

Thyroid hormones and BMI in obese children: One year follow up results

Obez çocuklarda tiroid hormonları ve VKİ: Bir yıllık sonuçlar

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ABSTRACT

Objectives: The aim of this study was to investigate the relationship between thyroid hormone levels and obesity, lipid levels and weight changes.

Patients and Methods: Five to eleven year old normal weight, overweight and obese children underwent measurements of thyroid stimulating hormone (TSH), free thyroxine (fT4), lipid profile and autoimmune thyroid antibodies. Children with high TSH were re-evaluated one year later without any intervention.

Results: Three hundred children (126 obese, 74 overweight, 100 normal weight) were evaluated in the study. The rates of high TSH levels were 1.0% in normal weight, 9.5% in overweight and 11.9% in obese group ($p=0.007$). fT4 levels of all the children enrolled in the study were in normal range. None of the children had autoimmune antibody positivity. Obese children with high TSH had higher triglyceride levels than children with normal TSH ($p=0.028$). One year later, a significant decrease in body mass index (BMI) was accompanied by a significant decrease in TSH levels.

Conclusion: TSH levels can be high in obese and overweight children. Obese and overweight children with elevated levels of TSH do not need to be treated pharmacologically, losing weight decreases TSH levels significantly.

Keywords: TSH, BMI, Child, Obesity, Overweight, Thyroid

ÖZET

Amaç: Bu çalışmanın amacı tiroid hormon düzeyleri ile obezite, lipid düzeyleri ve ağırlık değişiklikleri arasındaki ilişkiyi araştırmaktır.

Hastalar ve Yöntemler: Beş ve onbir yaş aralığında normal, fazla kilolu ve obez çocukların TSH, sT4, lipid profili ve otoimmün antikor değerlerine bakılmıştır. TSH düzeyi yüksek olan çocuklar herhangi bir müdahale yapılmadan bir yıl sonra yeniden değerlendirilmiştir.

Bulgular: Çalışmada 300 çocuk (126 obez, 74 fazla kilolu, 100 normal kilolu) değerlendirilmiştir. Yüksek TSH düzeyi sıklığı normal kilolu grupta %1.0, fazla kilolu grupta %9.5 ve obez grupta %11.9'dur ($p=0.007$). Bütün gruplarda sT4 düzeyleri normal bulunmuştur. Çocukların hiçbirinde otoimmün antikorlar pozitif değildir. Yüksek TSH'lı çocuklar normal TSH'lı çocuklara göre daha yüksek trigliserid düzeylerine sahiptir ($p=0.028$). Bir yıl sonra yapılan değerlendirmede, VKİ'de anlamlı düşüşle birlikte TSH düzeyinde de anlamlı bir düşüş saptanmıştır.

Sonuç: TSH düzeyleri obez ve fazla kilolu çocuklarda yüksek olabilir. TSH yüksekliği olan obez ve fazla kilolu çocukların farmakolojik olarak tedavi edilmesine gerek yoktur, kilo vermek TSH düzeylerinin anlamlı olarak azalmasını sağlar.

Anahtar kelimeler: TSH, VKİ, Çocuk, Obezite, Fazla kilolu, Tiroid

Introduction

Obesity in childhood is an important health problem all over the world and has great impact on child's health. Obesity is associated with many comorbidities including abnormalities of the endocrine, cardiovascular, gastrointestinal, pulmonary, orthopedic, neurologic, dermatologic, and psychosocial systems [1,2]. In recent years the effect of obesity on thyroid functions in children is emphasized. In some recent researches it has been shown that serum TSH levels were higher in obese children than in non-obese ones and this

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Submitted/Gönderilme: 22.04.2015 Accepted/Kabul: 25.08.2015

condition was associated with normal or slightly elevated free T4 (fT4) and/or free T3 (fT3) levels. Despite the results of some studies, a direct relationship between elevated TSH levels and obesity, as well as lipid profile and weight changes in children has not been established yet [3-8].

The aim of this study was to investigate the relationship between thyroid hormone levels and obesity, lipid profile and weight changes in children.

Patients and Methods

Participants

Children aged between 5-11 years who attended to Marmara University Faculty of Medicine Family Medicine outpatient clinics for various reasons between 01.04.2011 and 30.08.2011 and of whom parents gave consent were enrolled in the study. Primary school children have been chosen as they shared similar nutritional order and were not affected by hormonal changes of adolescence.

