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ORIGINAL RESEARCH

Weight homeostasis in hyperthyroidism and treatment with carbimazole

[1]Pravin Kumar Jha, [2]Rajesh Kumar Jha

[1]Assistant Professor, Dept. of Cardiology, D.M.C.H., Darbhanga, Bihar, India
[2]Assistant Professor, Dept. of Medicine, D.M.C.H., Darbhanga, Bihar, India

Correspondence:
Rajesh Kumar Jha
Assistant Professor, Dept. of Medicine, D.M.C.H., Darbhanga, Bihar, India

ABSTRACT

Background & objectives: Hyperthyroidism is related to expanded food consumption, energy use and modified body synthesis. This study was meant to assess the job of adipocytokines in weight homeostasis in patients with hyperthyroidism.

Methods: Patients (n=27, 11men) with hyperthyroidism (20 Graves' sickness, 7 harmful multinodular goitres) with a mean period of 31.3±4.2 years and 28 sound Body Mass Index (BMI) matched controls were examined. They went through an evaluation of Lean Body Mass (LBM) and total muscle to total body fat (TBF) by double energy X-ray absorptiometer (DXA) and a blood test was taken in the fasting state for estimation of leptin, adiponectin, ghrelin, insulin, glucose and lipids. Patients were reexamined following 3 months of treatment as at that point every one of them accomplished euthyroid state with carbimazole treatment.

Results: The LBM was higher (P<0.001) in sound controls when contrasted with hyperthyroid patients even after a change for body weight (BW), though the absolute muscle to fat ratio was similar between the two groups. Serum leptin levels were higher in patients with hyperthyroidism than controls (22.3±3.7 and 4.1±0.34 ng/ml, P<0.001), though adiponectin levels were tantamount. Plasma acylated ghrelin was higher in patients than in controls (209.8±13.3 versus 106.2±8.2 pg/ml, P<0.05). The accomplishment of euthyroidism was related to huge weight gain (P<0.001) and a huge expansion in slender weight (P<0.001). The total muscle versus fat additionally expanded however unimportantly from 18.4±1.8 to 19.9±1.8 kg. There was critical lessening (P<0.05) in serum leptin and acylated ghrelin yet adiponectin levels stayed unaltered after treatment. Serum leptin is decidedly associated with TBF and this connection persevered even after changes for BW, BMI, orientation and age (r=0.62, P=0.001). Nonetheless, serum leptin and acylated ghrelin didn't associate with the presence or nonattendance of hyperphagia.

Conclusion: Patients with hyperthyroidism transcendently had diminished slender weight which expanded after the accomplishment of euthyroidism with carbimazole. The hyperphagia and the modifications in weight homeostasis related to hyperthyroidism were autonomous of flowing leptin and ghrelin levels.

Keywords: Adipocytokines, body composition, ghrelin, hyperphagia, hyperthyroidism

INTRODUCTION

Hyperthyroidism is perpetually connected with weight reduction despite expanded appetite[1,2]. Thyroid chemical overabundance is related to expanded food admission in people and rodents, conceivably as a compensatory reaction to expanded energy consumption due to uncoupling of oxidative phosphorylation coming about in expanded thermogenesis[3,4] or

potentially its immediate impact on the nerve centre.

The instruments liable for the excitement of food admission by thyroid chemicals have not yet been completely elucidated[5,6]. Food admission is controlled by complex instruments including hypothalamic neuropeptides which react to fringe satiety signals like leptin and ghrelin. Leptin is viewed as a crucial sign for satiety to the cerebrum and increments thermogenesis subsequently assuming a significant part in energy homeostasis[7-9]. In creature models of T3 prompted thyrotoxicosis, it has been found that diminished plasma leptin levels or potentially diminished responsiveness of satiety focus to leptin could add to hyperphagia[7,8].

Ghrelin is an original peptide emitted from the fundus of the stomach. It improves yearning and craving and transduces signs to hypothalamic administrative cores that balance energy balance in ordinary physiology[10,11]. Notwithstanding expansion in craving in patients with hyperthyroidism, serum complete ghrelin level has been demonstrated to be ordinary or low[12,13]. In a larger part of the previous investigations, serum complete ghrelin was estimated rather than acylated ghrelin which is the organically dynamic form[10-13].

