SHORT REPORT

Serum leptin level in women with idiopathic intracranial hypertension

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Leptin is a protein secreted by adipose cells which influences regulation of energy balance and body weight. Idiopathic intracranial hypertension (IIH) is recognised as a neurological disorder mainly affecting obese females. The aim of this study was to evaluate the association between IIH and serum leptin level in 15 obese patients and compare the results with those for 16 obese and 15 non-obese women. A significantly higher serum leptin level was found in patients with IIH than in controls (p<0.0001), and this did not correlate with body mass index (BMI). Serum leptin levels were significantly associated with BMI in both control groups (p<0.0006). Additional factors must therefore be involved in the phenomenon of serum leptin increase beyond weight gain. The cause can only be hypothesised, but it seems that the origin is central, probably hypothalamic.

Leptin is a protein of the OB gene, is secreted by adipose tissue cells and circulates in plasma. The circulating plasma leptin is influenced by body weight and food intake and is a regulator of energy balance. The regulation of energy expenditure is mediated by adiposity signals originating in the hypothalamus. The key role of the hypothalamic endocrine system in regulation of body weight and food intake through serum leptin levels can be interpreted through the adipose tissue-hypothalamus and hypothalamus-adipose tissue endocrine axes. Neuropeptide Y7, agouti related peptide,2 and melanin concentrating hormone belong to the group of neuropeptides that affect leptin in the hypothalamic-adipose cell mediated axis, acting by increasing body weight and energy storage. Pro-opiomelanocortin,9 corticotropin releasing hormone,10 and cocaine amphetamine related transcript11 have the opposite effect and act as catabolic peptides. In the transmission of weight states from the periphery to the hypothalamus, leptin has a most important signalling role,12 as does insulin.13

The relation between idiopathic intracranial hypertension (IIH) and weight increase has been disputed.14 Reduction of weight may be of therapeutic benefit.15 IIH is a neurological disorder mainly of obese females. Examination of obese females with no other neurological complaints or deficits suggests that obesity explains the increase in cerebrospinal pressure in most of the patients with IIH. The increase in intra-abdominal and intrathoracic pressure and raised central venous pressure has been proposed as a cause. However, the relation between the increase in fluid pressure above normal and obesity is controversial and cannot explain the discrepancy between the very high percentage of obesity in the general population and low incidence of IIH.

To investigate whether patients with IIH have a disturbed leptin function, serum leptin level was measured under food restricted conditions and compared with a group of controls matched for age, sex, and weight.

PATIENTS AND METHODS

We studied serum leptin levels in women with IIH (group I). The decision to limit the inclusion criteria to women was based on the fact that the relation between IIH and obesity is stronger in women.19

Other inclusion criteria were age 18–50 years and completely normal endocrine profile, including cortisol profile, prolactin, follicle stimulating hormone, luteinising hormone, testosterone, androsterone, and thyroid stimulating hormone.

Exclusion criteria were the coexistence of any other neurological, metabolic, or infectious disease or liver or kidney dysfunction and the routine use of any drugs, except acetazolamide (Diamox). Each patient had a brain computed tomography scan; any abnormality was a reason for exclusion.

The blood sample for the single serum leptin measurement was drawn after overnight fasting (last food intake before 2100) between 0730 and 0830, at which time blood pressure, height, and weight were measured.

The results were compared with those for two control groups who fulfilled the inclusion and exclusion criteria: group II, obese women (body mass index (BMI) >27.5 kg/m2); group III, non-obese women (BMI >16 kg/m2).

Laboratory analysis

Blood samples (10 ml) were collected from the antecubital vein into vacutainer tubes (Becton Dickinson) and centrifuged at 1500 g for 10 minutes. The serum was divided into portions and stored at −70°C until analysed. Leptin was measured with the DSL-23100 kit (Leptin coated-Tube Immunometric Assay Kit; Diagnostic Systems, Webster, Texas, USA).

RESULTS

Table 1 presents some characteristics of the study population. The duration from first diagnosis of IIH in group I was 16.3 (SD 3.5) months (range 3–9). All patients were treated with acetazolamide (750 mg/day). BMI differed significantly by group (p<0.0001). Bonferroni pairwise comparison of means confirmed that groups I and II did not differ from one another in terms of BMI, but that group III had a significantly lower BMI than the other two groups.

As shown in table 1, mean serum leptin levels differed significantly by group (p<0.0001). Bonferroni comparison showed that women in group I had significantly higher serum leptin levels than women in group II or group III. The serum leptin levels in groups II and III were only marginally different from one another (p=0.02).

Linear regression analysis was used to examine association between the variables. No association was detected between age and serum leptin levels. Serum leptin levels were significantly associated with BMI (p=0.0006), such that BMI

Abbreviations: IIH, idiopathic intracranial hypertension; BMI, body mass index
accounted for about 26% of the variation in serum leptin levels. This association persisted in groups II and III, but not in group I.

**DISCUSSION**

Various studies have found that circulating serum leptin levels are proportionally to adipose cell mass, are related to food intake, and reflect energy balance. We found a significant correlation between serum leptin level and BMI in groups II and III. This association did not persist in patients with IHH, suggesting that, in addition to BMI, other factors must contribute to the variation in serum leptin levels. The very high level of leptin found exclusively in women with IHH indicates a link between IHH and leptin. A similar finding of raised serum leptin beyond the expected BMI, other factors must contribute to the variation in serum leptin levels.

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**REFERENCES**