Influence of Thyroid Status on Serum Immunoreactive Leptin Levels*

R. VALCAVI, M. ZINI, R. PEINO, F. F. CASANUEVA, AND C. DIEGUEZ

Second Division of Internal Medicine, Section of Endocrinology and Metabolism, Hospital S. Maria Nuova, Reggio Emilia, Italy; the Department of Medicine, Endocrine Area, Complejo Hospital (R.P., F.P.C.), and the Department of Physiology (C.D.), University of Santiago, Santiago de Compostela, Spain

ABSTRACT
Leptin, the product of the ob gene, is a recently discovered hormone secreted by adipocytes. Serum leptin concentrations increase in correlation with the percentage of body fat, but besides that, little is known about the physiological actions of leptin in humans. The aim of this study was to assess the influence of hypo- and hyperthyroidism on serum leptin levels.

Thirty-two patients (16 with hypothyroidism and 16 with hyperthyroidism) were studied before and after treatment with replacement doses of T4 (hypothyroid patients) or methimazole (hyperthyroid), when thyroid function was normal. Control serum for each group was obtained from healthy age-, sex-, and body mass index-matched subjects. Plasma leptin levels were measured by specific RIA.

The mean leptin level in the hypothyroid patients was lower before treatment (4.7 ± 0.7 μg/L) than that in the controls (8.6 ± 1.4 μg/L; P < 0.02) and was lower than that during treatment with T4 and normalization of thyroid function in the same group of patients (6.3 ± 0.8 μg/L; P < 0.05). Leptin levels in the hyperthyroid patients were similar before (7.2 ± 1.1 μg/L) and after normalization of thyroid function following treatment with methimazole (6.2 ± 1.1 μg/L) and were similar to the control value (8.8 ± 1.4 μg/L).

In conclusion, leptin levels are decreased in the hypothyroid patients and unchanged in hyperthyroidism. Whether decreased leptin levels may contribute to the decreased energy expenditure in patients with hypothyroidism merits further investigation. (J Clin Endocrinol Metab 82: 1632–1634, 1997)

Subjects and Methods
Sixteen patients (12 women and 4 men) with primary hypothyroidism due to autoimmune thyroid disease with a BMI of 24.4 ± 0.8, reduced free thyroid hormone levels (free T4 < 3 pg/mL; mean ± sem, 0.7 ± 0.1; normal range, 2–4.5 pg/mL; free T4 < 8 pg/mL; mean ± sem, 1.05 ± 0.2; normal range, 8–20 pg/mL), and elevated basal TSH levels (> 6 mU/L; mean ± sem, 121 ± 16; normal range, < 4.5 mU/L) were studied before and during replacement therapy with L-T4 (100–150 μg/day over 6–30 weeks) when thyroid function was normal and had a BMI of 21.9 ± 0.5 (mean ± sem). After antithyroid drug administration, all hyperthyroid patients had free thyroid hormone and TSH levels within the normal range. The length of euthyroidism at the time of study ranged from 2.1–4.5 months (mean ± sem, 3.4 ± 0.4 months) in the hypothyroid patients and from 2.2–6 months in the hyperthyroid group (mean ± sem, 5.4 ± 1.3 months). In addition, a group of control subjects matched for age, sex, and body mass index (BMI) were studied.

The ob gene is an adipocyte-specific gene that encodes leptin, a protein that regulates body weight by suppressing food intake and/or increasing energy expenditure (1–5). Recent data have clearly shown that the amount of leptin messenger ribonucleic acid in adipocytes correlates with body weight (6, 7). Furthermore, serum immunoreactive leptin levels show a strong positive correlation with body fat, being elevated in obesity (6, 8) and decreased in states of severe malnutrition such as anorexia nervosa (8a). Taken together, these data suggest that leptin is an adipocyte-synthesized hormone, the role of which is to inform the brain of the amount of the adipose tissue present in the body (9, 10).

