risk in Korean children

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KEYWORDS
Childhood overweight;
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Metabolic risk score;
Follow-up BMI

Abstract *Background and aims:* Leptin is an important regulator of energy metabolism. It is considered to be positively related to body adiposity and metabolic disorders in obese adults and children. The purpose of this study was to evaluate the relationship between baseline circulating leptin, insulin and adiponectin levels and future overweight and metabolic risks in a paediatric population-based cohort.
Methods and results: First-grade students, who entered elementary school at age 7 years in Gwacheon, a Korean city, were enrolled in this cohort study, and followed from 1st grade to 5th grade. Annual physical examinations from 2005 to 2009 were performed. In 2006, the levels of serum glucose, insulin, leptin and adiponectin and lipid profiles were examined. In 2008, the above parameters, except for adiponectin, were measured again in 381 children (202 boys and 179 girls) who participated. In 2006, 10.2% of the children were overweight (body mass index (BMI) $\geq$ 85th percentile), and after 2 years, an additional 3% became overweight. Compared with insulin and adiponectin, leptin was most highly associated with current and future BMI, and percent body fat. Boys in the highest tertile for initial leptin (T3) showed the highest prevalence of overweight and metabolic risk scores among three leptin tertile groups. Girls showed the same trends as boys. High initial leptin levels could be predictive of greater future BMI and metabolic risk score ($p < 0.001$).
Conclusion: These results suggest that elevated serum leptin concentrations among the childhood population could be a marker for future BMI and metabolic disorders.

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Introduction

Paediatric overweight is the most common health problem worldwide including Korea [1]. Childhood overweight could increase the risk of health problems such as insulin resistance and metabolic syndrome [2,3], as well as risks for the future development of adult obesity or cardiovascular disease [4]. Therefore, studies regarding early detection of childhood overweight and efficient prevention against future adult obesity are much needed.

In studies using adult subjects, body mass index (BMI) is used as a surrogate indicator of obesity. However, many studies have used multiple methods to define overweight in children such as gender- and age-specific cut-off points for BMI as described by Cole et al. [5]; the obesity index calculated using the ideal weight for height [6]; or gender- and age-specific BMI percentile chart based on the International Overweight Task Force standards or local reference data [7,8] because rapid growth in childhood should be considered. In the current study, overweight children were defined as those with a BMI for gender and age corresponding to $\geq$85th percentile, based on the child growth standards in Korea established by the Korean Center for Disease Control and Prevention (KCDC) [9].

In addition to anthropometric variables, leptin, adiponectin and insulin levels are strongly related to body fat or obesity [10,11]. Leptin secreted by adipose tissue plays a crucial role in regulating food intake and energy metabolism [12]. Cross-sectional and longitudinal studies have shown a positive relationship between serum leptin and obesity in adults and children [13–15]. While relatively few had function-altering genetic defects of the leptin receptor itself [16], the exacerbated fat accumulation in adipose tissues and subsequent hyperleptinaemia could cause leptin resistance in tissues including the hypothalamus, which may maintain energy balance positively [17]. Obesity could consequently affect the incidence of obesity-related metabolic disorder.

Although a recent study showed that high baseline serum leptin levels predict greater BMI and fat mass over time in children who are at high risk for adult obesity by virtue of their own overweight or because of their parents' overweight [18], the influence of leptin on future obesity in the general paediatric population is far less clear. Therefore, we conducted a prospective study on Korean early elementary students, who showed a relatively low prevalence of overweight, to determine the influence of serum leptin as a marker of future BMI and overweight status during childhood. The objective of this study was to investigate whether baseline leptin levels can predict future obesity and metabolic disorders in children.

Methods

Study population

This study was conducted as part of the Gwacheon Paediatric Cohort Study, which will follow this student cohort from their entry into elementary school at age 7 years to their graduation at age 13 years in Gwacheon City, Kyunggi Province, Korea. The objective of this paediatric cohort study was to identify early risk factors for obesity and associated metabolic diseases in urban Korean children. The sole inclusion criterion was being enrolled in the 1st grade, and no exclusion criteria were applied. At the year 2005, the physical examination data were obtained, but serum leptin level was not determined. At the year 2006, the 2nd year, there were 467 children in whom we obtained baseline leptin levels. At the year 2008, the 4th year, 381 students (202 boys and 179 girls) returned for the follow-up visit. These 381 children of the Gwacheon cohort were included in the present study. The longitudinal analysis of BMI variation could be done, as the physical examination data were also obtained at the years 2007 and 2009, with some missing data. Thus, we have 309 students (159 boys and 150 girls), 288 students (154 boys and 134 girls) and 349 students (184 boys and 165 girls), in the 1st, 3rd and 5th years, respectively.

This study was approved by the institutional review board of Inje University Seoul-Paik Hospital and KCDC. Informed consent was obtained from the children's parents.

Anthropometric measurements

Height was measured using an automatic stadiometer (DS-102; Jenix, Seoul, Korea). Weight was measured using a body composition analyser (BC418; Tanita, Tokyo, Japan). With the input data regarding height, age and gender, this bioelectrical impedance analysis (BIA) device provided both measurements of impedance and estimates of percent body fat. BMI was calculated as body weight divided by height squared ($kg \times m^{-2}$) and BMI *z*-score was calculated based on Korean reference data [9]. Waist circumference (WC) was measured at the midpoint between the lower border of the ribcage and the iliac crest using a non-elastic tape measure. Overweight children were defined as those with a BMI for age and gender corresponding to $\geq$85th percentile, based on the child growth standards in Korea [9]. Blood pressure was measured twice on the right arm using a mercury sphygmomanometer while the subject was resting in a seated position. From the year 2008, sexual maturity was assessed using the five-stage picture scale for the development of breast in girls and the development of genital in boys, according to Tanner [19].

Biochemical analyses

Blood samples were collected from an antecubital vein into vacutainer tubes between 0900 and 1100 h after a 12 h overnight fast. Within 30 min, aliquots of plasma and serum were separated and stored at $-80\ ^{\circ}C$ until further analysis. Triglyceride (TG) and high-density lipoprotein-cholesterol (HDL-C) levels were measured via enzymatic assays and an autoanalyser (model 7180; Hitachi, Tokyo, Japan). Fasting serum glucose was measured using the hexokinase method and a glucose analyser (model 7180; Hitachi). Concentrations of insulin, leptin and adiponectin were analysed within 1 month of serum storage. Because of change in the method of measurement, however, insulin level of the second stage was reanalysed in 2008. Fasting serum insulin was measured using a radioimmunoassay kit (Diagnostic