Adiponectin, an adipocytokine is a peptide especially emitted from the more modest adipocytes and upgrades insulin awareness in target tissues[14,15]. In patients with hyperthyroidism, adiponectin level is relied upon to be low and may add to insulin resistance[16]. Expansion in insulin opposition essentially may bring about an expansion in hunger with a special longing for carb foods[6,11].

A few examinations directed in patients with hyperthyroidism have shown conflicting outcomes in regards to the change in adipocytokines and ghrelin[11-16]. These investigations were either cross-sectional or had little example size and all the more critically body structure was not surveyed with fitting modalities to correspond with these modulators[11-16].

The current study was embraced to assess adjustment in body arrangement and its relationship with adipocytokines and ghrelin in patients with hyperthyroidism.

MATERIAL & METHODS

31 successive patients with hyperthyroidism were enlisted from the Endocrinology Out Patient Department of Darbhanga Medical College Hospital, Darbhanga, India, from November 2020 to July 2021. Every one of them was walking, and treatment credulous. Informed assent was acquired from all patients. Of these, 27 patients (16 female, 2 postmenopausal) were remembered for conclusive investigation. Considering body weight change (weight gain) as an agent of reaction boundary, an example size of 20 was satisfactory to recognize a weight gain of 4 kg following 3 months of treatment with carbimazole, in a two-sided matched 't-test with a 5 percent alpha mistake and 90 percent power. Considering misfortunes during the treatment time frame, an example size of something like 25 patients was chosen.

Subjects with diabetes, liver and kidney problems, cardiovascular disappointment and basic diseases were avoided. Not even one of them was an alcoholic, smoker or getting prescriptions known to modify glucose, lipid and weight homeostasis. The etiology of hyperthyroidism was Graves' illness in 20 patients and the excess seven had a poisonous multinodular goitre. 28 euthyroid subjects with comparative BMI were incorporated as controls. The controls were emergency clinic representatives and family members of patients who were not experiencing any thyroid issues and were generally solid. The two cases and controls were having a stationary way of life. They went through an evaluation of body synthesis and chemical profile including thyroid profile and serum leptin, adiponectin and ghrelin levels. Hyperthyroidism was analyzed given common signs and side effects, raised T3 and T4 and stifled thyroid stimulating hormone (TSH) levels contrasted with the reference range. "Recall method" was utilized to survey the food consumption throughout the previous

three days. Hyperphagia was characterized as an increment in calorie consumption by >30 percent when contrasted with before the beginning of the indications with practically no other co-morbidities. This depended on the typical models for critical modification in light of any type of treatment. Blood tests were taken after a short-term quick from an antecubital vein somewhere in the range of 0830 and 0900 h. The blood test was centrifuged and plasma aliquots were kept at - 20oC. The body organization including lean body mass (LBM), total body fat (TBF) and bone mineral content (BMC) and bone mineral density (BMD) was evaluated by Dual Energy X-ray Absorptiometer (DXA, Norland, XR46, USA). The accuracy mistake was ±1 percent assuming it was rehashed inside 24 h, and >2.5 percent on the off chance that it was rehashed following 2-6 months according to the producer's subtleties. The DXA was finished by a solitary expert. The patients were treated with a middle portion of 30 mg of carbimazole and encouraged to consume non-iodized salt. The patients were generally not on some other drugs and they were reconsidered at 6 weeks (information not shown) and twelfth week as at that point all patients accomplished euthyroid state.

HORMONE ASSAYS

Thyroid chemicals (T3 and T4) were assessed by radioimmunoassay and TSH by immunoradiometric assay (IRMA) utilizing commercial kits (Board of Radiation and Isotope Technology, India). The ordinary reach for T3 was 0.6-1.6 ng/ml, T4 4.5-12 µg/dl and TSH 0.5-5.2 µU/ml. Plasma leptin was estimated by sandwich ELISA examination (DRG, GmBH, Germany) with a base recognition breaking point of 1.0 ng/ml. The intra-and between test coefficients of variety were 3.5 and 6.5 percent, separately. Adiponectin levels were estimated by compound connected immunosorbent test (ELISA) utilizing the human adiponectin unit (Biovendor lab, Medicine, Inc, USA). The intra-and between examine coefficients of variety were 6.4 and 7.3 percent, individually and the least identification limit was 0.2 µg/ml. Plasma acylated ghrelin was estimated by ELISA (human acylated ghrelin, SPI, Montigmy Le Bretonneux, France) with intra-and between test coefficient of variety being 2.9 and 3.4 percent, separately. The lower identification cutoff of the examination was 1.5 pg/ml and the ordinary reach was 66.2-180 pg/ml.

