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Correlation between Serum Leptin Levels and BMI in Adults Residing in Pohang, Korea

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Abstract

Leptin is a small polypeptide hormone secreted primarily by adipocytes. Leptin regulates energy balance by decreasing food intake and increasing energy expenditure. This study investigated the relationships between serum leptin levels and BMI (body mass index) in 49 adults in Pohang, Korea. The subjects were 25 males and 24 females, aged 21 to 64 years attending an outpatient clinic at Handong University Sunlin Presbyterian Hospital. Values are given +/- the standard error of the mean. Our study shows that the serum leptin levels in these subjects were positively correlated with BMI. The leptin levels were higher in females (2.39+/-1.82 ng/mL) than in males (0.43+/-0.455 ng/mL), although lower than previously reported. We therefore compared the serum leptin levels from the male Korean subjects (BMI 24.3+/-0.74 kg/m^2) with serum from six British males with a similar BMI (23.4+/-1.48 kg/m^2). The serum leptin concentrations (1.76+/-0.76 ng/mL) were lower than that of plasma (4.28+/-1.66 ng/mL) in the British subjects. The serum leptin in the British subjects (1.76+/-0.76 ng/mL) was higher than that in the Koreans. There was no correlation between leptin levels and BMI in either male (slope 0.018±0.036, p=0.624) or female (slope 0.382±0.433, p=0.417) type 2 diabetic patients in Pohang, Korea. Taken together, our study shows that the serum leptin level in Koreans varies with the BMI, but is lower than that of BMI-matched British subjects.

Key words: body mass index (BMI), Pohang Korea, Britain, obese, leptin, type 2 diabetes

INTRODUCTION

During the last twenty years there has been a significant increase in the prevalence of obesity throughout the world, including Korea (1). Obesity is usually accompanied by related metabolic diseases such as dyslipidemia, type II diabetes, and cardiovascular diseases (2), consequently there is an increasing urgency for understanding more about the mechanisms that regulate the accumulation of adipose tissue.

Leptin, the 16 kD protein product of the ob gene (3), has been the object of much attention in obesity research. Leptin is mainly synthesized and secreted by adipocytes, and is thought to be involved in the regulation of energy balance by decreasing food intake and increasing energy expenditure (4-6). In animal studies, it has been shown that *ob/ob* mice (ob gene mutant mice that make non-functional leptin) exhibit hyperphagia, hypo-metabolic syndrome, insulin-dependent diabetes and obesity, but the administration of recombinant leptin into the mice reverses these phenomena by causing weight-loss by decreasing food intake and increasing energy expenditure (4-6). In humans, most obesity is associated with low responsiveness to endogenous leptin, termed leptin resistance; the administration of recombinant leptin to obese human subjects did not affect body weight (7,8). Since leptin is produced primarily in adipose tissue, the leptin concentration in the serum is positively related with the amount of body fat and reflects the amount of energy stored in adipose tissue (9,10). Few studies have investigated the effects of ethnicity on leptin concentration although certain ethnic groups are more or less affected by obesity than are others (11). Therefore, the role that leptin may play in the etiology of obesity in various ethnic groups is worthy of further investigation.

The relationship between leptin concentration and body mass index (BMI) among the Korean adult population in the Pohang region has not yet been studied. This study, therefore, investigated the correlation between serum leptin levels and BMI in an adult population in

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MATERIALS AND METHODS

Forty nine normal subjects, 25 males and 24 females, aged 21 to 64 years attending an outpatient clinic in Handong University Sunlin Presbyterian Hospital and twenty four diabetic patients, 17 males and 7 females, aged 21 to 60, diagnosed as type 2 diabetics at Handong University Sunlin Hospital with a record of previous treatment history were studied. Heights (m), weights (kg) and fasting leptin levels were measured.

Leptin analysis

Leptin analysis was performed by a solid phase sandwich ELISA based on the method of Hardie et al. (12). Briefly rabbit polyclonal IgG 2.5 mg/mL) raised against recombinant human leptin was immobilised on high affinity plates. After washing and blocking steps, wells were incubated with recombinant leptin standard (0.1 ~ 50 ng/mL) or test serum for 3 h at room temperature. Captured leptin was detected with biotynylated rabbit anti-leptin IgG (250 ng/mL), the signal enhanced with extravidin-peroxidase (1:4000) and visualized by the addition of the chromogenic substrate, tetramethylbenzidine. Optical densities were recorded at 450 nm on a plate spectrophotometer. Test samples were quantified from the leptin standard curve using a sigmoid fit of the data.

Statistics analysis

Linear regression was performed in Genstat 6th Edition (Release 6.1, Lawes Agricultural Trust, Rothamsted, Herts, UK) to investigate the relationship between leptin and BMI. Differences in intercepts and slopes were investigated by including country (or diabetes status) as factors in the regression analysis.

