Role of Leptin in Hyperthyroidism

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Received 20 April 2014 **Accepted 2 June 2014**

Abstract

Clinical hyperthyroidism is caused by the effects of excess thyroid hormone and can be triggered by different disorders**.** Hyperthyroidism presents with multiple symptoms that vary according to the age of the patient, duration of illness, magnitude of hormone excess and presence of comorbid conditions**.** Leptin is mainly synthesized and secreted by adipocyte. In addition to the white adipose tissue it can also be produced by brown adipose tissue, placenta, ovaries, skeletal muscle, stomach, mammary epithelial cells, bone marrow, pituitary and liver. It is a messenger of satiety from the fat cells to the brain, a regulator of insulin and glucose metabolism and plays a role in energy balance and body weight by neuroendocrine mechanisms.

This study was performed at the laboratories of Biochemistry Department, College of Medicine, University of Babylon. The collection of samples was conducted during the period from the of June 2013 till September 2013 at Al Hussain teaching hospital in Karblaa, including 48 patients diagnosed as hyperthyroidism with age ranging from 19-55 years. In addition to 30 apparently healthy individuals were taken as a control group. Measurement of serum T3, T4, TSH and leptin were done for all patients and control groups. Serums T3, T4, TSH were done by VIDAS technique with principle of combines a one-step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA), while the serum leptin done by ELISA technique with principle of Enzyme-Linked Immunosorbent Assay.

The mean age of patient was (38.25± 7.63) whereas the mean of control group was (36.90 ± 5.67) with no statistical differences. Majority of studied patients was female (75.6%). Body Mass Index (BMI) for patients group was (20.95 ± 3.59), majority (48.7%) were underweight. There were significant statistical differences between the mean of Leptin of patients (5.48± 2.72) ng/ml and the mean of control group (35.59 ± 10.74) ng/ml.

Low level of leptin might be the responsible cause of increased appetite in hyperthyroidism patient.

Keyword: Hyperthyroidism, Leptin.

دور اللبتين في فرط افراز الغدة الدرقية

الخلاصة

يعاني المريض صاحب فرط الغده الدرقية من آثار هرمونا لغدة الدرقية الزائد،ويمكن أن يكون سببها اضطرابات مختلفة. يتمثل مع أعراض فرط نشاط الدرق المتعددة التي تختلف وفق العمر المريض ،ومدة المرض،وحجم الهرمون الزائد وجود الظروف المرضية. اللبتين يتم تصنيعه أساسا ويفرز من قبل الخلايا الشحمية. بالإضافة إلى الأنسجة الدهنية البيضاء فإنه يمكن أيضا أن تنتجها الأنسجة الدهنية البنية والمشيمة والمبايض والعضلات والهيكل العظمي والمعدة وخلايا الظهارية الثديية ونخاع العظام والغدة النخامية والكبد.

وهو رسول الشبع من الخلايا الدهنية إلى الدماغ ،وهو منظم من الانسولين و الجلوكوز في عملية التمثيل الغذائي ويلعب دورا في توازن الطاقة ووزن الجسم عن طريق الآليات الهرمونية العصبية.

وقد أجريت هذه الدراسة في مختبرات قسم الكيمياء الحيوية،كلية الطب,جامعة بابل. وأجري جمع العينات خلال الفترة من ١ حزيران ٢٠١٣ حتى ٣٠ ايلول ٢٠١٣ في مستشفى الحسين التعليمي في كربلاء المقدسه، تضمنت الدراسه ٤٨ مريضا شخص تعاني فرط افراز الغده الدرقيه تتراوح اعمارهم ١٩–٥٥ سنة. بالإضافة إلى ٣٠ من الأفراد الأصحاء كمجموعة سيطره. وقد أجريت قياسT3وT4وTSHوهرمون الليبتين لجميع المرضى ومجموعة السيطره في موصول الدم. الأمصالT3،T4،TSHتم القيام قياسه بواسطة تقنية(VIDAS)بمبدأ خطوة واحدة انزيميه مناعية على شكل شطيرة مع كاشف الفلورسنت (ELFA)،في حين أن اللبتين في الدم قيس بتقنيةELISA مع مبدأ مقاييس الإنزيم المناعي المرتبط.