Study Design

Children were grouped according to their body mass index (BMI) percentiles as normal weight (5-85p), overweight (85-95p) and obese (>95p). Children with any disease that may cause obesity (syndromic, organic, hormonal causes) were excluded. All children underwent weight and height measurement, BMI calculation, general physical examination, measurement of TSH, fT4, glucose and lipid profile. BMI was calculated from the formula of weight(kg)/height² (cm²). BMI of children in the study were evaluated according to the percentiles of Turkish children. Thyroid hormone levels were evaluated according to the age matched percentiles. Autoimmune thyroid antibodies (anti-TPO, anti-thyroglobulin) were studied for children whose TSH levels were above 97.5 percentile.

One year later, thyroid hormone levels were re-evaluated in children with elevated TSH levels (>97.5 percentile). During this one year interval, no intervention has been executed. Children were recalled for TSH and fT4 analysis. Children were grouped into two groups according to weight status compared to the previous year. Children who gained weight formed group 1, children who lost weight formed group 2. TSH and fT4 levels were analysed according to the weight change.

Blood samples were studied at Marmara University Faculty of Medicine Biochemistry Laboratory. Informed consent was obtained by parents. Study was approved by Marmara University Ethics Committee (no:09.2011.0062).

Statistical Analysis

Data from obese, overweight and normal weight groups were analysed with SPSS 16 programme. Data about continuous variables were compared with Anova test, discrete variables were compared with Chi square test. Pearson correlation analysis method was used to evaluate correlation between variables. Differences between variables $p < 0.05$ was accepted as statistically significant.

Results

In this study 306 children were examined. Four children with hypothyroidism, one child with hyperthyroidism and one with Cushing syndrome were excluded from the study. A total of 300 children were evaluated. One hundred-fifty-nine (53.0%) of the children were female, 141 (47.0%) were male. Mean age value was 8.4 ± 2.1 ; 33.3% were 5-7 years, 27.7% were 8-9 years and 39% were 10-11 years old. One hundred-twenty-six of them (42%) were obese, 74 (24.7%) were overweight, 100 (33.3%) were normal weight. Mean weight of children was 39.7 ± 15.8 kg, mean height was 134.31 ± 4.9 cm and mean BMI was 21.25 ± 2.1 . There was no statistical difference among groups according to age and sex (respectively $p = 0.285$, $p = 0.42$) (Table I).

Table I. Distribution of variables according to groups

	Normal weight	Over weight	Obese	Total	p
<i>N</i>	100	74	126	300	
<i>Age</i>	8.1 ± 2.1	8.7 ± 2.1	8.5 ± 2.1	8.4 ± 2.1	0.28
<i>Sex(F/M)(n)</i>	59/41	40/34	60/66	159/141	0.42
<i>BMI(kg/m²)</i>	16.1 ± 1.8	20.3 ± 2.6	25.8 ± 4.1	21.5 ± 5.2	<0.001
<i>TSH(mIU/ml)</i>	2.7 ± 1.1	3.2 ± 1.5	3.5 ± 1.5	3.2 ± 1.4	<0.001
<i>fT4 (ng/dl)</i>	1.27 ± 0.16	1.27 ± 0.18	1.24 ± 0.16	1.26 ± 0.16	0.395
<i>TSH > 97.5p</i>	1	7	15	23	0.007

TSH levels were high according to their age matched percentiles (>97.5 percentile) in one child (1%) of the

normal weight group, in seven children (9.5%) of the overweight group and in 15 children (11.9%) of the obese group. The difference among groups was statistically significant ($p=0.007$, Chi square test). The sub-analysis detected statistically significant difference between obese and normal weight group ($p=0.002$) and between overweight and normal weight group ($p=0.008$).

Mean TSH values of the groups were 2.7 ± 1.1 mIU/ml for normal weight group, 3.2 ± 1.5 mIU/ml for overweight group and 3.4 ± 1.5 mIU/ml for obese group. Mean TSH levels, showed a significant difference among groups ($p<0.001$); the sub-analysis revealed that this difference was between obese and normal weight groups ($p<0.001$) (Table I).

There was a statistically significant but weak correlation between BMI and TSH levels ($p<0.001$) ($r=0.152$).

FT4 levels of all the children enrolled in the study were in normal range. Mean FT4 level was 1.27 ± 0.16 ng/dl for normal weight group, 1.27 ± 0.18 ng/dl for overweight group and 1.24 ± 0.16 ng/dl for obese group. There was not statistically significant difference between groups according to FT4 levels ($p=0.395$).