RESULTS AND DISCUSSION

Correlations of serum leptin levels with BMI in adults living in Pohang, Korea

Leptin levels were higher in females (2.39+/-1.82 ng/mL) than in males (0.43+/-0.46 ng/mL) but both were lower than in the small reference group of male and female British subjects (Fig. 1). In Korean males and females, the serum leptin level were positively correlated with BMI (Fig. 2A, B) accounting for 29.7% of the variance in females and 41.5% in males. The slopes were also significantly different from each other ($p<0.001$) and from zero (female, slope $\pm$ SE 0.296 ± 0.097, $p=0.006$; male, slope $\pm$ SE 0.079 ± 0.020, $p<0.001$). The higher level of serum leptin in females is in accordance with numerous previous studies (13). There are several reasons for this gender difference: firstly females have a higher fat mass than men: secondly there is a difference in fat distribution between the genders, women having more subcutaneous fat than men - leptin secretion rate is about twofold higher in subcutaneous than in the omental adipose tissue; thirdly within the subcutaneous depot mRNA levels are higher in women (14,15) indicating that differences may be due to the sex steroid concentrations and action (16).

Serum leptin levels of Korean subjects compared to BMI-matched British subjects

The serum leptin level of Korean subjects, however, seems to be lower than values previously reported for subjects on a western diet (17). This might be due to the lower detection value from our plate reader. We therefore compared the serum leptin levels from the male Korean subjects (BMI 24.3+/-0.74 kg/m^2) with serum from six British male subjects. As shown in Fig. 1B,

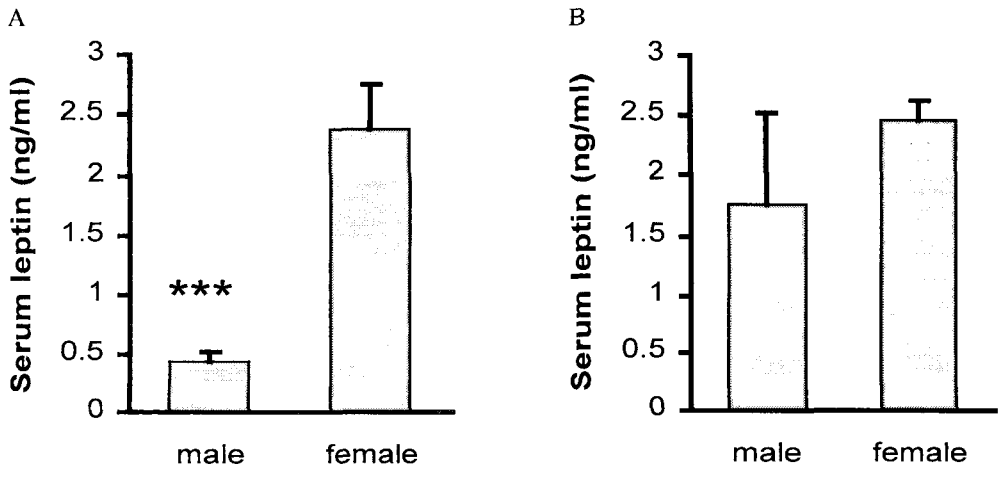

Fig. 1. Average serum leptin in male and female Koreans and Europeans.
A) Korean subjects, n=25 males, n=24 females ($^{***}p<0.001$), B) European reference subjects, n=6 males, n=3 females.