STATISTICAL ANALYSIS

Statistical analysis was carried out with Microsoft Excel data analysis and SPSS 10.0 for windows, (Chicago Illinois, USA) using simple correlation. Mean values were compared using the Student's t-test. Normality of data was checked by KolmogorovSmirnov method. Pearsons correlation was used to find out the relationship between adipocytokines and ghrelin with various other parameters. The hormone levels measured at baseline and after the achievement of euthyroidism were compared by paired t-test.

RESULTS

The study groups comprised 31 patients and 27 of them (men 11) finished the review as three patients were lost to follow up and one got radio ablation. The mean age of the patient's groups was 31.3±4.2 years and the median lag time between the beginning of indications and analysis was a half year. 22 (81.5%) out of 27 patients had hyperphagia. The mean BMI of the patients' gathering was 20.5±0.7 kg/m2 and the abdomen outline was 73.4±2.3 cm. The LBM and TBF as surveyed by DXA at gauge were 32.6±1.6 and 18.4±1.8 kg, separately. The BMD and BMC were 0.88±0.04 g/cm2 and 2226.0±60.8 g, individually. The controls (men 14) had a tantamount BMI of 21.6±0.6 kg/m2 and higher LBM (46.3±1.3 kg, $P<0.001$). This fundamentally higher LBM in controls persevered after factual change for body weight. In any case, they had a comparative TBF of 18.7±1.2 kg when contrasted with patients. The

BMD (P<0.05) and BMC (P<0.001) in the benchmark group was higher at 0.98±0.02 gm/cm2 (P=0.02) and 2767.9±63.0 gm (P<0.001) when contrasted with the patient's groups. The pattern serum T3, T4 and TSH in the patient's groups were 4.0±0.5 ng/ml, 23.3±2.9 µg/dl and 0.1±0.0 µU/ml individually. Serum fatty substance level was 150.6±18.0 mg/dl and HOMA IR 1.4±0.02. The mean serum leptin and adiponectin in hyperthyroid patients and solid controls were 22.3±3.7 versus 4.1±0.3 ng/ml (P<0.001) and 12.5±2.3 µg/ml versus 10.4±4.3 (P=0.75) individually. The mean plasma acylated ghrelin level at the pattern in patients with hyperthyroidism was 209.8±13.3 pg/ml (typical reach 66.2-186 pg/ml) which was higher when contrasted with solid controls (106.2±8.2 pg/ml, P=0.05).

Table I Baseline characteristics of the patients and controls

Parameter	Hyperthyroid patients (n=27)	Healthy controls (n=28)
Age (yr)	31.3 ± 2.2	30.0 ± 1.8
Weight (kg)	53.2 ± 2.0**	67.9 ± 2.1
BMI (kg/m^2)	20.5 ± 0.7	21.6 ± 0.6
LBM (kg)	32.6 ± 1.6***†	46.3 ± 1.3
TBF (kg)	18.4 ± 1.8†	18.7 ± 1.2
% BF	34.7 ± 0.7†	27.2 ± 0.9
BMD (g/cm^2)	0.88 ± 0.04*	0.98 ± 0.02
BMC (g)	2226.0 ± 60.8***	2767.9 ± 63.0
HOMA-IR	1.4 ± 0.02*	0.8 ± 0.01
Leptin (ng/ml)	22.3 ± 3.7***	4.1 ± 0.3
Adiponectin (µg/ml)	12.5 ± 2.3	10.4 ± 4.3
Acylated ghrelin (pg/ml)	209.8 ± 13.3*	106.2 ± 8.2

Values are given as mean ± SEM
BMI, Body mass index; TBF, total body fat; %BF, percentage body fat; LBM, Lean body mass; BMC, bone mineral content; BMD, bone mineral density; HOMA-IR, homeostasis model assessment-insulin resistance
†The significance remained unchanged after statistical adjustment for body weight
*P**<0.05, **<0.01, ***<0.001 compared to controls

After 12 weeks of treatment with carbimazole (median dose of 30 mg/day), all patients achieved a euthyroid state with a significant decrease in T_3 (1.6±0.1 ng/ml), T_4 (9.6±0.6 µg/dl) and increase in TSH levels (0.6±0.1 µU/ml, range 0.6-3.3). All patients had a significant (*P*<0.001) weight gain after carbimazole therapy and had an increase (*P*<0.001) in lean body mass. Though the total body fat also increased from 18.4±1.8 to 19.9±1.8 kg, it could not achieve statisticalsignificance. The BMD did not increase but BMC increased significantly after treatment (*P*<0.05). There was a significant improvement in HOMA-IR (*P*<0.05) after treatment and a decrease (*P*<0.05) in leptin levels, however, the adiponectin level did not change.

