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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Subclinical hypothyroidism in obese children

Obez çocuklarda subklinik hipotiroidi

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ABSRACT

Objective: Thyroid functions in obese children and adolescents were evaluated in order to determine subclinical and clinical hypothyroidism.

Materials and methods: In this study, 85 obese (Body mass index >97th percentile) children, aged 2-14 years, as well as 47 healthy controls were enrolled. Levels of serum free triiodothyronine (fT_3), free thyroxine (fT_4) and thyroid-stimulating hormone (TSH) of the two groups were compared. Obese children with TSH level above 5.4 IU/ml were also analyzed for thyroid autoantibodies and thyroid ultrasounds were performed.

Results: Obese children showed higher serum concentrations of TSH and fT_3 than the controls but no significant difference in serum fT_4 levels was found between the two groups (P=0.001). One child had high auto antibodies and 32 had high TSH levels. Of 28 children with TSH >5,4 IU/ml, 25 children had normal thyroid ultrasound findings and three had nodules or thyroiditis but no enlargement of the thyroid gland.

Conclusion: TSH and fT_3 levels were found to be higher in obese children compared with non-obese children with no difference of fT_4 levels between two groups.

Key words: Body mass index, obesity, thyroid functions

ÖZET

Amaç: Çocukluk çağı obezitesinde tiroid fonksiyonlarının değerlendirilmesi, subklinik-klinik hipotiroidinin saptanması amaçlanmıştır.

Gereç ve yöntem: Çalışmamızda, 2-18 yaş arasında 85 obez (Vücut kitle indeksi >97. persentil), 47 obez olmayan hastanın, serbest triiyodotironin (sT_3) ve tiroksin (sT_4) ve tiroid stimülan hormon (TSH) düzeylerine bakıldı. Obez grupta, TSH düzeyi 5,4 IU/ml'nin üzerinde saptanan hastaların, tiroid otoantikor düzeyleri ölçüldü ve tiroid ultrasonu yapılarak tiroid vo-lümü hesaplandı.

Bulgular: Obez hastaların sT_3 ortalamaları ve TSH değerleri, kontrol grubunun değerlerinde istatistiksel olarak anlamlı derecede yüksek bulunurken (P=0,001), sT_4 ortalamalarında iki grup arasında fark saptanmadı. TSH >5,4 IU/ml olan hastalardan birinde otoantikor düzeylerinde yükseklik saptandı. TSH >5,4 IU/ml olan 28 hastadan 25'inin tiroid ultrasonu normal iken, kalan 3 hastada tiroidit veya nodül saptandı ancak tiroid büyümesi yoktu.

Sonuç: Obez çocuklarda sT_3 ve TSH düzeyi obez olmayanlara kıyasla yüksek, sT_4 ise normal bulundu.

Anahtar kelimeler: Beden kitle indeksi, obezite, tiroid fonksiyonları

INTRODUCTION

Obesity is a complex, multifactorial disease characterized by behavioral, endocrine and metabolic changes. Few systems of an organism are remained unaffected by obesity. In particular, obesity-related complications of endocrine functions and the cardiovascular system are well-defined.[1]

Thyroid functions in obesity reveal a variety of inconsistencies from normal to elevated TSH and/or fT_3 levels. Many studies have shown increased TSH levels in obese subjects.[2] Subclinical hypothyroidism (i.e., normal fT_3 and fT_4 levels but high TSH levels) is typically observed in adults but incidence is increasing among children and adolescents. In this study, we aimed to determine the thyroid func-

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tions and subclinical-clinical hypothyroidism in childhood obesity.

MATERIALS AND METHODS

Eighty-five children (aged between 2-14 years old) who were found to be obese in anthropometric measurements and 47 healthy control group were included in the study. The study was conducted between September 2009 and September 2010 at the Bezmialem Vakif University Departments of Pediatrics. We obtained written informed consent from parents and approval from our university's Ethical Committee. The patients who had systemic or chromosomal disease, multiple endocrine disorders, a history of drug use or those diagnosed with congenital or acquired hypothyroidism were excluded from the study. The control group consisted of children evaluated in the pediatric clinic for other nonendocrine-related problems.