كان متوسط عمر المرضى (٣٨.٢٥ ± ٧.٦٣) في حين كان متوسط مجموعة السيطره (٣٦.٩٠ ± ٥.٦٧) مع عدم وجود فروق ذات دلالة إحصائية. وكان غالبية المرضى الخاضعين للدراسة الإناث (٧٥.٦٪). مؤشر كتلة الجسم (BMI) لمجموعة من المرضى كان (٢٠.٩٥ ± ٣.٥٩)،وكانت الغالبية (٤٨.٧٪) يعانون من نقص الوزن. كانت هناك فروق ذات دلالة إحصائية بين متوسط اللبتين من المرضى (٥.٤٨ ± ٢.٧٢) نانو غرام / مل ومتوسط مجموعة السيطره (٣٥.٥٩ ± ١٠.٧٤) نانو غرام / مل.

انخفاض مستوى هرمون الليبتين قد يكون السبب المسؤول عن زيادة الشهية في المريض فرط نشاط الغده الدرقيه.

الكلمات الافتتاحيه : فرط الغده الدرقيه , لبتين

Introduction

Clinical hyperthyroidism is caused by the effects of excess thyroid hormone and can be triggered by different disorders; etiologic diagnosis influences prognosis and therapy and the prevalence of hyperthyroidism in community-based studies has been estimated at 2 percent for women and 0.2 percent for men [1].Hyperthyroidism presents with multiple symptoms that vary according to the age of the patient, duration of illness, magnitude of hormone excess and presence of comorbid conditions [2].Many people with hyperthyroidism feel warm even in a cool room; their skin may become moist as they tend to sweat profusely, and they may develop "myxedema" which is known to occur in various forms of hypothyroidism, and also in Graves' disease [3].

Thyroid function, even within the reference range, is associated with changes in body weight [4]. However, the pathogenesis of this link between thyroid function and body weight is not clear and it must consider not only changes of thyroid hormones, but also body fat distribution [5]. Leptin is mainly synthesized and secreted by adipocyte [6]. In addition to the white adipose tissue (the major source of leptin) it can also be produced by brown adipose tissue, placenta (syncytiotrophoblast). Ovaries, skeletal muscle, stomach (low part of fundic glands), mammary epithelial cells, bone marrow, pituitary and liver [7]. It is a messenger of satiety from the fat cells to the brain, a regulator of insulin and glucose metabolism and plays a role in energy balance and body weight by neuroendocrine mechanisms [8]. Leptin circulates in the plasma in a free form or bound to leptin-binding proteins, leptin is produced in larger quantities in subcutaneous adipose tissue than in visceral adipose tissue [9]. A fall in leptin mediates weight gain through the hypothalamus to increase appetite, decrease energy expenditure and modify neuroendocrine functions [10]. Main function of leptin involved in energy

balance and as a mediator of the adaptation to fasting [11]. Increased levels in the blood positively correlate with fat stores in many species [12].In addition to regulation of appetite, thermogenesis and body weight, leptin has multiple other biological actions. Leptin also modulates different other functions by direct peripheral action in various tissues or through activation of thermo genic and cardio renal sympathetic nerve activity [13].

Thyroid hormones act on several aspects of metabolic and energy homeostasis controlling body weight, thermogenesis, as well as lipolysis in adipose tissue. Similarly, adipocytokines have multiple effects on several tissues acting on the energy homeostasis. Hence the increased concern about the possible relationship between adipocytokines, thyroid status, and thyroid dysfunction [14].

Material and methods

This study was performed at the laboratory of Biochemistry Department, College of Medicine, University of Babylon. The collection of samples was conducted during the period from June 2013 till September 2013 at Al Hussain Teaching Hospital in Karbala.

The patients group subjected in this study was (48) persons ranging from 19-55 years old, the mean ± standard deviation (SD) was (37.73 ± 6.94 years). Majority (75.6%) of the study respondents and control were female.

