Circulating Leptin Levels in Elderly Subjects With and Without Cerebrovascular Disease

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ABSTRACT
Serum concentrations of leptin was investigated in 40 patients with ischemic stroke, in context of the size of the lesion and also in 40 non-diseased controls, matched according to age, gender and waist hip ratio. Serum leptin concentrations were determined in ng/ml with ELISA and computer tomography (CT) scan was performed in patients to estimate lesion size in cms.

Serum leptin concentrations were found to be significantly higher (p < 0.001) in stroke patients (51.61±1.39), compared with controls (37.76±1.207). Moreover, positive correlation (r=0.93) existed between serum leptin level and infarction size in patients with stroke.

Key words: Leptin. Ischemic stroke. Infarction size.

The protein product of the ob gene leptin may be an important link between obesity, the insulin resistance syndrome and an increased risk for vascular disease.1 Recent studies have provided evidence, that leptin also has significant effects on vascular development and repair.1 The combination of high leptin levels and high blood pressure was associated with a strong positive interaction in males, with stroke.2 Cerebrovascular Disease (CVD) is one of the leading causes of morbidity amongst elderly individuals. The study was planned to investigate the levels of circulating leptin in subjects, with and without cerebrovascular disease and the relationship between serum concentrations of leptin and the infarct size.

Eighty subjects between the age of 50 and 70 years (40 each) with and without CVD according to inclusion criteria, age, gender, waist hip ratio and socioeconomic status matched, were selected from Ziauddin and Liaquat National Hospitals, Karachi. Amongst them, 21 were males and 19 females. Informed consent was obtained from all the subjects and the study was approved by the Ethical Committee of Ziauddin University. Waist and hip circumference was measured and classified as obese, if the waist/hip ratio (WHR) was greater than 0.8 in women and 0.95 in men.

Smokers and alcohol consumers, patients with concurrent major cardiac, renal, hepatic and cancers diseases, infection, stroke due to any vascular malformation, recent (within 1 month) history of head trauma, transient ischemic attack, intracerebral haemorrhage, those with collagen disease, acute viral infections and CT/MRI results inconclusive for the lesion location, were excluded from the study.

Fasting plasma samples were obtained within 48 hours from stroke onset and were stored at -80°C for subsequent assay. Leptin was determined by enzyme linked immunoassay (ELISA).3 Fasting and random blood glucose was determined by glucose oxidase method, using kit obtained from Merck. All the CT examinations were performed on a CT Systec 3000 plus (GEC) scanner.4

Data was shown as mean and standard error of mean. Analysis was performed using the statistical package for the social sciences (version 12). P-value was determined by Student’s t-test. Pearson correlation analysis was used to evaluate the bivariate relationship between leptin and infarction size. P < 0.05 was considered statistically significant.

The clinical characteristics of the subjects are shown in Table I. The mean plasma level of leptin was significantly higher in stroke patients compared to controls (51.61±1.39 vs. 37.76±1.207, p < 0.001).

**Table I:** Characteristics of subjects with and without CVD. Values are expressed as mean and standard error of mean (SEM).

<table>
<thead>
<tr>
<th></th>
<th>Normal controls (40)</th>
<th>Stroke patients (40)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.02±0.890</td>
<td>58.15±0.865</td>
<td>0.920</td>
</tr>
<tr>
<td>Waist hip ratio</td>
<td>0.82±0.005</td>
<td>0.83±0.005</td>
<td>0.843</td>
</tr>
<tr>
<td>Fasting blood glucose</td>
<td>5.33±0.115</td>
<td>5.58±0.208</td>
<td>0.300</td>
</tr>
<tr>
<td>Random blood glucose</td>
<td>8.92±0.151</td>
<td>9.39±0.400</td>
<td>0.275</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>37.76±1.207</td>
<td>51.61±1.39</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

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higher (51.61 ng/ml versus 37.76 ng/ml, p < 0.001) in those with CVD, than in those without CVD. No significant difference was found in the groups’ age, WHR, fasting blood glucose and random blood glucose. Significant positive correlations existed between leptin and infarction size (r = -0.93, p < 0.01, Figure 1).

Figure 1: Correlation coefficient (r) of leptin vs. infarction size. Leptin is expressed as ng/ml and infarction volume as cm³.

Leptin is an adipose hormone endowed with angiopoietic, neurotrophic, and neuroprotective properties. Leptin acts synergistically with fibroblast growth factor-2 and vascular endothelial growth factor to stimulate angiogenesis and thus, influence vascular permeability. Exogenous leptin administration protects against ischemic neuronal injury in vitro and in vivo in a c-Rel-dependent manner in a study by Valerio et al. Recently, it has been suggested that insulin resistance with compensatory hyperinsulinemia may be an important pathogenetic factor of atherothrombotic brain infarction. Elevated triglycerides interfere with entry of leptin in brain. Once leptin resistance is induced by high non-fasting triglycerides, then the surplus leptin communicates to leptin receptors on the platelets and makes them more sticky. This results in a combination of too much sludge in the circulation along with platelets that are primed to clot inappropriately. Carotid artery lesions from symptomatic patients are characterized by inflammation and revascularization. Leptin promotes angiogenesis and activates inflammatory cells, and the leptin receptor (ob gene-encoded receptor), ObR, is expressed in advanced atherosclerotic lesions. Sodenberg et al. reported leptin to be more responsible for cerebrovascular disease than adiponectin. Thus, leptin along with other cytokines contributes to cerebrovascular disease.

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REFERENCES