Standing height was measured to the nearest 0.1cm with a Harpenden fixed stadiometer. Body weight (BW) was measured on a SECA balance scale to the nearest 0.1 kg, with each subject dressed in a light T-shirt and shorts. Body mass index (BMI) was calculated by dividing weight by height (kg/m²). Obesity was defined as a BMI >97th percentile, the definition of the International Task Force of Obesity in Childhood and Population-specific Data.[3] All the patients' fT_3, fT_4 and TSH levels were measured by a direct chemiluminesance technique (ADVIA Centaur XP, USA). The norm values for respective range were between 0.8 -5.4 uIU/ml for TSH, between 4.3-8 pmol/l for fT_3 and between 10.3-25.7 pmol/l for fT_4. The anti-Tg and anti-TPO levels were measured with using a chemiluminesence competitive immune test (ADVIA Centaur, USA) in the patients whose TSH levels were determined above 5.4 IU/ml. Patients whose anti-TPO (0-35 IU/ml) and anti-Tg (0-115 IU/ml) levels were above the reference ranges were evaluated for autoimmune thyroid disease. Thyroid ultrasound examinations was used to analyze the heterogenity of the thyroid tissue, nodularity and to determine thyroid volume.[4]

Statistical analysis was performed with NCSS 2007, paired t-test was used to calculate the difference of two parameters in groups; Tukey multiple comparison test was used to calculate of the difference of two parameters in groups with more than two in the same group and t test was used for calculation of difference between different groups. Categorical data were evaluated using the chi-square test, $p<0.05$ was accepted as statistically significant.

RESULTS

Age and gender distribution were not statistically different between the control and study groups (p=0.730 and p=0.219, respectively). The mean ages of the patients were 10.9±2.7 years in the obese group and 11.1±4.0 years in the control group. Mean BMI was 26.5±4.0 in the obese group, a statistically significant difference from the 17.5±2.7 of the control group ((p = 0.0001) (Table 1).

Group		Control (n=47)		Obese (n=85)		p
Age (years)		11.2±4.1 (3.4-15.6)		10.9±2.7 (2.67-15.9)		0.730
BMI (kg/m²)		17.6±2.7 (13-20)		26.5± 4.1 (21-39)		0.0001
BMI SDS		-0.17±0.6 (-1.9-1.8)		2.2±0.3 (1.7-3.03)		<0.001
BMI %		44.6±20.6 (12.4-83.7)		98.1±1.18 (95.7-99.8)		<0.001
Gender	Male	18	38.3%	42	49.4%	0.219
	Female	29	61.7%	43	50.6%	

Table 1. The demographical features and mean body mass index (BMI) of obese and control groups [mean±standard deviation (range)]

Averages of the fT_3 levels were significantly higher in obese group than the control group (p=0.002), but the mean fT_4 levels observed between the control and study groups (p=0.818) showed no statistically significant difference (Table 2). TSH levels in the obese group were significantly higher than in the control group (p=0.001), and the risk of developing subclinical hypothyroidism in obese group was 2.55 times higher than in the nonobese group (Table 3).

Only one of the 32 patients with TSH levels > 5.4 also had high anti-TPO and anti-Tg levels. The patients with high TSH levels underwent thyroid ultrasound. Thyroid volumes were calculated as normal in all cases, 3 cases were found to have evidence of thyroiditis without thyroid enlargement.