All patients were examined by surgeon in hospital, clinical symptoms and signs of those patients were recorded.

Exclusion criteria include:Patients under antithyroid drug,Patients with previous therapy of steroid and women patient in this study were not pregnant and no history of contraceptive drugs. Control group include thirty apparently healthy individuals.

Venous blood samples collected to the two groups. Sera were separated, divided into three parts in sterile eppendorffs tubeand frozen until assay time under -20C.

Determination of serum T3, T4 and TSH for all patients and control group were done by (Mini-VIDAS,BioMerieux (France)) and serum leptin by (ELISA system,Creative diagnostic (U.S.A))

Results

Age

The mean age ±SD of hyperthyroid patient was (38.25± 7.63) where- as the mean ±SD of control group was (36.90 ± 5.67). Majority of study respondent was female (75.6%).There was no significant mean difference between patients with hyperthyroidism and control $p > 0.05$ Fig (1).

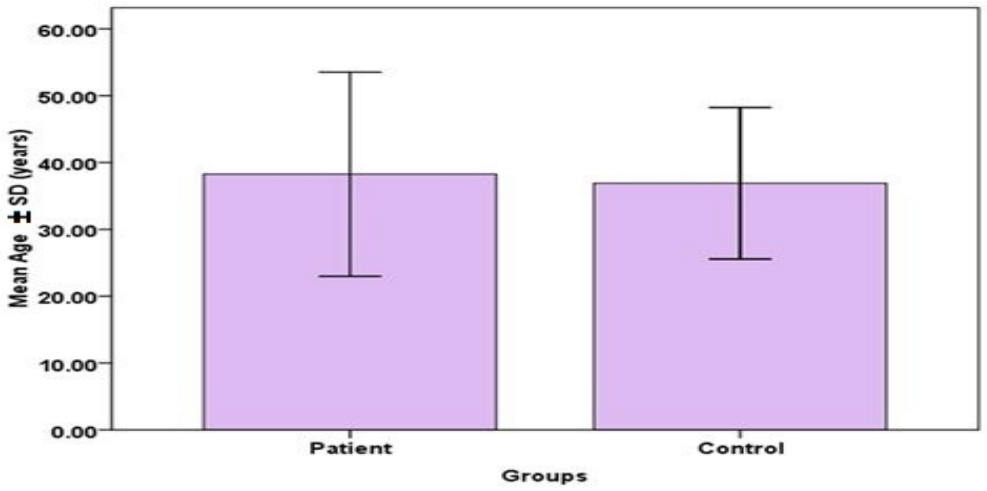

Fig (1): Mean difference of study groups by age

The patients mean Body Mass Index (BMI) was (20.95 ± 3.59) and ranged from (17.08 – 39. 26) kg/ m^2. Majority (48.7%) of study respondents were underweight, meanwhile only (34.6%) were normal weight and only (16.7%) were overweight .The control mean BMI was (25.89±2.53) There was significant statically difference between patients with hyperthyroidism and control $p \leq 0.05$.

The mean ±SD of T3, T4,and TSH of the study respondents. There were significant mean differences between patients with hyperthyroidism and control by TSH, T4, T3, and leptin showed in table (1).

Fig (2) showed the mean differences of leptin by study groups. There were significant differences between the mean leptin of patient (5.48± 2.72) ng/ml and the mean of control (35.59 ± 10.74) ng/ml ($p< 0.001$).

Variable	Groups	N	Mean	S.D	t-test	P value
TSH	Patient	48	0.05	0.0	15.873	<0.01**
	Control	30	1.54	0.67		
T4	Patient	48	149.72	59.31	10.134	<0.01**
	Control	30	82.97	13.46		
T3	Patient	48	4.14	1.21	12.301	<0.01**
	Control	30	1.36	0.21		

** p value ≤ 0.05 is significant

Table (1) Mean differences of study groups by TSH, T4, T3, and Leptin.