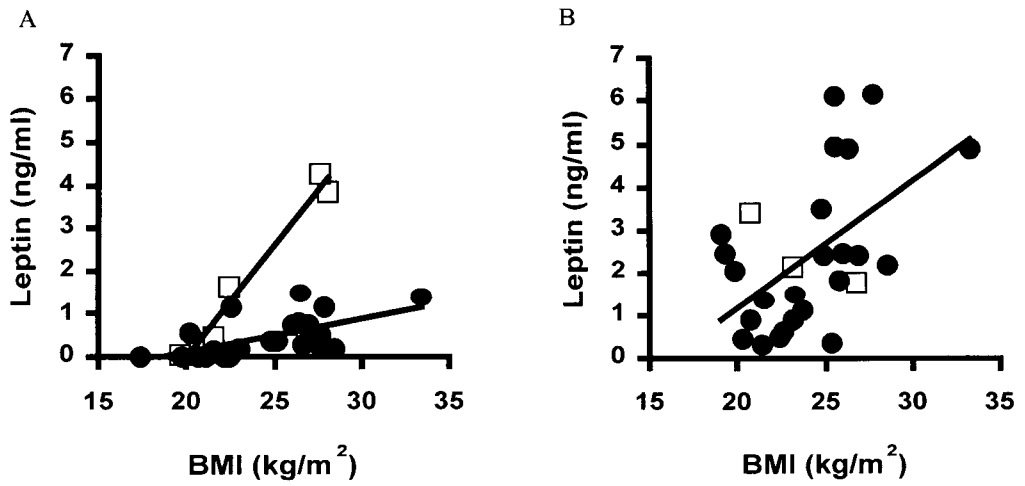

Fig. 2. Serum leptin and Body Mass Index (BMI) in Koreans (●). Values for the reference group of Europeans (□) are included for comparison. A) Korean males: n=25, leptin=-1.48+0.079BMI, R^2=0.415, slope $p<0.001$; British males: n=6, leptin=-10.13 +0.509BMI, R^2=0.97, slope $p<0.001$. Differences in slope between Korean and British males, n=31, $p<0.001$. B) Korean females: n=24, leptin=-4.74+0.296BMI, R^2=0.297, slope p=0.006; British female leptin values (n=3) are not significantly different from Koreans for this small reference group. Difference in slope between Korean males and females, n=49, p=0.024.

the serum leptin level in the British male subjects (1.76+/-0.76 ng/mL) was significantly higher than in Korean males, and the slope (0.509±0.044 R^2=97.1%, $p<$ 0.001) of the regression of leptin on BMI (Fig. 2A) was significantly different (n=31, $p<0.001$) from that for Korean males. In contrast, there was no significant difference between Korean female and British female leptin levels-albeit with a very small sample size (n=3). Values from British subjects seem to be similar to other reports for Caucasians (17). There are a few reports concerning the differences in leptin levels among different ethnic groups. None the less, this is the first report demonstrating the differences in serum leptin levels between Korean and British male subjects (18). This might be due to the differences in body composition and fat distribution between the Korean and British populations, but there are numerous possibilities and further study is needed to elucidate the reasons for these differences.

Correlations between serum levels and BMI among type 2 diabetic patients

We also tested the relationships between serum leptin levels and BMI of type 2 diabetic patients. The subjects were 24 (17 males and 7 females, aged between 21 to 60) diagnosed with type 2 diabetics at Handong University Sunlin Hospital but no record of previous treatment history. In this small sample there was no correlation between leptin levels and BMI in either male (slope 0.018±0.036, p=0.624) or female (slope 0.382± 0.433, p=0.417) type 2 diabetic patients (Fig. 3) and no significant difference between slopes (n=24, p=0.163).

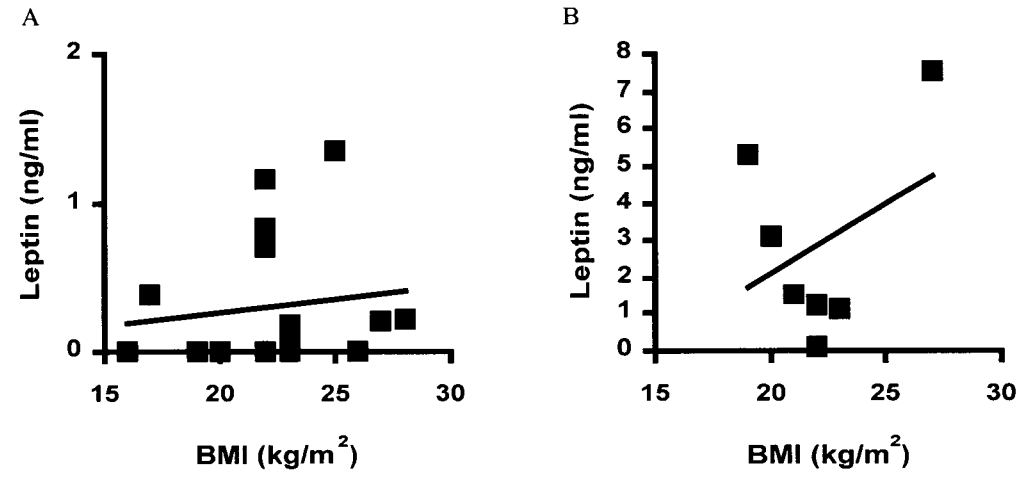

Fig. 3. Serum leptin and Body Mass Index (BMI) in diabetic Koreans. A) Korean males: n=17, leptin=-0.097+0.018BMI, R^2=0.016, slope p=0.624. B) Korean females: n=7, leptin=-5.56+0.382BMI, R^2=0.135, slope p=0.417. Difference in slopes between diabetic Korean males and females, n=24, p=0.163.

This contrasts with the strong correlation found between BMI and leptin in subjects with type 2 diabetes, from Europe and America. It has been reported that both type 2 diabetic and non-diabetic subjects showed positive correlation of leptin with the BMI from in a study of 80 type 2 diabetic and 80 nondiabetic subjects (19).

