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The Plasma Levels of Leptin were Correlated with the Metabolic Cardiovascular Risk Factors such as Obesity and Dyslipidemias in Healthy Subjects

Yuichi Ishikawa¹, Shuzou Gomikawa¹, Shingo Sasada³, Mako Taguchi², Masako Uchi¹, Akihiko Oda², and Takahiro Taniguchi².

Leptin, the gene product of the ob gene, may play an important role in regulating body weight by signalling the size of the adipose tissue mass. It has been reported that the plasma levels of leptin were correlated with the body mass index (BMI). The obesity is associated to the insulin resistitant state. So we investigated the relation between the plasma leptin levels and the plasma levels of glucose and lipids such as cholesterol, triacylglycerol (TG) and high density lipoprotein cholesterol in healthy subjects.

The plasma levels of leptin in female were significantly higher than that in male. The plasma levels of leptin were well correlated with BMI in both male and female. The plasma glucose levels in female correlated with the plasma leptin levels, but not in male. The plasma levels of cholesterol in both male and female were not correlated with the plasma leptin levels. The plasma TG levels in female correlated with the plasma leptin levels, but not in male. We also measured the plasma levels of tumor necrosis factor-alpha, but there was no correlation with the plasma leptin levels.

The plasma leptin level may reflect the adipose tissue mass and might relate with coronary risk factors.

Key Words
Leptin, Obesity, Lipid metabolism, Insulin–resistance, Tumor necrosis Factor–alpha.

Introduction
Leptin, the gene product of the ob gene, may play an important role in regulating body weight by signalling the size of the adipose tissue mass to the brain through ob receptor. It is also reported that ob gene is overexpressed in adipose tissue of human obese subjects. The plasma levels of leptin were correlated with body mass index (BMI) and also body fatness. The obesity is associated to the insulin resistant state and in this state plasma levels of lipids are also abnormal.

In this study, we investigate the correlation between plasma levels of leptin and BMI and plasma glucose and plasma lipid levels in healthy subjects.

Materials and Methods
Ninty eight healthy subjects, 42 males
Ishikawa et al. (mean age 43 ± 14 years old) and 56 females (mean age 37 ± 14 years old), were studied. Body height and body weight were measured at the admission to the Health Promotion Center (Day 1) and BMI was calculated.

At day 2, venous blood was sampled at fasting state and total cholesterol, triacylglycerol (TG), high density lipoprotein (HDL)—cholesterol and glucose were measured. Plasma levels of leptin were measured using commercially available kit (Human leptin measurement kit, Japan Immunoresearch Laboratories, Takasaki, Japan). Plasma tumor necrosis factor—alpha (TNF–α) was measured using commercially available kit (TNF–α Elisa Kit, R & D system, Mineapolis, USA).

Values were expressed as mean ± standard deviation (SD) or standard error of mean (SE) as indicated. Relationships were assessed by Pearson’s correlation coefficient analysis. The significance of difference in each group was determined by non—paired Student’s t—test (two tailed). P values of less than 0.05 were considered statistically significant.

Results

Subject Characteristics

Table Characteristics of the Subjects

<table>
<thead>
<tr>
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<th>male (n=42)</th>
<th>female (n=56)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Age (years old)</td>
<td>43 ± 14</td>
<td>37 ± 14</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>168 ± 7</td>
<td>156 ± 6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.1 ± 13.6</td>
<td>57.9 ± 8.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>25.3 ± 5.3</td>
<td>23.8 ± 3.3</td>
<td>n.s</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>94.7 ± 32.4</td>
<td>83.1 ± 13.0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>209 ± 45</td>
<td>204 ± 40</td>
<td>n.s</td>
</tr>
<tr>
<td>Triacylglycerol (mg/dl)</td>
<td>216 ± 206</td>
<td>108 ± 53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dl)</td>
<td>52.8 ± 14.0</td>
<td>56.7 ± 12.6</td>
<td>n.s</td>
</tr>
</tbody>
</table>

Values were expressed as mean ± standard deviation.

n.s: not significant

The subjects were generally healthy. The anthropometric data and blood chemicals were summarized in table.