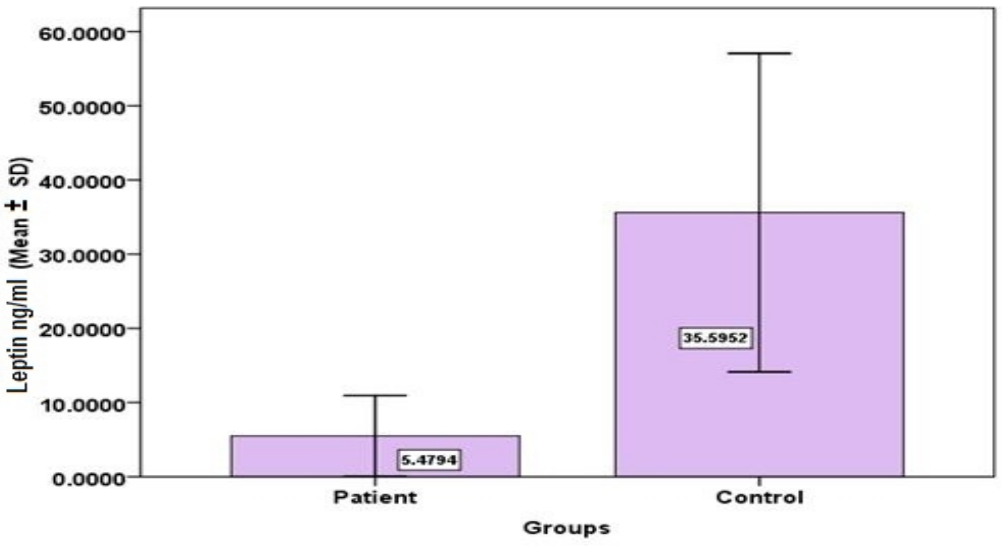

Fig (2): Mean differences of leptin in study groups.

Table (2) showed the correlation of leptin with T3, T4 and TSH for patients. There was significant correlation between leptin and T3 among patients; whereas there were no significant correlations between leptin and each of T4, TSH among patients.

Variable	Mean	S.D	r	P value
TSH	0.005	0.0	0.0	---
T4	194.72	59.31	-0.151	0.306
T3	4.139	1.21	**-0.329**	**0.022***

*p value ≤ 0.05 is significant

Table (2): Correlations of lipten withT3, T4 and TSH for patients.

Discussion

The inter relationship between obesity and thyroid hormones in determining that the circulating levels of leptin is still a matter of discussion, although the major determinates of leptin levels, are gender and amount of fat, other factors are likely to be implicated in determining circulating leptin concentrations, thyroid hormones exert a negative effect on leptin secretion in vitro; thus, leptin levels were lower than normal in hyperthyroid patients [15].

In the current study there were significant statistical differences

between the mean of serum leptin level of patients and the mean of control group. Leptin concentrations were lower in hyperthyroidism patients than control group. Decreased leptin levels could cause reduction in energy expenditure, which is not seen in hyperthyroidism due to hypermetabolic state of high thyroid hormones levels. This finding of low leptin level could be explain by stimulation of Beta adrenergic receptors in hyperthyroidism with hyperadrenergic state exists at the level of the adipocyte causing the suppresses of expression of circulating leptin levels. Low serum level of leptin may stimulate increase appetite state of patient with hyperthyroidism by hypothalamus stimulation.

This finding of low leptin level is consistent with many other studies [16][17] which showed leptin concentrations were significantly decreased in all hyperthyroid patients as compared with that of controls. That is because of the thyroid hormones which produce over activity of sympathetic nervous system, resulting in the increase release of norepinephrine from sympathetic nerve endings in adipose tissue, the fat cells express adrenergic receptors that are stimulated by norepinephrine, causing fatty acid hydrolysis and also uncouple energy production from fat store of hyperthyroid patients, low serum leptin level in hyperthyroid patients is due to hyperadrenergic state found in these patients and /or it may be the result of suppression of leptin gene expression due to over activity of TSH receptors by auto antibodies [18] [19].

Conclusion

Low level of leptin might be the responsible cause of increased appetite in hyperthyroidism patient

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