

Original Article

Serum Ghrelin Changes in Thyroid Dysfunction

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Background: Thyroid dysfunction is associated with changes in the appetite. Ghrelin can regulate feeding behavior. The aim of this study was to evaluate whether ghrelin plays a role in the appetite changes in different states of thyroid dysfunction.

Methods: The serum ghrelin levels were measured in 45 newly diagnosed hyperthyroid and 45 newly diagnosed hypothyroid patients before and after medical treatment. Forty-five healthy subjects were also studied as control group.

Results: The ghrelin levels did not change significantly in patients with hyperthyroidism or hypothyroidism before and after the treatment. The ghrelin levels were not different from those of the control group.

Conclusion: Ghrelin is not likely to be the primary determinant of appetite changes in thyroid dysfunction.

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Keywords: Appetite • ghrelin • hyperthyroidism

Introduction

Ghrelin, a recently discovered hormone secreted mainly from the gut, is a growth hormone secretagogue.¹ It is found to regulate feeding behavior.² Ghrelin administration induces weight gain in rats.³ There is compelling evidence for a role of ghrelin in energy balance.⁴ A premeal rise in the ghrelin level has been reported in human. Also, ghrelin administration induces hunger.^{5,6} Although ghrelin is expected to play a role in obesity, it has been found that the serum ghrelin level is lower in obese individuals.⁷ Furthermore, negative energy balance conditions are associated with increased ghrelin levels.⁸

As alterations in body weight and appetite are hallmarks of thyroid disorders,⁹ it seems rational to assess the changes in the serum ghrelin levels in different states of thyroid dysfunction and explore

the role of ghrelin in appetite changes in these patients.

Materials and Methods

Forty-five patients newly diagnosed as having hypothyroidism and 45 patients newly diagnosed as having thyrotoxicosis were recruited and studied before and after medical treatment. The patient groups were compared to a group of 45 healthy individuals, age and body mass index (BMI) were matched, by the control group. Table 1 summarizes the characteristics of the subjects.

Fasting serum samples were taken from all subjects for measurement of total T4, T3, TSH, and ghrelin levels. Age, sex, and weight of the subjects were recorded. Human ghrelin was measured using a commercially available radioimmunoassay (RIA) kit (DRG International Inc., Germany); thyroid hormones were measured by RIA (Kavoshyar Iran Co.); and TSH was measured by immunoradiometric assay (IRMA) (Kavoshyar Iran Co.).

Statistical analysis

Data were presented as mean \pm SD. SPSS

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Table 1. Baseline characteristics of the participants.

	Hyperthyroid group	Hypothyroid group	Control group
*Age (year)	36.6 (13.04)	38.9 (12.8)	35.9 (12.6)
**BMI (kg/m ²)	21.8 (3.8)	27.04 (4.7)	22.02 (3.5)
Sex			
Male	53%	32%	20%
Female	47%	68%	80%

*Data are presented as mean \pm (SD); **BMI = body mass index.

Table 2. Mean \pm (SD) baseline thyroid function tests of the subjects.

	Hyperthyroid group	Hypothyroid group	Control group
T4 (μ g/dL)	19 (3.9)	2.2 (1.7)	7.8 (1.9)
T3 (μ g/dL)	459 (178)	67 (30)	126 (27)

software (version 11.5) was used for statistical analysis.

The ghrelin levels before and after treatment were compared by paired *t*-test. The ghrelin levels of hyperthyroid and hypothyroid patients, and control group were compared by unpaired *t*-test. Pearson correlation was used to measure the level of association between ghrelin and other variables. $P < 0.05$ was considered significant.

Results

The characteristics of the subjects and control group are shown in Table 1. Table 2 shows the mean values of T3, T4, and TSH in hyperthyroid, hypothyroid, and control groups.

The serum ghrelin levels before and after treatment are shown in Figure 1, which reveals a slight rise in the ghrelin levels in hyperthyroid patients after treatment, but it was not statistically significant ($P = 0.19$).

