



ARAŞTIRMA / RESEARCH

Effects of thyroid homeostasis, insulin resistance and some parameters on weight loss

Tiroid homeostazisi, insülin direnci ve kan parametrelerinin kilo verme üzerine olan etkileri

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Abstract

Purpose: Many studies show that obesity is associated with increased serum thyrotropin [TSH] but the relationship between obesity, free thyroid hormones (including free triiodothyronine [FT3] and free thyroxine [FT4]) is still unclear. The aim of this study was to evaluate the effects of thyroid homeostasis, insulin resistance and blood parameters on weight loss in an obesity center.

Materials and Methods: Of 3918 patients applied to an obesity center between November 1st, 2018 and March 13th, 2020, 417 were found suitable and accepted in this obesity prevention program and retrospective, descriptive, cross-sectional study.

Results: A total of 417 patients were interviewed, 383 were female in this study. The mean age of participants was 48.20±11.03 years. In the group who lost weight; TSH, FT3, BMI, WC, HC, HbA1c and HOMA-IR index values were significantly lower in the sixth month. According to these results, the blood parameters, TSH, FT3 and insulin resistance of the patients are decreased who lose weight. Hip circumference, BMI, BFP, FT3, HbA1c and FBG were important determinants of weight loss in our univariate analyses. FT3 (odds ratio [OR]: 1.854; 95% CI: [1.223-2.811]; p=0.004), BMI (OR: 0.948; 95% CI: [0.914-0.984]; p=0.005) and FBG (OR: 0.984; 95% CI: [0.973-0.996]; p=0.007) were defined as multivariate predictors affecting weight loss.

Conclusion: This study advises that lower BMI and FBG levels, and higher FT3 concentrations are related with a better potential to lose weight in obese patients.

Keywords: Obesity, insulin resistance, thyroid hormones, weight loss

Öz

Amaç: Birçok çalışma, obezitenin artmış serum tirotropin [TSH] ile ilişkili olduğunu göstermektedir, ancak obezite, serbest tiroid hormonları (serbest triiyodotironin [FT3] ve serbest tiroksin [FT4] dahil) arasındaki ilişki hala net değildir. Bu çalışmada bir obezite merkezinde tiroid homeostazisi, insülin direnci ve kan parametrelerinin kilo verme üzerine olan etkilerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Obezite merkezine 1 Kasım 2018 ile 13 Mart 2020 tarihleri arasında başvuran 3918 hastadan 417'si uygun bulunarak bu obezite önleme programı ve retrospektif, tanımlayıcı, kesitsel çalışmaya kabul edilmiştir.

Bulgular: Çalışmada 383'ü kadın hasta olmak üzere toplam 417 hasta ile görüşüldü. Hastaların ortalama yaşı 48.20 ± 11.03 yıldır. Kilo veren grupta; 6. ayda TSH, FT3, BMI, WC, HC, HbA1c ve HOMA-IR indeks değerleri anlamlı olarak daha düşüktü. Bu sonuçlara göre kilo veren hastaların kan parametreleri, TSH, FT3 ve insülin direnci azalmıştır. Kalça çevresi, BMI, BFP, FT3, HbA1c ve FBG, tek değişkenli analizlerimizde kilo kaybının önemli belirleyicileriydi. FT3 (olasılık oranı [OR]: 1.854; %95 CI: [1.223-2.811]; p = 0.004), BMI (OR: 0.948; %95 CI: [0.914-0.984]; p = 0.005) ve FBG (OR: 0.984; %95 CI: [0.973-0.996]; p = 0.007) kilo kaybını etkileyen çok değişkenli prediktörler olarak tanımlandı.

Sonuç: Bu çalışma, daha düşük BMI ve FBG seviyelerinin ve daha yüksek FT3 konsantrasyonlarının, obez hastalarda daha iyi bir kilo verme potansiyeli ile ilişkili olduğunu önermektedir.