Autoimmune thyroid antibodies were not positive in any of the children with high TSH levels.

Mean triglyceride value was 80.7 mg/dl for normal weight group, 89.9 mg/dl for overweight group, 109.8 mg/dl for obese group. Mean total cholesterol value was 159.6 mg/dl for normal weight group, 160.2 mg/dl for overweight group, 170.4 mg/dl for obese group. Mean HDL cholesterol value was 57.8 mg/dl for normal weight group, 51.8 mg/dl for overweight group, 48.1 mg/dl for obese group. Mean LDL cholesterol value was 85.4 mg/dl for normal weight group, 90.3 mg/dl for overweight group and 99.5 mg/dl for obese group. As BMI increases, mean triglyceride, mean LDL cholesterol and mean total cholesterol levels increased significantly but mean HDL cholesterol level decreased significantly ($p<0.05$).

The analysis of the relationship between TSH and lipid profile showed that in obese group, children with high TSH had significantly higher triglyceride levels (141.8 mg/dl) than children with normal TSH levels (104.8 mg/dl) ($p=0.028$). There was not a similar relationship between overweight and normal weight group. Total, LDL and HDL cholesterol levels did not change according to TSH levels in any of the groups.

One year after the first analysis, four out of 23 children with elevated TSH levels did not come to the reanalysis. There were 8 children in group 1 who gained weight.

Compared to baseline parameters in group 1 mean BMI increased from 23.4 to 24.4 ($p=0.12$). Mean TSH of group 1 changed from 5.5 mIU/ml (TSH 1) to 5.3 mIU/ml (TSH 2). This change was not statistically significant ($p=0.234$). Mean FT4 level changed from 1.34 ng/dl to 1.36 ng/dl. This change was not significant also ($p=0.68$). In group 2 there were 11 children who lost weight. Their mean BMI decreased from 25.6 to 22.9 ($p=0.03$). By this change, mean TSH of the group decreased from 6.6 mIU/ml to 4.1 mIU/ml ($p<0.001$). Mean FT4 level was 1.16 ng/dl previously and it was 1.2 ng/dl one year later ($p=0.76$) (Figure 1).

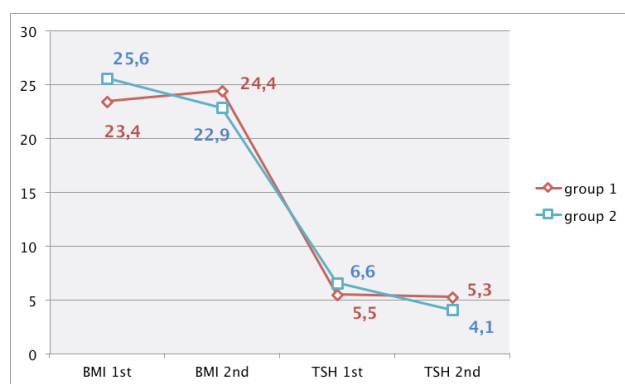


Figure 1. TSH change according to BMI change

Discussion

In our study, one child in normal weight group (1%), seven children in overweight group (9.5%) and 15 children in obese group (11.9%) had TSH levels over 97.5 percentile. These results were compatible with the results of several other studies. Grandone et al. found high TSH levels (>4.2 mIU/ml) in 12.8% of 938 obese children aged between 4.5-16 years [9]. In Bhowmick et al.'s study high TSH (>4 mIU/ml) rate was 11.7% in 308 obese children aged 6-17 years [10]. In a retrospective study by Mutlu et al., age matched TSH levels over 97.5 percentile have been accepted as high, the percentage was 12.9% in 132, 5-18 year-old obese children [11]. There was statistically significant difference between TSH levels of obese and normal weight group ($p=0.002$) and between overweight and normal weight group ($p=0.008$). This difference did not exist between overweight and obese group. Similarly, Kumar et al. could not find any significant difference between TSH levels of 20 overweight children and 30 obese children [12]. These findings suggest that increased body weight results in increased TSH levels; but there is no relationship between the severity of obesity and TSH level (Table II).

