Effect of Low Calorie Diet and Exercise on Thyroid Hormones and Leptin Levels

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Abstract

Aim of the Work: To investigate the effect of low calorie diet alone and the effect of low calorie diet and exercise on the levels of thyroid hormones, leptin, and BMI. Also we tried to investigate if there is a relation between thyroid hormones and leptin levels.

Subjects and Methods: Two groups of normal male subjects, each group consists of 25 person matched for age and BMI. Group I had low calorie diet program for one month (1200-1500 Kcal). Group II had the same low calorie diet in addition to program of therapeutic exercise on treadmill with moderate intensity every other day for one month. Evaluation of free T3, freeT4, TSH, leptin levels, and BMI were done before and after the study. Correlation between thyroid hormones and leptin levels were done.

Results: This study showed significant increase in Free T3, T4, and significant decrease in TSH, leptin and BMI after one month of low calorie diet program (group I) compared to their levels before the study.

After one month of low calorie diet and the exercise program (group II), a highly significant increase in free T3, T4 and highly significant decrease in TSH, leptin and BMI compared to their levels before the study.

Comparing the studied parameters of both groups after the study showed that there is a more significant increase in T3 & T4 and a more significant decrease in TSH & BMI in group II compared to group I. Leptin level showed no statistically significant difference. A positive correlation between BMI and leptin was found in both groups. We found no relation between thyroid hormones and leptin levels.

Conclusion: Low calorie diet caused increase in the level of circulating thyroid hormones, and a decrease in TSH, leptin levels and BMI. Low calorie diet and moderate intensity therapeutic exercise caused more significant increase in the level of circulating thyroid hormones, more significant decrease in TSH level and BMI. No statistically significant difference in leptin level of both groups after the study. We found no relation between leptin level and thyroid hormone levels.

Key Words: Diet – Exercise – Thyroid hormones – Leptin.

Introduction

OBESITY is a serious illness that can lead to many medical complications. Low calorie diet and exercise are essential part in the treatment of obesity [1].

Effect of exercise on circulating levels of thyroid hormone (which are important in body weight regulation) remains controversial [2].

Thyroid hormones act on several aspects of metabolic and energy homeostasis influencing body weight, thermogenesis, and lipolysis in adipose tissue.

Several research groups have reported that exercise results in significant reduction in T3, T4, and TSH concentrations. Other studies have reported that exercise to exhibit no influence on thyroid hormone concentrations, and some other studies have reported increased hormonal levels in response to exercise [3]. The ambiguity within the research findings suggests that further investigations are necessary on this topic [4].

Adipocytokines are biologically active substances produced by adipocyte with different physiological functions. These substances have multiple effects on several tissues acting on the intermediate and energy metabolism. Leptin, a signal of satiety to the brain and regulator of insulin and glucose metabolism, reflects the amount of fat storage and is considered as a pro-inflammatory adipocytokine [5]. Although it is known that plasma leptin concentrations correlate with the amount of adipose tissue in the body, little information is available on the long-term effects on leptin concentrations of changes in diet and exercise. Thyroid hormones act on several aspects of metabolic and energy homeostasis influencing body weight, thermogen-
esis, and lipolysis in adipose tissue. Leptin, the product of the adipose specific ob gene, regulates food intake and energy expenditure. However, little is known about the effects of thyroid status on plasma leptin. For these reasons, attention has been focused on the possible relationship between adipocytokines, thyroid status, and thyroid dysfunction.

The aim of this study is to find the effect of therapeutic exercise and diet restriction on the thyroid hormone and leptin levels and to find if there is a relationship between thyroid hormones and leptin.

**Subjects and Methods**

The study was conducted on fifty healthy males divided into two equal homogenous groups (group I and group II) matched for age and sex. Their age ranged from 20–40 years, and their BMI ranges from 30–35. Inclusion criteria: Normal subjects who had no medical problems by history taking and physical examination. Exclusion criteria: Subjects who had illness related to the endocrine, musculo skeletal, or cardiopulmonary systems. Subjects that received any medications or who are cigarette smokers were also excluded. Group I subjects were assumed to maintain identical low calorie diet (1200-1500 Kcal) for one month without therapeutic exercise. Group II were maintained on low calorie diet and therapeutic exercise on electrical treadmill (motorized, 2.5 horses. Made in Taiwan, 2004) between 50% and 70% of the maximal heart rate, the maximal heart rate is calculated by subtracting the age of the subject from 220 [6]. The subjects performed this exercise for one month every other day. For all subjects BMI was calculated before and after the study [BMI = Body weight (kg) ÷ height (m)²]. Serum samples were drawn from both groups before and after the study for estimation of free T3, free T4, TSH, and leptin level. Serum concentrations of the thyroid stimulating hormone (TSH), free thyroxin (T4) and free triiodothyronine (T3) were determined by time-resolved radioimmunoassay. All determinations were performed in duplicate. Serum leptin concentrations were measured in duplicate by radioimmunoassay in venous blood sample using sensitive human leptin. The minimum detectable concentration of the assay is 0.05ng/mL. The mean intra-assay concentration variations (CV) were 4.5% according to manufacturer recommendation.