Anahtar kelimeler: Obezite, insülin direnci, tiroid hormonları, kilo kaybı

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INTRODUCTION

Obesity is defined as excessive or abnormal fat accumulation which has extended all over the world and it is associated with increased incidence of hypertension, cardiovascular heart disease, hypothyroidism, type 2 diabetes mellitus, mental disorders, obstructive sleep apnea, several cancers and musculoskeletal disorders¹⁻⁵. In 2016; more than 650 million adults, 124 million children and adolescents were obese worldwide. At least 2.8 million people die as a result of being overweight/obese each year⁶.

Many studies show that obesity is associated with increased serum thyrotropin [TSH] but the relationship between obesity, free thyroid hormones (including free triiodothyronine [FT3] and free thyroxin [FT4] is still unclear⁷⁻¹⁰. Studies showed that the prevalence of subclinical hypothyroidism and hypothyroidism was highly common in obese population¹¹⁻¹². Benserior et al. reported that there was a positive association between TSH levels, insulin resistance and metabolic syndrome¹³. Recently, 29 studies have evaluated the relationship between serum TSH levels and BMI in euthyroid patients. 18 Of the studies found a positive correlation between TSH levels and adiposity measurements. There is no single, precise information about the circulating levels of thyroid hormones in obese individuals because most studies declared normal/low levels of FT4 in obese patients and high/normal/low FT3 levels.

The aim of this study was to establish the independent predictor of weight loss in the obesity center within 6 months and to show the relationship between thyroid function tests, HOMA index and obesity.

MATERIAL AND METHODS

Of 3918 patients applied to an obesity center between November 1st, 2018 and March 13th, 2020, 417 were found suitable and accepted in this obesity prevention program and retrospective, descriptive, cross-sectional study.

The essential situations for the acceptance to our obesity program are as follows; age \geq 18, BMI \geq 30 kg/m², to get approval from 5 different physicians consulted (department of internal medicine, psychiatry, cardiology, general surgery and physical therapy/rehabilitation). Patients with cardiac insufficiency, major depression and under 18 years of

age were never accepted obesity center. These are the common rules received by the ministry of health for all obesity centers in Turkey. In Turkey all obesity centers use the agreed program named "Obezit" founded by the ministry¹⁴.

In this study, patients were excluded for any of the following cases: having type 2 diabetes mellitus, having hypothyroidism/hyperthyroidism, taking any drugs, any other abnormal situation that could affect thyroid homeostasis, having Cushing syndrome, those with growth hormone deficiency, those at risk of developing obesity due to neuromuscular disorder.

Overall functioning and operation

In this center 5 healthcare providers including a nurse, physician, psychologist, dietician and secretary work continuously. There are two physiotherapists who come to this center for 2 hours a day once a week. All health workers of this center receive 'obesity basic knowledge certificate and 'Obezit' system basic knowledge certificate training¹⁵.

Education is given at the obesity center 5 days a week. Each group consists of about 20 obese patients. Patients are invited to the obesity center by the central secretary in at least 1-year period. In trainings, patients are directed to have a healthy lifestyle suggested by the ministry of health for all obesity centers in Turkey.

Patients with diabetes, hypertension, hypothyroidism or hyperthyroidism and other some diseases are treated by a doctor working in the center. All of the aforementioned services are free and they are all covered by insurances.

The research was managed under the original Declaration of Helsinki and its later recruitments or comparable ethical standards and was confirmed by the local ethics committee of the Selçuk University, Faculty of Medicine, (Reference number: 2020/156, date: 01.04.2020). All participants signed an informed consent.

Data collection tools

Participants admitted to this center were asked to complete a form to define their sociodemographic characteristics and the sociodemographic information form was routinely managed to all patients admitted to this center on first entrance. This socio-demographic information form included questions about the participants' gender, weight,

height, hip circumference, waist circumference, BMI, educational status, occupation and income levels.