Table II. Studies investigating relationship between obesity and TSH

	Obese TSH↑	Overweight TSH↑	Normal weight TSH↑	Total
Grandone et al.	12.8%	-	-	938
Bhowmick et al.	11.7%	-	-	308
Mutlu et al.	12.9%	-	-	140
Kumar et al.	30%	20%		50
Ekinici et al.	11.9%	9.5%	1%	300

TSH↑: High level of thyroid stimulating hormone

In our study, correlation between BMI and TSH levels was low but statistically significant. Knudsen et al. found positive correlation between BMI and TSH also between gaining weight during 5 years and progressive increase in serum TSH levels [13]. Our results suggest a positive correlation between weight gain and TSH levels as confirmed by several studies [3,9,14]. In controversy Mutlu et al. and Kumar et al., stated that TSH level and BMI did not correlate significantly [11,12].

Autoimmune thyroiditis has been expressed as a rare reason of elevated TSH in childhood obesity [4,15]. Dekelbab et al., detected 3% autoimmune thyroiditis in their study with obese and non obese children with high TSH [5]; Grandone et al.'s study result was 7% in 938 obese children and adolescents [9]; in our study none of the children were positive for thyroid autoantibodies.

There are some hypothesis to explain the increase of TSH in obesity. Mostly emphasised hypothesis is proTRH production by leptin, hormone produced mostly by adipocytes. Some researchers showed that leptin could change hypothalamic TRH production [16,17]; TSH secretion was regulated by hormones and transmitters such as neuropeptide Y, alfa-MSH that regulated body weight and satiety and also by aguti related peptide that innervates hypophysiotrophic TRH neurons. These transmitters were also affected by leptin [17,18]. Besides, it was shown that TSH could stimulate leptin secretion by direct effect on adipocytes. All these findings suggest that TSH levels, as a result of obesity, reflect the change of energy balance in obesity [19].

In obesity, free thyroid hormone levels might be elevated as well as TSH levels. Although the reason is not clear yet, thyroid hormone resistance may play role, or elevated thyroid hormones, by increasing resting and total energy expenditure can cause an adaptation process to decrease energy that can be converted into fat [18,19]. In studies of Reinehr [20] and Stichel et al. [4] fT3 level of obese group was significantly higher than that of the control group, while fT4 levels did not differ. Similarly in our study fT4 levels did not differ between normal weight, overweight and obese groups. Children with high TSH levels also had normal fT4 levels. According to these data, it could be suggested that fT4 and fT3 levels do not increase at the same level for every case, and probably there are different hormonal and environmental factors specific to every person that can affect this relation.

With the increase of BMI, mean triglyceride, LDL and total cholesterol levels were increased, while mean HDL cholesterol level decreased significantly. Similarly, in a study performed with overweight and obese children showed higher triglyceride and lower HDL levels in obese children [21]. Adiposity is associated with high blood lipid levels and obese and overweight children are prone to increased metabolic risk caused by dyslipidemia.

Analysis of the relationship between TSH and lipid profile showed that in obese group, children with high TSH had significantly higher mean triglyceride level (141.8 mg/dl) than children with normal TSH levels (mean triglyceride level=104.8 mg/dl) (p=0.028). We did not find such a relation between TSH and triglyceride levels in overweight and normal weight groups; as well we did not find any significant relationship between total, LDL, HDL cholesterol and TSH levels in any group. There are conflicting results about relationship between elevated TSH level and lipid profile. Beside studies showing no significant relationship [9, 20] there are some studies that showed a relationship between TSH and triglyceride, total and LDL cholesterol levels [22,23]. So there is no agreement on this point. Thyroxine treatment of obese children with moderately increased TSH did not change their lipid profile [24] so disturbed lipid profile may be the result of obesity but not of elevated TSH.

There is a disagreement about treatment of children with mildly elevated TSH and normal total or fT4. In obese and overweight children, mildly elevated TSH is frequently seen but it is not absolute to lower TSH by giving thyroxine treatment. There are different opinions but mostly accepted one is that this condition is not the reason but the result of obesity. Eliakim et al., showed that giving thyroxine

treatment to obese children with mildly elevated TSH, did not change their weight status and lipid profile [24]. As shown in our study and in other studies by losing weight TSH levels decreased significantly [9,20,25]. However some studies found no relationship between weight loss and normalization of TSH values [26,27]. Our current knowledge does not support the use of thyroxine treatment for elevated TSH in obese children [28,29].

In our study, TSH levels of obese group were found to be significantly higher than normal weight group and a similar relation was also present between overweight and normal weight groups. TSH levels did not differ significantly between obese and overweight groups and there was no relationship with elevated levels of TSH and the severity of obesity. Obese and overweight children with elevated levels of TSH do not need to be treated pharmacologically, losing weight decreases TSH levels significantly.

Conflict of Interest

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors

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