Table II Body composition parameters in hyperthyroid patients before and after treatment with carbimazole

Parameters	Before treatment (95% CI)	After treatment (95% CI)
Weight (kg)	53.0 ± 2.0 (48.9 - 57.2)	56.9 ± 2.1 (52.7-61.2)**
BMI (kg/m^2)	20.5 ± 0.7 (18.9-21.7)	21.9 ± 0.6 (20.2-22.7)**
Waist circumference (cm)	73.4 ± 2.3 (68.7-78.2)	76.4 ± 2.0 (72.2-80.5)**
LBM (kg)	32.6 ± 1.6 (29.2-35.9)	35.4 ± 1.6 (31.9-38.8)**
TBF (kg)	18.4 ± 1.8 (14.7-22.1)	19.9 ± 1.8 (18.1-23.6)
%BF	34.6 ± 1.2 (31.3-36.4)	34.6 ± 0.7 (32.1-36.9)
T-score	-1.3 ± 0.2 (-1.6-1.0)	-1.3 ± 0.2 (-1.6-1.0)
Z-score	-0.9 ± 0.2 (-1.3-0.5)	-0.7 ± 0.2 (-1.1-0.3)
BMD (g/cm^2)	0.88 ± 0.03 (0.8-1.0)	0.89 ± 0.04 (0.8-1.0)
BMC (g)	2226.0 ± 60.8 (2101-2351)	2260.0 ± 61.8 (2183.5-2387)*

Values are given as mean ± SEM
LBM, lean body mass; TBF, total body fat; BMD, bone mineral density; BMC, bone mineral content
P<0.05, **<0.001 compared to before treatment

The plasma acylated ghrelin level decreased significantly (P<0.05) after the achievement of euthyroidism. The improvement in insulin resistance commensurated with decrease in serum triglyceride (r=0.62, P=0.01) and decrease in leptin levels (r=0.43,P=0.02).

There was a significant positive correlation observed between serum leptin with hip circumference(r=0.41, P=0.03), TBF (r=0.62, P<0.001), BMD (r=0.45, P=0.02) and serum triglyceride levels (r=0.55, P<0.001**)**. However, no significant correlation could be observed with the presence or absence of hyperphagia, BMI, LBM, serum T_3, T_4 and HOMA- IR. After adjustment for BMI, gender and age, the correlation between serum leptin with TBF (r=0.50, P<0.02) and BMD (r=0.60, P=<0.001) persisted. The serum adiponectin level had only a positive correlation with T_3 (r=0.59, P=0.001) and T_4 (r=0.44, P=0.02), while no correlation was observed with total body fat, HOMA-IR and triglyceride. After adjustment for BMI, age and gender the correlation between adiponectin and T_3 persisted (r=0.85, P<0.001). Ghrelin positively correlated with serum total cholesterol (r=0.45, P=0.021) and negatively correlated with serum T_3 level (r=0.40, P=0.04). However, no correlation was found with the presence or absence of hyperphagia, serum insulin, blood glucose, triglyceride, HOMA-IR, TBF, LBM, BMC and BMD. After treatment with carbimazole, no correlation was observed between serum leptin, adiponectin, ghrelin with TBF, BMD and presence or absence of hyperphagia.

DISCUSSION

This study shows that patients with hyperthyroidism had weight reduction overwhelmingly because of diminishing in fit weight notwithstanding expanded food consumption. It went with expanded serum leptin and ghrelin levels. Treatment with carbimazole brought about significant expansion in slender weight with modest expansion in fat mass and abatement in

both leptin and ghrelin levels. Modifications in body synthesis and hunger in subjects with hyperthyroidism give off an impression of being free of circling leptin and ghrelin levels.