Laboratory evaluation

The blood parameters were routinely measured at the center on first arrival and every 3 months. The blood parameters and anthropometric measurements of the patients that were taken routinely at the center for approximately 1.5 years in 3-month periods were retrospectively screened and evaluated. In our hospital; the laboratory reference range for serum TSH is 0.57-5.60 mIU/L; for FT4 is 0.70-1.74 ng/dL; for FT3 is 2.20-4.0 pg/mL.

Risk factor documentation

According to the Turkish Society of Endocrinology and Metabolism [TEMD] guide, patients with a BMI ≥ 30 -34.99 kg/m² were defined as class I obese, 35.00-39.99 kg/m² as class II obese, 40.00-49.99 kg/m² as class III obese, and ≥ 50.00 kg/m² as super obese¹⁶. Insulin resistance was assessed using the homeostasis model assessment for insulin resistance (HOMA-IR) based on the formula: fasting glucose (mg/dL) \times insulin (mIU/mL) / 405¹⁵.

Statistical analysis

All data were recorded into the IBM Statistical Package for the Social Sciences (SPSS) 22.0 computer program (Armonk, NY). Frequency (n), percentage (%), mean \pm standard deviation, min (minimum) – max (maximum) values were used as descriptive statistics to evaluate the data obtained from the research. The normality of the datum was controlled using the Kolmogorov-Smirnov test. The t-test and

logistic regression analysis were used to crosscheck the averages of the continuous variables of the datum. Pearson correlation analysis was used to investigate correlations. All analyses were conducted within a 95% confidence range. A p-value < 0.05 was considered as meaningful.

RESULTS

In this study, a total of 417 patients were interviewed, 383 were female. The mean age of the patients was 48.20 \pm 11.03 years. When the participants were evaluated according to BMI, 30.2% (n=126) were slightly obese, 34.3% (n=143) were moderately obese, 30.7% (n=128) were morbidly obese, and 4.8% (n=20) were super obese. While 56.4% (n=235) of them lost weight, 43.6% (n=182) could not lose weight (Table 1). Table 2 summarizes the comparison of patients' with/without weight loss according to thyroid homeostasis, insulin resistance and some parameters. In the group who lost weight; TSH, FT3, BMI, WC, HC, HbA1c and HOMA-IR index values were significantly lower in the sixth month. According to these results, the blood parameters, TSH, FT3 and insulin resistance of the patients are decreased who lose weight. The single and multivariate logistic regression determinants of weight loss are shown in Table 3 and Table 4. Hip circumference, BMI, BFP, FT3, HbA1c and FBG were important determinants of weight loss in our univariate analyses (Table 3).

FT3 (odds ratio [OR]: 1.854; 95% CI: [1.223-2.811]; p=0.004), BMI (OR: 0.948; 95% CI: [0.914-0.984]; p=0.005) and FBG (OR: 0.984; 95% CI: [0.973-0.996]; p=0.007) were defined as multivariate predictors affecting weight loss (Table 4).

Table 1. Socio-demographic characteristics of patients (n=417).

| Socio-demographic Characteristics | Category | n | % |
|---------------------------------------|--------------------------------|-----|------|
| Gender | Female | 383 | 91.8 |
| | Male | 34 | 8.2 |
| Age Mean \pm SD (min-max) | 48,20 \pm 11,03 (18-76) | | |
| Age (years) | 18-49 | 215 | 51.6 |
| | 50-65 | 188 | 45.0 |
| | 66 and \uparrow | 14 | 3.4 |
| BMI Mean \pm SD (min-max) 1st month | 38.45 \pm 5.69 (30.00-58.50) | | |
| BMI Categorical | Class I obesity | 126 | 30.2 |
| | Class II obesity | 143 | 34.3 |
| | Class III obesity | 128 | 30.7 |
| | Super obese | 20 | 4.8 |