The baseline serum ghrelin levels were slightly higher in hyperthyroid patients compared to the

control group, but this was not statistically significant (Figure 1) ($P = 0.06$).

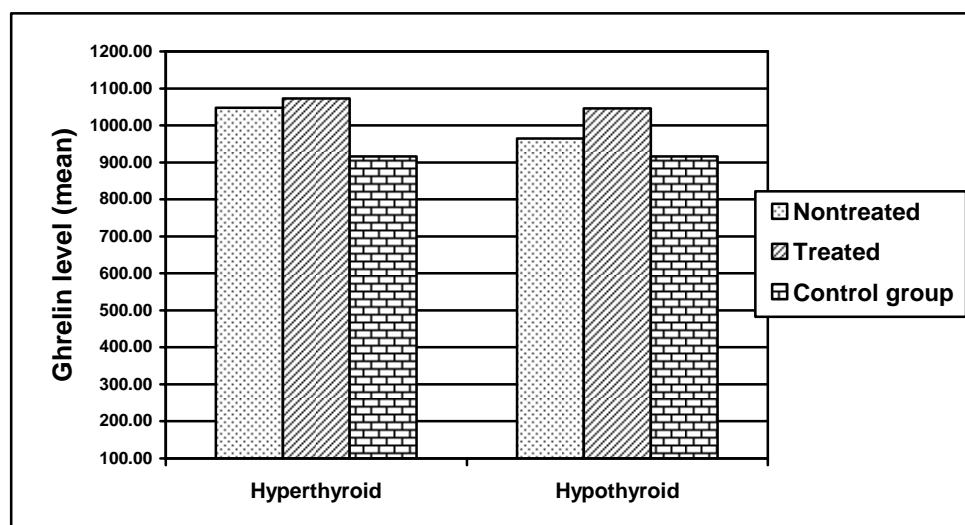
The baseline serum ghrelin levels were slightly, but not significantly, lower in hypothyroid subjects compared to hyperthyroid ones ($P = 0.29$).

The analysis of variance (ANOVA) did not show any significant difference between the mean ghrelin levels in different groups.

There was no significant correlation between the ghrelin levels and BMI, age, T4, and TSH in any of the groups. Although, a weak inverse correlation existed between ghrelin and BMI, and a weak positive correlation between ghrelin and TSH.

Discussion

We assessed the relationship between the plasma ghrelin levels in thyroid dysfunction and anthropometric parameters of the patients. The ghrelin levels are expected to be higher in patients with hyperthyroidism as in other negative energy balance states⁸; but in our study, the ghrelin levels

**Figure 1.** Serum ghrelin levels in hyperthyroid and hypothyroid patients before and after treatment.

were slightly lower in hyperthyroid patients before treatment compared with posttreatment values. This was true for the control group too.

Although the pretreatment values were lower in our study, but the difference was not significant ($P = 0.59$). In a study on nine patients with Graves' thyrotoxicosis, the ghrelin levels were lower in pretreatment stage compared with posttreatment values.¹⁰ In another study on 24 hyperthyroid patients, similar results were obtained. In that report, the authors concluded that the changes in the ghrelin levels were due to insulin resistance induced by thyrotoxicosis rather than negative energy balance.¹¹

These findings are similar to the results of Purnell et al and Hansen et al who reported the elevation of the ghrelin level in obese subjects after weight loss.^{12, 13}

As well as in patients with anorexia nervosa^{5, 14} and bulimia nervosa,¹⁵ it can be hypothesized that the change in food intake in patients with hyperthyroidism is regulated by other mechanisms, which in turn, may inhibit gastric ghrelin release through a feedback inhibition.

In our study, 45 hypothyroid patients, which is the largest studied group so far, were investigated. In this group, the ghrelin levels before and after treatment were not statistically different. The levels were not different with those of the control group either ($P = 0.19$).

In agreement with our results, there is a recent study on 17 hypothyroid patients, which showed no significant change in the ghrelin levels before and after treatment.⁸ In that study, there was no significant correlation between the plasma ghrelin levels and anthropometric parameters, which is similar to our results

Finally, we conclude that ghrelin is not likely to have a primary role in appetite changes in patients with thyroid dysfunction.