The impacts of thyroid chemicals on body arrangement have been portrayed widely in the literature[1,2]. In patients with hyperthyroidism, before antithyroid medication treatment, a significant lessening in slender weight, an unobtrusive reduction in fat mass and BMD have been described[2]. Our review gives similar perceptions. After treatment with antithyroid treatment, there was weight gain, which was mostly contributed by expansion in slender weight and unobtrusive increase in fat mass, likely because of abatement in thermogenesis and protein catabolism, which is reliable with the past studies[2-4].

At the hour of analysis of hyperthyroidism, there is a significant weight reduction regardless of the expansion in craving and food consumption in the greater part of the patients. Weight reduction in patients with hyperthyroidism is owing to misrepresented thermogenesis interceded by uncoupling of oxidative phosphorylation by thyroid hormones5. Weight reduction despite expanded craving can be clarified by the way that either the calorie admission was not significant to hold over the misrepresented basal metabolic rate or a few different variables like adipocytokines may be balancing weight reduction in patients with hyperthyroidism. Past investigations have shown variable plasma leptin levels (high or low typical to ordinary) in patients with hyperthyroidism which can be clarified by factor span and seriousness of the infection, shifting measure of muscle versus fat and inconstancy in leptin assay[18-22]. We attempted to defeat these restrictions in the current review and showed that the plasma leptin levels were higher in these patients when contrasted with sound controls with comparative BMI and muscle versus fat. This might be credited to coordinating the impact of thyroid chemicals on leptin mRNA articulation as shown by in vitro investigations of modified leptin digestion and expanded insulin obstruction in hyperthyroid state[16,22]. In typical physiology, leptin is related to weight reduction by its impact on the nerve center through neuropeptide Y (NPY) articulation along these lines bringing about diminished food admission and upgrading thermogenesis[3,23]. The perception of weight reduction despite expanded hunger in these patients with higher leptin levels can be clarified by differential leptin responsiveness, that is its diminished awareness at the nerve center (taking care of focus) while protected activity at the outskirts brings about expanded craving and misrepresented thermogenesis, separately. On the other hand, expanded appetite and food admission might be connected with a vague flagging pathway from the fringe, actuated by misrepresented thermogenesis to the nerve centre. The absence of a relationship among's leptin and hyperphagia and thyroid chemicals recommends that the impact of leptin is overwhelmed by expanded thermogenesis initiated by thyroid chemicals. The decline in serum leptin notwithstanding expansion in muscle versus fat after treatment with carbimazole might be because of these instruments and a huge improvement in insulin obstruction as serum leptin level and insulin opposition go hand in hand[16,21,22]. Our concentrate additionally showed that serum ghrelin levels were higher at benchmark and standardized after accomplishment of euthyroidism as displayed earlier[11,12]. A couple of studies in patients with hyperthyroidism have shown variable ghrelin levels. One of the past reviews has shown a moment to minute variety in serum ghrelin level connected with insulin responsiveness during hyperinsulinaemic, euglycaemic clasp concentrate rather than thyroid chemical level[11]. The higher ghrelin level in our review was potentially a compensatory reaction to negative energy balance as depicted in patients with anorexia nervosa and stout patients on weight reduction programme[24-26]. The past investigations didn't show expanded ghrelin levels perhaps in light of polyclonal tests and estimating complete rather than acylated ghrelin[12]. In the current review, plasma ghrelin levels didn't relate to hyperphagia as likewise presented in past studies[12,21,25-27].

Serum adiponectin levels are conversely connected with the level of adiposity and insulin

obstruction in solid subjects and type 2 diabetes mellitus[14,15,21]. In the current review serum, adiponectin levels were tantamount among patients and controls conceivably due to comparative complete muscle to fat ratio mass. Additionally, serum adiponectin levels stayed unaltered even after the accomplishment of euthyroidism due to immaterial expansion in absolute muscle versus fat. This is additionally validated by the perception that thyroid chemicals don't influence adiponectin mRNA articulation as shown by in vitro studies[16,22]. Comparable perception has been made in past studies[21,23].

The qualities of the review incorporate the presence of control groups, assessment of acylated ghrelin and follow up after enemy of thyroid treatment, while constraints included the absence of genuine rules to characterize hyperphagia, absence of an evaluation of thermogenesis and brief length of follow up.

CONCLUSION

Taking everything into account, patients with hyperthyroidism have a decline in fit weight, which was recaptured after the accomplishment of euthyroidism with carbimazole treatment. The hyperphagia went with weight reduction in hyperthyroidism was free of leptin and ghrelin.

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