| | | | |
|-----------------------|-------------------------|-----|-------|
| Educational level | Illiterate | 21 | 5.0 |
| | Elementary school | 253 | 60.7 |
| | High school | 76 | 18.2 |
| | University and ↑ | 67 | 16.1 |
| Marital status | Married | 359 | 86.1 |
| | Single / Divorced | 58 | 13.9 |
| Weight Loss Condition | Yes | 235 | 56.4 |
| | No | 182 | 43.6 |
| Occupation | Housewife | 345 | 82.7 |
| | Retired | 31 | 7.4 |
| | Artisan/Self-employment | 10 | 2.4 |
| | Public personnel | 27 | 6.5 |
| | Private sector | 4 | 1.0 |
| Income status | Low | 17 | 4.1 |
| | Middle | 149 | 35.7 |
| | Good | 251 | 60.2 |
| Total | | 417 | 100.0 |

Table 2. Comparison of patients' with/without weight loss according to thyroid homeostasis, insulin resistance and some parameters (Mean±SD)

| Parameter | Weight loss (+) | | Weight loss (-) | | p | |
|--------------------------|-----------------|--------------|-----------------|--------------|----------|----------|
| | Baseline | 6 months | Baseline | 6 months | Baseline | 6 months |
| TSH | 2.98±3.33 | 2.08±0.63 | 2.60±2.41 | 2.95±1.14 | 0.104 | <0.001 |
| FT3 | 3.00±0.55 | 2.34±0.25 | 3.19±0.55 | 3.05±0.81 | 0.002 | <0.001 |
| FT4 | 1.21±0.18 | 1.70±0.86 | 1.27±0.29 | 1.80±0.81 | 0.898 | <0.001 |
| BMI (kg/m ²) | 39.84±5.08 | 35.55±4.74 | 37.96±6.01 | 38.84±5.95 | 0.439 | <0.001 |
| WC (cm) | 111.88±11.17 | 98.10±10.54 | 108.36±16.40 | 107.14±16.86 | 0.084 | <0.001 |
| HC (cm) | 130.72±11.39 | 117.13±10.82 | 128.24±12.25 | 127.85±12.31 | 0.004 | <0.001 |
| HbA1c (%) | 6.05±0.87 | 5.39±0.37 | 5.73±0.48 | 6.19±0.48 | 0.017 | <0.001 |
| HOMA-IR index | 3.67±2.01 | 1.99±0.97 | 3.43±2.38 | 4.20±2.03 | 0.344 | <0.001 |

TSH: Thyroid-stimulating hormone; FT3: Free triiodothyronine; FT4: Free thyroxine; BMI: Body mass index; WC: Waist circumference; HC: Hip circumference; HbA1c: Hemoglobin A1c; HOMA-IR: Homeostasis model assessment of insulin resistance.

Table 3. Univariate logistic regression analysis of demographic characteristics of patients and some parameters of the first month on weight loss

| Univariate analysis | p | OR (95% CI) |
|--------------------------|-------|---------------------|
| HC (cm) | 0.008 | 0.977 (0.960-0.994) |
| BMI (kg/m ²) | 0.001 | 0.939 (0.906-0.974) |
| FT3 | 0.001 | 2.019 (1.327-3.070) |
| HbA1c (%) | 0.001 | 0.612 (0.455-0.822) |
| FBG | 0.003 | 0.983 (0.972-0.994) |

HC: hip circumference; BMI: Body mass index; FT3: Free triiodothyronine; HbA1c: Hemoglobin A1c; FBG: Fasting blood glucose; OR: Odds ratio; CI: Confidence interval.

Table 4. Multivariate analysis showing independent determinants of patients with weight loss

| Multivariate analysis | p | OR (95% CI) |
|--------------------------|-------|---------------------|
| FT3 | 0.004 | 1.854 (1.223-2.811) |
| BMI (kg/m ²) | 0.005 | 0.948 (0.914-0.984) |
| FBG | 0.007 | 0.984 (0.973-0.996) |

Adjusted for age and gender; FT3: Free triiodothyronine; BMI: Body mass index; FBG: Fasting blood glucose; OR: Odds ratio; CI: Confidence interval.