**Results**

The results shown Tables (1-4).

**Table (1): Mean ± SD of the studied parameters before and after diet program in group I.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before diet</th>
<th>After diet</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>F T3 (ng/dl)</td>
<td>0.392±0.132</td>
<td>0.663±0.176</td>
<td>&lt;0.05**</td>
</tr>
<tr>
<td>F T4 (ng/dl)</td>
<td>1.706±0.655</td>
<td>2.740±0.556</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>TSH (µIU/ml)</td>
<td>2.506±1.286</td>
<td>0.872±0.183</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>26.720±6.435</td>
<td>22.705±5.009</td>
<td>&lt;0.001 **</td>
</tr>
<tr>
<td>BMI</td>
<td>32.22±1.44</td>
<td>30.49±1.87</td>
<td>&lt;0.05*</td>
</tr>
</tbody>
</table>

*p significant.  **p highly significant.

**Table (2): Mean ± SD of the Studied parameters before and after diet program and exercise in group II.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before diet</th>
<th>After diet</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>F T3 (ng/dl)</td>
<td>0.400±0.105</td>
<td>1.233±0.367</td>
<td>&lt;0.001 **</td>
</tr>
<tr>
<td>F T4 (ng/dl)</td>
<td>1.780±0.587</td>
<td>3.784±0.995</td>
<td>&lt;0.001 **</td>
</tr>
<tr>
<td>TSH (µIU/ml)</td>
<td>2.527±0.174</td>
<td>0.505±0.269</td>
<td>&lt;0.001 **</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>26.466±5.573</td>
<td>21.712±3.794</td>
<td>&lt;0.001 **</td>
</tr>
<tr>
<td>BMI</td>
<td>32.352±1.236</td>
<td>28.988±2.013</td>
<td>&lt;0.001 **</td>
</tr>
</tbody>
</table>

*p significant.  **p highly significant.

**Table (3): Comparison between group I and group II in all studied parameters after one month.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I</th>
<th>Group II</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>F T3 (ng/dl)</td>
<td>0.663±0.176</td>
<td>1.233±0.367</td>
<td>&lt;0.001 **</td>
</tr>
<tr>
<td>F T4 (ng/dl)</td>
<td>2.740±0.556</td>
<td>3.784±0.995</td>
<td>&lt;0.001 **</td>
</tr>
<tr>
<td>TSH (µIU/ml)</td>
<td>0.872±0.183</td>
<td>0.505±0.269</td>
<td>&lt;0.001 **</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>22.705±5.009</td>
<td>21.712±3.794</td>
<td>0.433</td>
</tr>
<tr>
<td>BMI</td>
<td>30.49±1.87</td>
<td>28.988±2.013</td>
<td>&lt;0.05**</td>
</tr>
</tbody>
</table>

*p significant.  **p highly significant.

**Table (4): Correlation between leptin level and thyroid functions & BMI before the study in all studied subjects (n=50).**

<table>
<thead>
<tr>
<th>Leptin</th>
<th>Free T3</th>
<th>Free T4</th>
<th>TSH</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson test (r)</td>
<td>0.137</td>
<td>-0.216</td>
<td>0.028</td>
<td>0.296</td>
</tr>
<tr>
<td>Sig. (p value)</td>
<td>0.344</td>
<td>0.132</td>
<td>0.845</td>
<td>0.037*</td>
</tr>
</tbody>
</table>

*p significant.

**Discussion**

Leptin is an adipocytokine protein, of 146 amino acids, not only important in the regulation of food intake and energy balance, but it has also a function as a metabolic and neuroendocrine hormone. It is now clear that it is involved in glucose metabolism, sexual maturation and reproduction. It also interacts with the hypothalamic-pituitary adrenal axis, thyroid and growth hormone axes, and even with hematopoiesis and the immune system [7]. Thyroid function is linked to energy expenditure and thyroid hormones increase the metabolic rate, thus being a major regulator of energy homeostasis. Physical activity influences energy metabolism in human
subjects by increasing activity induced energy expenditure and resting metabolic rate for several hours after exercise. Effects of exercise on circulating thyroid hormones values remain controversial [2]. A frequently asked question is: Does therapeutic exercise have an effect on the levels of thyroid hormones? And does that affect weight reduction. Our study is thought to clarify the effect of diet program only and therapeutic exercise with fixed diet on the level of circulating thyroid hormones, leptin level and weight reduction. Also we tried to find if there is a relation between leptin level and thyroid hormone levels.