The difference in the correlation value of serum leptin level and BMI between our and other Korean group may be due to the smaller size of samples in our study and these results need to be confirmed by further study with a larger number of diabetic patients.

REFERENCES

1. Lee TH, Kim SM, Lee DJ, Kim YS. 2000. Assessment of anthropometric indices of obesity in Korea. *Korean J Obesity Studies* 9: 276-282.
2. Ginsberg HN. 2000. Insulin resistance and cardiovascular disease. *J Clin Invest* 106: 453-458.
3. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. 1994. Positional cloning of the mouse obese gene and its human homologue. *Nature* 372: 425-432.
4. Campfield LA, Smith FJ, Guisez Y, Devos R, Burn P. 1995. Recombinant mouse OB protein: evidence for a peripheral signal linking adiposity and central neural networks. *Science* 269: 546-549.
5. Haalas JL, Gajiwala KS, Maffei M, Cohen SL, Chait BT, Rabinowitz D, Lallone RL, Burley SK, Friedman JM. 1995. Weight-reducing effects of the plasma protein encoded by the obese gene. *Science* 269: 543-546.
6. Pelleymounter MA, Cullen MJ, Baker MB, Hecht R, Winters D, Boone T, Collins F. 1995. Effects of the obese gene product on body weight regulation in *ob/ob* mice. *Science* 269: 540-543.
7. Frederich RC, Hamann A, Anderson S, Lollmann B, Lowell BB, Flier JS. 1995. Leptin levels reflect body lipid content in mice: evidence for diet-induced resistance to leptin action. *Nat Med* 1: 1311-1314.
8. Heymsfield SB, Greenberg AS, Fujioka K, Dixon RM, Kushner R, Hunt T, Lubina JA, Patane J, Self B, Hunt P, McCamish M. 1995. Recombinant leptin for weight loss in obese and lean adults: a randomized, controlled, dose-escalation trial. *JAMA* 282: 1568-1575.
9. Haffiner SM, Gingerich RL, Miettinen H, Stern MP. 1996. Leptin concentrations in relations to overall adiposity and regional body fat distribution in Mexican Americans. *Int J Obes Relat Metab Disord* 20: 904-908.
10. Considine RV, Sinha MK, Heiman ML, Aidas K, Thomas WS, Mark RN, Joanna PO, Cheryl CM, Linda JM, Thomas LB, José FC. 1996. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. *N Engl J Med* 334: 292-295.
11. Ruhl CE, Everhart JE. 2001. Leptin concentrations in the United States: relations with demographic and anthropometric measures. *Am J Clin Nutr* 74: 295-301.
12. Hardie L, Trayhurn P, Abramovich D, Fowler P. 1997. Circulatingeptin in women: a longitudinal study in the menstrual cycle and during pregnancy. *Clin Endocrinol* 47: 101-106.
13. Donahue RP, Zimmet P, Bean JA, Decourten M, DeCarlo Donahue RA, Collier G, Goldberg RB, Prineas RJ, Skyler J, Schneiderman N. 1999. Cigarrete smoking, alcohol use, and physical activity, in relation to serum leptin levels in a multiethnic population: the Miami Community Health Study. *Am J Epidemiol* 9: 108-114.
14. Lonnqvist F, Arner P, Nordfors L, Schalling M. 1995. Overexpression of the obese (ob) gene in adipose tissue of human obese subjects. *Nature Med* 1: 950-953.
15. Gottschling-Zeller H, Birgel M, Scriba D, Blum WF, Hauner H. 1999. Depot-specific release of leptin from subcutaneous and omental adipocytes in suspension culture: effect of tumor necrosis factor-α and transforming growth factor-β1. *Eur J Endocrinol* 141: 436-442.
16. Wabitsch M, Blum WF, Muche R, Braun M, Hube F, Rascher W, Heinze E, Teller W, Hauner H. 1997. The contribution of androgen to the gender difference in leptin production on obese children and adolescents. *J Clinical Investigation* 100: 808-813.
17. Blum WF, Juul A. 1997. Reference ranges of serum leptin levels according to body mass index, gender, and developmental stage. In *Leptin the voice of adipose tissue*. Blum WF, Kiess W, Rascher WJA, eds. Thieme, Stuttgart/Barth, Leipzig, Heidelberg. p 318-326.
18. Wagner DR, Heyward VH. 2000. Measures of body composition in blacks and whites: a comparative review. *Am J Clin Nutr* 71: 1392-402.
19. Shim DJ, Kim SH, Kim YS, Choi YS, Jeong US, Lee HY, Choi HY, Kim JY, Lee SJ. 1999. Serum leptin concentration in diabetic and nondiabetic Koreans. *Korean J Obesity Studies* 8: 102-108.

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