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 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.

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.

Other inclusion criteria were age 18–50 years and completely normal endocrine profile, including cortisol profile, prolactin, follicle stimulating hormone, luteinising hormone, testosterone, androstenedione, 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
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 proportional 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 III, 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 III indicates a link between III and leptin. A similar finding of raised serum leptin beyond the expected BMI values has also been shown in patients after hypothalamic surgery. Brabant et al showed a significantly higher blood level of leptin after craniopharyngeal removal. In about 40% of the patients, serum leptin levels were higher than expected for their BMI as compared with the sample taken before surgery. The weight gain corresponded to the increase in leptin level in only about 50% of patients. There were no similar findings in patients who had received non-hypothalamic surgery or in healthy controls.

The relation between defective weight regulation and high circulating leptin level is seen in the db/db mouse and fa/fa Zucker rat. Dysfunction of the leptin receptor in the hypothalamus with overexpression of the ob gene and increased circulating leptin is probably caused by a polymorphism of the leptin receptors. This was also assumed to be the case in patients with severe early onset of obesity. Clement et al reported an association between mutation of a human leptin receptor and severe obesity and pituitary dysfunction. A failure in the transport of leptin from the cerebrospinal fluid into the brain and desensitisation of the hypothalamic structures were proposed as mechanisms of this phenomenon.

In conclusion, severe obesity in the presence of significantly raised circulating leptin levels was found to be present in women with III and may have a central origin, probably hypothalamic dysfunction. Further studies are needed to clarify and ascertain the exact mechanism of these disturbances.

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**REFERENCES**