On the other hand, alterations in thyroid hormone levels are frequently associated with changes in body weight. Thus, patients with hypothyroidism usually exhibit an increase in body weight, whereas, on the contrary, hyperthyroid patients tend to lose weight (11). To study the effect of chronic thyroid hormone excess and deficiency on serum leptin levels, in the present work we measured leptin levels in hypothyroid and hyperthyroid patients before and during treatment, when thyroid function was normal. In addition, a group of control subjects matched for age, sex, and body mass index (BMI) were studied.
Leptin levels were detectable in all subjects studied. Leptin levels in the hypothyroid patients were lower before treatment (mean ± sem, 4.7 ± 0.7 µg/L) than in the controls (8.6 ± 1.4 µg/L; P < 0.02) and were lower during treatment with T4 and normalization of thyroid function (6.3 ± 0.8 µg/L; P < 0.05). Leptin levels in the hypothyroid patients were similar before (7.2 ± 1.1 µg/L) and after treatment with methimazole and normalization of thyroid function (6.2 ± 1.1 µg/L) and similar to the control value (8.8 ± 1.4 µg/L) (Fig. 1).

Discussion

The discovery and antiobesity effects of leptin offer a breakthrough in the understanding of adipose tissue regulation and will help us to understand the pathophysiology of different clinical entities associated with changes in body weight and body composition. Although the intrinsic mechanisms through which leptin exerts its effects are far from being completely understood, the accepted working hypothesis at present is that it acts as an afferent satiety signal in the brain to reduce food intake as well as to increase energy expenditure (9, 10).

Data gathered in vitro and in vivo in experimental animals have shown that leptin gene expression and leptin secretion are regulated by various hormones and by body lipid content (10). However, little is yet known regarding the mechanisms that influence leptin secretion in humans. This is an important consideration, taking into account that the physiology of adipocytes is quite different in rodents and primates. Furthermore, remarkable differences have been observed in leptin levels between obese mice and obese humans. Although the ob/ob mice, which are hyperphagic and obese, show no production of leptin, serum leptin concentrations as well as the levels of ob messenger ribonucleic acid are elevated in obese subjects (6–8).

Thyroid status markedly influences body weight and food intake. Thus, in a large number of hyperthyroid patients (85%) there is a decrease in body weight, whereas in 59% of hypothyroid patients there is an increase (11). These changes in body weight are not due to changes in food intake; on the contrary, appetite is increased in 65% of hyperthyroid patients and decreased in 45% of hypothyroid patients (11). Taking into account that leptin has been shown to decrease food intake and increase energy expenditure, it was of great interest to investigate whether changes in serum leptin levels could account for the disturbances in these two parameters in both hypothyroid and hyperthyroid patients. Our findings of decreased leptin levels in the patients with hypothyroidism and unchanged leptin levels in the hyperthyroid patients were somewhat unexpected and suggest that changes in leptin levels do not explain the alterations in appetite usually found in these patients. On the other hand, decreased leptin levels could contribute to the decrease in energy expenditure in hypothyroidism, but not to its increase in hyperthyroidism. Interestingly, in the hypothyroid state, a relatively higher BMI was associated with lower leptin levels; in the same subjects after treatment, BMI and leptin levels were higher. Taking into account that serum leptin levels appear to be related to BMI, these data could indicate that normal thyroid hormone levels are needed to achieve an adequate leptin gene expression. However, there are no data available to prove this hypothesis. Finally, the possibility that thyroid hormone levels regulate leptin bioactivity and, therefore, its effects on appetite and energy expenditure by influencing leptin-binding proteins (13) and or leptin receptors merits further investigation.

In conclusion, our data show that although physiological thyroid hormone levels are needed to ensure normal circulating leptin levels, excess thyroid hormones levels do not lead to a further increase. Whether the decrease in leptin levels observed in the hypothyroid patients is due to decreased leptin gene expression or increased clearance rate remains to be established.

Acknowledgment

We thank Ms. Mary Lague for her kind technical assistance.

References


Fig. 1. Mean ± sem serum leptin concentrations in the control subjects and the patients with hypothyroidism (hypo) or hyperthyroidism (hyper) before and during treatment with T4 or methimazole (Meth). *P < 0.05.