References

- 1 Kojima M, Hosoda H, Date Y, Nakazato M, Matsuo H, Kangawa K. Ghrelin is a growth hormone releasing peptide from stomach. *Nature*. 1999; **402**: 656 – 660.
- 2 Wren AM, Small CJ, Ward HL, Murphy KG, Dakin CL, Taheri S, et al. The novel hypothalamic peptide ghrelin stimulates food intake and growth hormone secretion. *Endocrinology*. 2000; **141**: 4325 – 4328.
- 3 Wren AM, Small CI, Abbott CR, Dhill WS, Seal LJ, Cohen MA, et al. Ghrelin causes hyperphagia and obesity in rats. *Diabetes*. 2001; **50**: 2540 – 2547.
- 4 Horvath TL, Diano S, Sotonyi P, Heiman M, Tschop M. Minireview: ghrelin and the regulation of energy balance—a hypothalamic perspective. *Endocrinology*. 2001; **142**: 4163 – 4169.
- 5 Cummings DE, Purnell JQ, Frayo RS, Schmidova K, Wisse BE, Weigle DS. A preprandial rise in plasma ghrelin level suggests a role in meal initiation in human. *Diabetes*. 2001; **50**: 1714 – 1719.
- 6 Wren AM, Seal LJ, Cohen MA, Brynes AE, Frost GS, Murphy KG, et al. Ghrelin enhances appetite and increases food intake in human. *J Clin Endocrinol Metab*. 2001; **86**: 5992 – 5995.
- 7 Tschop M, Weyer C, Tataranni PA, Devanarayan V, Ravussin E, Heiman ML. Circulating ghrelin levels are decreased in human obesity. *Diabetes*. 2001; **50**: 707 – 709.
- 8 Otto B, Cuntz U, Fruehauf E, Wawarta R, Folwaczny C, Riepl RL, et al. Weight gain decreases elevated plasma ghrelin concentration of patients with anorexia nervosa. *Eur J Endocrinol*. 2001; **145**: 669 – 673.
- 9 Ingbar DH. The thyroid gland. In: Wilson D, Foster DW, eds. *Textbook of Endocrinology*. Philadelphia: Elsevier Science; 1985: 976 – 1170.
- 10 Riis AL, Hansen TK, Moller N, Weeke J, Jorgensen JO. Hyperthyroidism is associated with suppressed circulating ghrelin levels. *J Clin Endocrinol Metab*. 2003; **88**: 853 – 857.
- 11 Gimenez-Palop O, Gimenez-Perez G, Mauricio D, Berlanga E, Potau N, Vilardell C, et al. Circulating ghrelin in thyroid dysfunction is related to insulin resistance and not to hunger, food intake or anthropometric changes. *Eur J Endocrinol*. 2005; **153**: 73 – 79.
- 12 Purnell JQ, Cummings D, Weigle DS. Changes in 24-h area-under-the-curve ghrelin values following diet-induced weight loss are associated with loss of fat-free mass, but not with changes in fat mass, insulin levels or insulin sensitivity. *Int J Obes (Lond)*. 2007; **31**: 385 – 389.
- 13 Hansen TK, Dall R, Hasoda H, Kojima M, Kangawa K, Christiansen JS, et al. Weight loss increases circulating levels of ghrelin in human obesity. *Clin Endocrinol (Oxf)*. 2002; **56**: 203 – 206.
- 14 Shirya T, Nakazato M, Mizuta M, Data Y, Mondal MS, Tanka M, et al. Plasma ghrelin levels in lean and obese humans and the effect of glucose on ghrelin secretion. *J Clin Endocrinol Metab*. 2002; **87**: 240 – 244.
- 15 Tanaka M, Naruo T, Muranaga T, Yasuhara D, Shiiya T, Nabazato M, et al. Increased fasting plasma ghrelin levels in patients with bulimia nervosa. *Eur J Endocrinol*. 2002; **146**: R1 – R3.