The present study tried to answer these questions on two groups of subjects. The first group was given a low calorie diet program for one month. The second group was given a program of treadmill exercise every other day for one month with low calorie diet program. Evaluation of thyroid hormone level, leptin level, and BMI before and after exercise was done. Subjects participated in this study were males only. Females and males typically play different roles in survival of the species and would be expected to respond differently to food scarcity or excess [8]. Guevara, et al. (2008) have investigated whether differences between male and female rats described in response to 40% caloric restriction (CR) were influenced by circulating level variations of sex hormones and/or insulin and leptin. They found that insulin levels were decreased by CR in both genders, but was more evident in female rats than males. Leptin serum levels were higher in male rats than in females, and CR caused a circulating leptin level reduction only in males [9]. Because of that we selected all our patients with the same sex (all were males).

We found that in group I, there was a significant increase in free T3, and T4 while there was a significant decrease in TSH, and BMI after the program of diet control. These results were coinciding with the results of Pucci, et al. (2000) who reported that the thyroid hormones, in particular T3 can stimulate metabolic rate and increase adipose tissue lipolysis, potentially via an interaction with the catecholamines. The combined effects of thyroid hormones and catecholamines enhance mobilization of triglycerides from adipose tissues and increase fatty acid lipogenesis in the liver [10]. Also the results of our study come in agreement with Yamaki, et al. (1991) who suggested that increased T3 exposure causes an increase in mitochondrial density, which elevates resting metabolic rate. Thus with consumption of an isocaloric intake, elevated T3 results in weight loss [11]. On the contrary, increasing T3 and T4 in our study after one month of low calorie diet are not in agree with McCargar, and Crawford (1992) and Nindl, et al. (1997) who reported that there is decline in T3 and T4, with concomitant decline in basal metabolic rate after hypocaloric diet [12-13]. Also the results of our study are not in agree with those of Robert, et al. (2005) who reported that fasting causes circulating T3 to decline, which lowers resting metabolic rate [14]. Also Luigi Fontana et al. (2006) reported in their study that serum T3 concentrations were lower in the caloric restriction group than the sedentary or exercising subjects eating a western diet, in contrast, no significant differences in serum TSH, T4 were detected between groups in their study. They explained that the mechanism responsible for the decrease in serum T3 concentrations induced by caloric restriction is likely related to caloric restriction itself, rather than changes in body composition [15]. In the same context, the results of our study are not consistent with the findings of Walford, et al. (2002) and Luigi Fontana, et al. (2006) [16-18]. They reported that a series of studies have shown that short term (2 weeks up to 6 months) fasting or severe caloric restriction decreases serum T3 in obese subjects who are actively losing weight. This may be explained by Braverman and Utiger, 2004, who hypothesized that energy deprivation can modulate serum T3 concentration by reducing the activity or concentrations of iodothyronine deiodinase, which leads to conversion of T4 to T3 [17].

