Role of Leptin in Hyperthyroidism

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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 Karbala, 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 الليبتين في فرط افراز الغدة الدرقية

الخلاصة

يعاني المريض صاحب فرط الغدة الدرقية من آثار هرمونها لغدة الدرقية الزائدة ويمكن أن يكون سببها اضطرابات مختلفة. يُتمثل مع أعراض فرط نشاط الدرق المتعددة التي تختلف وفق العمر المريض ونوع المريض وحجم الهرمون الزائد وجود الظروف المرضية. الليبتين يتم تصنيعه أساساً ويزرع من قبل الخلايا الشحمة. بالإضافة إلى الأنسجة الدهنية البيضاء فإنه يمكن أيضاً أن تنتجها الأنسجة الدهنية البنية والشيمة والبؤس والعضلات والهيكل العظمي والأنابيب والخلايا الطهارية الثابتة وندخع العظام والغدة النخامية والكبد.
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 tube and frozen until assay time under -20C. Determination of serum T3, T4 and TSH for all patients and control group were done by (MiniVIDAS, 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/ m². 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 (\( p < 0.001 \)).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Groups</th>
<th>N</th>
<th>Mean</th>
<th>S.D</th>
<th>t-test</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>Patient</td>
<td>48</td>
<td>0.05</td>
<td>0.0</td>
<td>15.873</td>
<td>&lt;0.01**</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>30</td>
<td>1.54</td>
<td>0.67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>Patient</td>
<td>48</td>
<td>149.72</td>
<td>59.31</td>
<td>10.134</td>
<td>&lt;0.01**</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>30</td>
<td>82.97</td>
<td>13.46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>Patient</td>
<td>48</td>
<td>4.14</td>
<td>1.21</td>
<td>12.301</td>
<td>&lt;0.01**</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>30</td>
<td>1.36</td>
<td>0.21</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

** p value \( \leq 0.05 \) is significant

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>S.D</th>
<th>r</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>0.005</td>
<td>0.0</td>
<td>0.0</td>
<td>---</td>
</tr>
<tr>
<td>T4</td>
<td>194.72</td>
<td>59.31</td>
<td>-0.151</td>
<td>0.306</td>
</tr>
<tr>
<td>T3</td>
<td>4.139</td>
<td>1.21</td>
<td>-0.329</td>
<td>0.022*</td>
</tr>
</tbody>
</table>

*p value ≤ 0.05 is significant

**Table (2): Correlations of leptin with T3, 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

**Reference**

2- Jack DeRuiter. (2002). Thyroid hormone tutorial: thyroid pathology.Endocrine module (pypp 5260), Thyroid Section, spring.