Table 2. Thyroid hormone levels in obese and nonobese patients [mean±Standard deviation (range)]

	Nonobese group (n=47)	Obese group (n=85)	p
fT_3 (pmol/L)	5.4±0.9 (4.1-6.7)	5.9±1.1 (3.04-8.6)	0.002
$f T_4$ (pmol/L)	16.9±2.4 (14.1-24)	16.8±2.01(11.8-22.6)	0.818
TSH (UI/ml)	3.2±1.1 (1.2-6.1)	3.9±1.4 (1.3-7.7)	0.001

Table 3. The risk of devoloping subclinical hypothyroidism in both groups

	Nonobese group n (%)	Obese group n (%)	Difference	
TSH level ≥5.4	38 (80.9)	53 (62.4)	χ^2:4,84	2,55
TSH level >5.4	9 (19.1)	32 (37.6)	p=0,028	1,1-5,9

DISCUSSION

The effects of thyroid hormones on energy balance and adipose tissue is an issue, which should be emphasized. Studies performed to determine the relationship between thyroid hormones and obesity suggested that, TSH, fT_3 and fT_4 levels highlight the different results in obese subjects.[5-8] In our study, TSH and fT_3 levels were found to be high in obese children compared with non-obese children although fT_4 levels were comparable between the two groups. Similar results have been obtained by Stichel et al.,[9] i.e., T_4 levels did not differ, while that the medians of TSH and T_3 concentrations were normal, but higher in the obese group than in the controls to a statistically significant degree. The effect of weight loss on thyroid functions in obese children was evaluated by Reinehr et.al[10] who concluded that fT_3 and TSH and thyroid hormone levels were moderately increased in obese children and that weight loss led to a reduction in the levels of these hormones. This reduction supported the theory that the elevation of these hormones was a consequence rather than a cause of obesity. This subclinical hypothroidism demonstrated with modarate increase in TSH and fT_3 levels was related to the resistance to thyroid hormones in periferial tissues and decreased negative feedback between TSH and the peripheral thyroid hormones.[11]

Some studies that showed serum TSH levels elevated without any change in fT_3 and T_4 in obese children. A higher prevalence of TSH elevation was observed in the obese of the study conducted by Bhowmick et al., and positive thyroid peroxidase and thyroglobulin antibodies were observed more in the obese subgroup with an elevated TSH levels.[12] In their study, higher TSH levels were associated with positive thyroid peroxidase and thyroglobulin antibodies due to thyroid disease. In our study, only one of the 32 patients with TSH levels > 5.4 UI/ml had high anti thyroid peroxidase and anti-thyroglobulin levels. Studies showing the high prevalence of antibody in obese patients confirmed that these findings were not related with thyroiditis but were related with the increased presentation of antigen presenting to the thyroid gland because thyroid iodine uptake and thyroid volumes in these patients were normal.[9,13-14] Also the negative feedback between TSH and the peripheral thyroid hormones may be decreased in obese patients so both TSH and peripheral thyroid hormones are increased in obesity. The study conducted by Bastemir et al. supported the idea that serum TSH levels were positively correlated with the degree of obesity and some of its metabolic consequences in overweight people with normal thyroid function.[15] The prevalence of positive thyroid autoantibodies was increased in the obese children (for the most part in those with elevated TSH) and was not related with autoimmune thyroititis or iodine deficiency.

The relationship between the obesity, BMI, weight gain, waist circumference and thyroid functions in the adult patients those were euthyroid, overt hypothyroid or, subclinical hypothyroid was studied by Karakurt et al. who found that obesity was related with TSH and fasting insulin levels and

HOMA-IR independent from serum T_3 and T_4 levels.[15] One of the most comprehensive studies about the relationship between thyroid functions and obesity was conducted by Knudsen et. al[16] with 4,082 adult patients. They found that serum TSH levels were correlated positively with weight gain during 5 years with an association between obesity (BMI > 30 kg/m²) and serum TSH levels. They concluded that elevated serum TSH levels were associated with an increse in the occurance of the obesity; therefore, thyroid function could be one of several factors acting in concert to affect body weight in a population.

In conclusion, the present study supports previous findings, that obesity is the cause of moderate increase in TSH and fT_3 levels but has no relationship with autoimmune thyroiditis or hypothyroidism in children. These children should not be unnecessarily treated with thyroid hormone replacement for mildly TSH elevation but should be encouraged to implement appropriate diet and exercise programs for normalization of the thyroid functions.

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