In our study we found that after one month of therapeutic exercise on treadmill with a low calorie diet program there were highly significant changes in the FT3, FT4, TSH, and BMI that were more significant compared to group I. Comparing the results obtained after one month of diet program only (group I) with the results obtained after one month of therapeutic exercise with diet program (group II) revealed significant increase of T3, T4 and significant decrease of TSH, and BMI. The results of our study are supported by the results of Kanaka (2005) who reported that strenuous endurance training seems to have rather transient changes of the function of the thyroid gland. However since thyroid hormones play a key role in adaptation to physical stress and considerably affect the organism’s metabolic rate by both affecting oxidation of substrates and muscular function, changes in thyroid hormone metabolism may rather reflect the metabolic rate of the organism [18]. The results of our study come in consistent with other reports of Refsum, and Stromme (1979) Schmid, et al. (1982) and Krotkiewski, et al. (1984) who suggested that hemoconcentration could be a cause of changes in circulating TSH [19,20,21]. The results
of our study concerning BMI after the exercise agree with Peter Klijn, et al. (2007), who had an increase in body weight in his study group and who designed his exercise treatments to increase energy expenditure or to increase negative energy balance, although the major impact on energy balance occurs through decreasing caloric intake. Indeed, they reported that the effects of exercise can add to dietary interventions to enhance loss of fat mass and improve long-term maintenance [23]. Chicharro, et al. (2001) reported a significant increase of T3 and decrease of TSH; they evaluated the thyroid hormone levels during a 3-week professional road cycling competition. They found that although TSH and total T3 levels remained partially stable before and during the two weeks of professional cycling. However, there was a significant increase in the T3 and T4 levels in the third week compared to all other times investigated. They explained increasing T3 and T4 levels after three weeks of exercise may reflect the accumulated physical stress and also may be due to increased action of the plasma catecholamines which are known to potentiate actions of thyroid hormones [24]. Significant changes in T3 level after exercise in our study agree with Wensheng H., et al. (2004) who reported that significant changes of circulating T3, T4 and TSH values after acute exercise appeared due to plasma volume alterations because such changes became trivial after hematocrit adjustment. Also in this study, circulating TSH levels increased shortly after exercise [24]. Our results are not in agree with the results of Kanaka (2005) who reported that although thyroid hormones are only transiently or significantly changed during strenuous exercise, adequate caloric intake should be guaranteed in highly performing athletes in order to counteract the relative negative energy balance and prevent alterations in endocrine metabolic profile [18]. Our results are not in agree with the results of Rone, et al. (1992), Hackney & Gulledge (1994) and Chicharro, et al. (2001) [23,25,26]. Their studies did not demonstrate any significant changes outside the normal range for TSH and T3 level during strenuous exercise in elite strength athletes. Baylor, et al. (2003) reported that resting thyroid hormones do not appear to change with exercise training unless the training is extremely strenuous [27]. Also WenSheng H., et al. (2004) stated that physical exercise has been reported to stimulate peripheral deiodination of T4 and an increased uptake of T4 in the liver during exercise [24]. Tremblay (1997) studied the effect of exercise training on components of energy expenditure and related hormones reported that when exercise training is associated with a substantial negative energy balance, energy expenditure and levels of related hormones are also transiently decreased [28].

Steinacker, et al. (2005) reported that chronic exercise is a factor that gives the signal to save energy and, in turn, induced decreased levels of leptin and hypothalamic-pituitary-thyroid axis. Thus, because of the down regulation of the thyroid axis, a shortage of T3 develops, which saves energy. This effect on thyroid hormones may have an impact on skeletal muscles, and thereby on muscular training response [29].

Although it is known that plasma leptin concentrations correlate with the amount of adipose tissue in the body, little information is available on the long-term effects on leptin concentrations of changes in diet and exercise. Leptin plays a vital role in the regulation of energy balance in rodent models of obesity. However, less information is available about its homeostatic role in humans. Our study showed that leptin level decreased significantly after one month of low calorie diet and this coincides with the result of Sucajtys-Szule, et al. (2008) who found that rats maintained on restricted diet displayed lower serum NPY, leptin and insulin concentrations and higher serum corticosterone concentration [30]. Reseland, et al. (2001) found that long-term changes in lifestyle consisting of decreased intake of dietary fat and increased physical activity reduced plasma leptin concentrations in humans beyond the reduction expected as a result of changes in fat mass [31]. Koutsari, et al. (2003) found that daily moderate intensity exercise, without concomitant changes in body fat mass, suppressed fasting and postprandial circulating leptin concentrations after consumption of a short-term high-carbohydrate diet [32].

Our study showed that leptin level was decreased in group II subjects after diet and exercise for one month, and this does not coincide with the result of Dirlewanger, et al. (1999) who found that a moderate physical activity performed over a 3-day period does not alter plasma leptin concentrations, even when energy balance is slightly negative. This argues against a direct effect of physical exercise on plasma leptin concentrations, when body composition is unaltered [33].

