SHORT COMMUNICATION

Serum leptin and insulin concentrations in patients with insulinoma before and after surgery

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Abstract

Inferential studies suggest that circulating insulin concentrations positively regulate leptin secretion by adipocytes. In humans, however, insulin requires prolonged periods of time, and relatively artificial set-ups before a relationship with leptin can be observed. In the present work, serum leptin concentrations were measured in five patients with insulinoma before and one month after surgery and in five control subjects matched by sex and body mass index (BMI).

The control subjects presented a mean serum leptin concentration of 6.7 ± 1.5 μg/l and a BMI of 24.9 ± 1.1. The mean serum leptin concentration in patients with insulinoma was 11.8 ± 3.1 μg/l (P < 0.05 vs controls), with a BMI of 26.3 ± 1.9. After surgery, there was a non-significant reduction in BMI (25.8 ± 1.7), and a clear reduction in serum leptin concentration (5.6 ± 2.4 μg/l, P < 0.05 vs pre surgical values and no difference vs control subjects). The fasting area under the curve (AUC) of insulin concentration (in mU/l per 120 min) before surgery was 14 421 ± 4981 and after surgery was 1306 ± 171 (P < 0.05). Before surgery, serum leptin concentrations significantly correlated with BMI (r = 0.71) and AUC of insulin (r = 0.82), a correlation that was lost after surgery.

In conclusion, serum leptin concentrations are significantly elevated in patients with chronically high insulin levels due to insulinoma. After surgical treatment and normalization of insulin values, leptin levels return to normal.

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fasting, which was stopped in all cases after 24 h due to the presence of signs and symptoms alleviated by i.v. glucose. The presence of the insulin-secreting tumor was confirmed by histology after surgery. Blood samples were obtained early in the morning after a brief breakfast and none of the subjects was taking medication or drugs. All subjects provided informed consent and the study was approved by the Hospital Ethical Committee.

Insulin was measured by a commercial RIA kit (INEP, Belgrade, Yugoslavia) with intra- and interassay coefficients of variation of 6.1% and 13% respectively. Serum leptin levels were measured by radioimmunoassay (Linco Research, St Louis, MO, USA) with a limit of sensitivity of 0.5 μg/l and intra- and interassay coefficients of variation of 6.2% and 8.3% respectively. The area under the curve (AUC) for insulin was calculated by a trapezoidal method, after determinations every 15 min for 2 h. A Wilcoxon test was used to compare values, and a regression analysis was performed. Results are expressed as means ± S.E.M. and values of \( P < 0.05 \) were considered significant.

**Results**

Control subjects presented a serum leptin concentration of 6.7 ± 1.5 μg/l and a BMI (calculated as body weight in kg divided by the square of height in meters) of 24.9 ± 1.1. On the other hand, the mean serum leptin concentration in patients with insulinoma was 11.8 ± 3.1 μg/l (\( P < 0.05 \) vs controls), with a BMI of 26.3 ± 1.9 (Fig. 1). After surgery, a non-significant reduction in BMI was observed (25.8 ± 1.7) with a clear reduction in serum leptin concentrations of 5.6 ± 2.4 μg/l (\( P < 0.05 \)), not different from the control subjects. The fasting AUC of insulin concentration before surgery was 14 421 ± 4981 mU/l per 120 min, and after surgery was 1306 ± 171 mU/l per 120 min (\( P < 0.05 \)). Before surgery, serum leptin concentrations significantly (\( P < 0.05 \)) correlated with BMI (\( r = 0.71 \)) and AUC of insulin (\( r = 0.82 \)), a correlation that was lost after surgery.

**Discussion**

On the one hand, leptin seems to modulate insulin action (16), and on the other hand the close association between hyperinsulinemia and hyperleptinemia suggests that ob gene expression may be mediated by insulin (17). Although leptin and insulin evolve in parallel in fasting and overfeeding, the interrelationship is not at all simple, with controversial experimental results being reported (18, 19). Data gathered in humans supports a positive correlation between fasting concentrations of insulin and leptin, and a long-term stimulatory effect of insulin on leptin production in vivo and in vitro (14). However, the studies that demonstrated an effect of insulin on the regulation of leptin production required a 72-h hyperglycemic clamp, casting doubt regarding the final mechanism of this action, i.e. is it a direct one or a tropic effect of insulin plus glucose on the adipocyte?

In the present study, it has been shown that chronic endogenous hyperinsulinemia in patients with insulinoma tumors is significantly associated with enhanced leptin secretion, an action that is reversed after successful surgery. As no changes in BMI were observed after surgery, the clear-cut reduction in leptin serum concentrations probably reflects the reduction and normalization of insulin levels.

In conclusion serum leptin levels decrease after the successful cure of patients with endogenous chronic hyperinsulinemia due to insulinoma. This may suggest that insulin has a stimulatory role in regulating serum leptin levels. Further studies are needed in these patients in order to understand whether the insulin-mediated serum leptin increase could contribute to the development of insulin resistance.

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**References**


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**Figure 1** Serum leptin concentrations, AUC of serum insulin, and BMI in five patients with insulinoma before (open bars) and one month after (solid bars) surgical cure. Values are means ± S.E.M. *P < 0.05 vs pre-surgical values.


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