DISCUSSION

In our study, BMI, fT3 and FBG were demonstrated to be the independent predictors of weight loss in obese patients followed-up in an obesity center. In addition, in those who lose weight; serum TSH and fT3 levels, WC, HC, HbA1c and HOMA-IR index are significantly reduced. There was no association between fT4 levels and weight loss.

Obesity is a systemic chronic disease with important alterations in thyroid hormones. Xu et al. showed that obese/overweight subjects had high serum levels of fT3 and low levels of fT4; compared to underweight subjects¹⁷. 36 of 308 obese children aged 6-17 were found to have high TSH levels compared to normal weight children¹⁸. Similarly, Bastemir et al. investigated TSH levels among adult obese women and found it higher compared to women with normal weight¹⁹. Contrarily, it was shown that no significant difference was found between the serum TSH and fT4 levels of obese patients and the control group in another study conducted in Turkey²⁰. In the current study we did not evaluate thyroid hormones in terms of comparison between obese and healthy patients. Serum fT3 hormone was the only independent predictor of weight loss among thyroid hormones, which is consistent with the current literature^{21,22}. Moreover, Kazma et al. reported no significant relationship between fT4 and obesity that is also one of the important results of our study²³.

Admission BMI is the other independent predictor of weight loss which may have several underlying mechanisms to explain. BMI has been already associated with weight loss in a recent study²⁴. Marzullo et al. represented that there is a positive relationship between short-term weight loss and thyroid hormones (TSH, fT3, fT4) while no relation with BMI was found²¹.

Since the patients have been followed-up for six months in our study, it is comprehensible to detect BMI as an independent predictor of weight loss in contrast to four week follow-up by Marzullo et al.²¹ In other research performed by Chomard et al. defined that during the 6-week slimming therapy, the BMI decreased by about 10 per cent, with a slow decrease in the rate of weight loss in 17 moderately obese women, however BMI has not been investigated in terms of independent prediction for weight loss²⁵. The underlying mechanisms for the effect of BMI may be the environmental and

psychological factors of the participants or the adherence to the obesity center.

FBG has been usually applied as a confidential marker in the follow-up of obese patients²⁶. It was positively correlated with fT4 levels and negatively correlated with TSH levels in overweight and obese participants¹⁷. Thyroid hormones are one of the key factors in the glucose homeostasis. Metabolic investigations revealed that hypothyroidism/subclinical hypothyroidism may be responsible from the insulin resistance and high-normal serum levels of TSH was positively associated with insulin resistance^{27,28}. Our results showed that fT3 and FBG were detected as the independent predictors marking weight loss. Since the association between thyroid hormones and metabolic risk factors were defined, thyroid hormones may be the triggering factors effecting body weight and the co-morbidities of obesity.

Our research had a number of strengths and limitations. We worked on a group with similar characteristics that met the conditions to join the obesity center. Standard anthropometric and biochemical measurements were performed on all patients. A standard exercise and diet program is applied to patients attending the obesity center but, we are unable to suppose connection because this was a cross-sectional and retrospective study.

In conclusion, we observed an association between high fT3 and a weight loss. Also, we found serum TSH and fT3 levels, BMI, WC, HC, HbA1c and HOMA-IR index values were significantly decrease after 6 months in the group that lost weight. FBG and BMI were independent predictors affecting weight loss. This study advises that lower BMI and FBG levels, and higher fT3 concentrations are related with a better potential to lose weight in obese patients. The underlying reason of the challenge in weight loss may be due to fluctuations in the serum hormones (leptin, insulin, neuro peptide y, cortisol) related to obesity.

Yazar Katkıları: Çalışma konsepti/Tasanımı: DİY; Veri toplama: DİY; Veri analizi ve yorumlama: DİY, MAE; Yazı taslağı: DİY; İçeriğin eleştirel incelenmesi: MAE, DİY; Son onay ve sorumluluk: MAE, DİY; Teknik ve malzeme desteği: DİY, MAE; Süpervizyon: MAE, DİY; Fon sağlama (mevcut ise): yok.

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