Attention has been focused on the possible relationship between adipokines, thyroid status, and thyroid dysfunction. Leptin, a signal of satiety to the brain and regulator of insulin and glucose metabolism, reflects the amount of fat storage and is considered as a pro-inflammatory adipocytokine.
Several reports indicate that leptin regulates thyroid function at hypothalamic-hypophyseal level and, conversely, thyroid hormones might control leptin metabolism at least in some animals studies [3]. In our study we found no relation between leptin level and thyroid hormones. Kokkinos, et al. (2007) investigated possible alterations of important energy regulators such as leptin, adiponectin, and ghrelin in relation to changes in thyroid hormones. They found that T3 and T4 levels were inversely correlated to leptin. Leptin seems mainly to be involved in the thyroid hormone effects on energy homeostasis [34]. Diekman, et al. (1998) showed that thyroid states modulates serum leptin concentrations independent of BMI, with a small decrease in hypothyroidism and a small increase in thyrotoxicosis [38]. Sreenan, et al. (1997) showed that there was a significant positive correlation between BMI and leptin level irrespective of the thyroid status. These data suggest that leptin levels are not affected by thyroid dysfunction [36]. Oge, et al. (2005) investigated the relationship between thyroid hormones and leptin levels in patients with overt hypothyroidism and hyperthyroidism before and after successful treatment. They found that serum leptin levels were correlated with BMI and thyrotropin (TSH) in both hypothyroid and hyperthyroid patients. Serum leptin levels are affected in thyroid disorders and the correlation of leptin with TSH is independent of thyroid hormones [37]. Hanan, et al. (2001) showed that thyroid hormones do not have an independent effect on circulating serum leptin and they do not operate through changes in serum leptin level to regulate energy expenditure [38].

Thyroid stimulating hormone (TSH) is correlated to the metabolic hormones leptin and insulin, and may be used as indicator of metabolic control. Because the hypothalamus integrates various error signals (metabolic, hormonal, sensory afferents, and central stimuli), the pituitary’s releasing hormones represent the functional status of an athlete [29]. Hsieh (2005) found that circulating thyroid hormone plays a relevant role in regulating leptin metabolism independent of BMI and body fat [39]. Simsch, et al. (2002) found that leptin (L) is associated with body-weight-regulating and adipostatic functions. Its receptors also may be found centrally. Thyroid hormones regulate metabolic processes mainly by binding at peripheral receptors. They speculated a high energy flux during intensified training (RT) caused the decrease of L and the hypothalamic thyroid axis (HTA), independent of BMI or body fat. Thus, they conclude a depression of L and HTA is associated with training intensity [40].

Fasting induces profound changes in the hypothalamus-pituitary-thyroid (HPT) axis. The alterations observed in humans and rodents are similar in many ways, although they may be more pronounced and more acute in rodents. The molecular mechanisms underlying the resetting of HPT axis regulation in the framework of caloric deprivation are still incompletely understood. Studies in rats and mice have shown a dramatic downregulation of thyrotropin-releasing hormone (TRH) gene expression in hypophysiotropic paraventricular nucleus (PVN) neurons during fasting. Direct and indirect effects of decreased serum leptin, as well as effects of increased local triiodothyronine (T3) concentrations, in the hypothalamus during food deprivation contribute to the decreased activity of TRH neurons in the PVN. However, the relative contributions of these complex determinants remain to be defined in more detail. Pituitary thyroid-stimulating hormone (TSH) beta mRNA expression decreases during fasting, and this may be relatively independent of leptin and/or TRH, since leptin administration in this setting does not fully restore pituitary TSH expression, while it does restore TRH expression in the PVN. There may be a role for pituitary peptides, such as neuromedin B, in altered TSH gene expression during fasting. The observed decrease in serum thyroid hormone concentrations results to some extent from diminished thyroidal secretion of thyroid hormones, especially in rodents. Decreased thyroxine (T4) and T3 contribute to the downregulation of T3-responsive genes such as liver D 1. The overall result of these complex HPT axis changes in various tissues during fasting is downregulation of the HPT axis, which is assumed to represent an energy-saving mechanism, instrumental in times of food shortage [41]. Prolonged fasting is associated with a number of changes in the thyroid axis manifested by low serum T3 and T4 levels and, paradoxically, low or normal TSH. This response is, at least partly, caused by suppression of proTRH gene expression in neurons of the hypothalamic paraventricular nucleus (PVN) and reduced hypothalamic TRH release. Because the fall in thyroid hormone levels can be blunted in mice by the systemic administration of leptin, Légrádi, et al. (1997) raised the possibility that leptin may have an important role in the neuroendocrine regulation of the thyroid axis, through effects on hypophysiotropic neurons producing proTRH [42].

Conclusion:

From our study we found that, low caloric diet results in increase in free T3, free T4, decrease in TSH, leptin levels and BMI. Both low caloric diet
and moderately intensive therapeutic exercise had a more significant effect on the levels of circulating thyroid hormones, leptin and BMI than diet alone. A positive correlation between leptin and BMI was found. We found no relation between thyroid hormone levels and leptin level.

**Recommendations:**
Further studies are needed to investigate the influence of exercise with different intensities, the long term effect of exercise on the level of circulating thyroid hormone, and leptin level.

**References**