Correlation between Plasma Levels of Leptin and Age.

The plasma levels of leptin were not correlated with age.

Comparison of Plasma Levels of Leptin in Male and Female

The mean plasma levels of leptin in male were 8.7 ± 1.3 ng/ml and that in female were 14.7 ± 1.6 ng/ml. The plasma levels of leptin in female were significantly higher than that in male (P< 0.05, Fig.1).

Correlation between Plasma Level of Leptin and BMI

The BMI was 23.8 ± 3.3 in female and 25.3 ± 5.3 in male. The plasma levels of leptin were correlated with BMI in both gender (P<0.001, Fig.2).

Correlation between Plasma Level of Leptin and Fasting Plasma Glucose level.

The plasma level of leptin significantly correlated with plasma level of fasting glucose in female (P<0.003), but not in
Leptin and Cardiovascular Risk Factors

Fig. 1. Comparison of plasma levels of leptin in male and female. Values were expressed as mean ± standard error of mean.

Correlation between Plasma Level of Leptin and Plasma Levels of Cholesterol, TG and HDL-Cholesterol.

The plasma level of leptin were not correlated with plasma levels of cholesterol. The plasma levels of leptin significantly correlated with plasma levels of TG in female (P<0.01) but not in male (Fig.4). The plasma levels of leptin showed the tendency of negative correlation with plasma levels of HDL-cholesterol (not significant).

Fig. 2. Relationship between plasma levels of leptin and BMI.

Fig. 3. Relationship between plasma levels of leptin and fasting glucose levels.
Correlation between Plasma Level of Leptin and TNF-α.

The plasma levels of TNF-α were 2.5 ± 1.4 pg/ml in 40 subjects. The plasma levels of leptin were not correlated with the plasma levels of TNF-α.

Discussion

Leptin, the gene product of the ob gene, may play an important role in regulating body weight by signalling the size of the adipose tissue mass. A leptin receptor was also identified, which was a single membrane-spanning receptor most related to the gp130 signal-transducing component the IL-6 receptor, the G-CSF receptor, and the LIF receptor. The ob gene was overexpressed in adipose tissue of human obese subjects. It was reported that leptin levels reflect body lipid content in mice and human. In diabetic mice abnormal splicing of the leptin receptor was identified and it could related to the abnormal signal transduction through a leptin receptor.

As plasma leptin levels are elevated in most overweight individuals, obesity may be associated with leptin resistance.

In this paper, we reported that the plasma leptin levels were associated to BMI. Considine reported that serum immunoreactive leptin concentrations in obese humans were higher than that in normal weight and this result is compatible to our result. The high plasma levels of leptin may reflect either body fatness or leptin resistance.

Plasma levels of leptin were significantly higher in females compared to males. Rosenbaum also reported that leptin was higher in pre- and post-menopausal females compared to males and pointed that plasma leptin levels were determined by primarily by the absolute fat mass rather than the relative degree of adiposity.

We also indicated that the plasma levels of leptin were correlated with the plasma levels of TG and fasting glucose. Leyva reported that there were a negative correlation between leptin and insulin sensitivity. Although we measured neither fasting insulin levels nor insulin resistance, high plasma levels of TG and glucose and obesity may related to insulin resistance.

TNF-α is expressed and secreted from adipose tissue and induced insulin resistance. However we could not find
positive correlation between TNF-α and leptin levels. Other factors such as fatty acids may related to these conditions.

In conclusion, plasma levels of leptin are correlated with TG and insulin resistance and these results suggest leptin is correlated with coronary risk factors. Further studies are needed to determine whether plasma leptin levels may aggravate coronary atherosclerosis.

References