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Determination of the Rate of Treatment with Over or Underdose of Patients Under Levothyroxine Replacement Therapy

Levotiroksin Replasman Tedavisi Alan Hastaların Yüksek veya Yetersiz Doz ile Tedavi Edilme Oranlarının Belirlenmesi

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ÖZET

Amaç: Primer hipotiroidizm, hipotiroidizm vakalarının %95'inden fazlasını oluşturur. Primer hipotiroidili hastaların levotiroksin sodyum (LT4) replasman tedavisi ile hedeflenen tiroid uyarıcı hormon (TSH) düzeyine ulaşılarak ötiroid hale gelmesi amaçlanır. Bu çalışmada optimal tedavi edilemeyen hastaların değerlendirilmesi ve aşırı doz veya eksik doz ile tedavi edilen hasta sıklığının belirlenmesi amaçlanmıştır.

Yöntemler: Bu retrospektif çalışma, Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi hastanesinde Ocak 2015 ile Aralık 2016 tarihleri arasında takip edilmiş olan 18 yaş üzeri, tiroid malignitesi olmayan, son 6 aydır sabit doz LT4 replasman tedavisi alan primer hipotiroidi tanılı 500 hasta üzerinde gerçekleştirilmiştir. Hastaların tiroid hormon durumunu belirlemek için serum TSH, serbest triiyodotironin (sT3) ve serbest tiroksin (sT4) seviyeleri kullanılmıştır. Tüm hastaların vücut kitle indeksi (VKİ) değerlendirilmiştir. Hastaların düşük yoğunluklu lipoprotein(LDL), yüksek yoğunluklu lipoprotein(HDL), çok düşük yoğunluklu lipoprotein(VLDL), trigliserit ve total kolesterol verileri analize dahil edildi.

Bulgular: LT4 replasman tedavisi alan hastaların %66.8'inde (n=334) TSH seviyeleri istenen hedef aralığında değildi. Hastaların %50,8' inde TSH düzeyi istenen hedef aralığından yüksekken (yetersiz dozla tedavi), hastaların %16.0' sında TSH düzeyi istenen hedef aralığından düşüktü (fazla dozla tedavi). Hastaların sadece %20, 6'sı normal vücut ağırlığındaydı. Dislipidemi prevalansı erkeklerde %69.2, kadınlarda %68.9'du ve cinsiyetler arasında anlamlı farklılık yoktu (p = 0.968).

Sonuç: Çalışmamızda LT4 replasman tedavisi altındaki çoğu hastanın istenen TSH aralığında olmadığı görüldü. LT4 tedavisi ile serum TSH seviyeleri normalize edilemediğinde disiplinler arası bir tanısal yaklaşım ve dikkatli öykü alınması gerekmektedir.

Anahtar Kelimeler: Primer hipotiroidizm, Hedef TSH, Aşırı doz, Yetersiz doz, Dislipidemi

ABSTRACT

Purpose: Primary thyroid disease accounts for over 95 percent of cases of hypothyroidism. It is aimed that patients with primary hypothyroidism become euthyroid by reaching the target thyroid stimulating hormone (TSH) level with levothyroxine sodium (LT4) replacement therapy. In this study, it was aimed to evaluate the patients who could not be treated optimally and to determine the frequency of patients treated with overdose or underdose.

Methods: This retrospective study was carried out on 500 patients diagnosed with primary hypothyroidism who were followed up at Necmettin Erbakan University Meram Faculty of Medicine hospital, are over 18 years of age, without thyroid malignancy, and who had been receiving fixed dose LT4 replacement therapy for the last 6 months between January 2015 and December 2016. Serum TSH, free triiodothyronine (fT3) and free thyroxine (fT4) levels were used to determine the thyroid hormone status of the patients. Body mass index (BMI) of all patients were evaluated. Low density lipoprotein (LDL), high density lipoprotein (HDL), very low density lipoprotein (VLDL), triglyceride and total cholesterol data of the patients were included in the analysis.

Results: TSH levels were not within the desired target range in 66.8% (n=334) of patients under LT4 replacement therapy. While TSH level was higher than the desired target range in 50.8% of the patients (treatment with underdose), 16.0% of the patients had TSH levels below the desired target range (treatment with overdose). Only 20.6% of the patients had normal body weight. The prevalence of dyslipidemia was 69.2% in men and 68.9% in women and there was no significant difference between the genders (p = 0.968).

Conclusion: In our study, it was observed that most patients under LT4 replacement therapy were not in the desired TSH range. When serum TSH levels cannot be normalized with LT4 therapy, an interdisciplinary diagnostic approach and careful history should be taken.

Key words: Primary hypothyroidism, Target TSH, Overdose, Underdose, Dyslipidemia

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INTRODUCTION

The prevalence of primary hypothyroidism, which is one of the most common endocrinological diseases, has been reported between 3.8-4.6% in the general population, and its annual incidence has been reported as 4.1/1,000 in women and 0.6/1,000 in men(1). It may progress asymptomatically, as well as symptomatic such as decreased quality of life, mood disorders, fatigue, cold intolerance. Levothyroxine sodium (LT4) replacement therapy is used in the treatment. Symptoms and signs of hypothyroidism are not specific or sensitive to the disease. Therefore, treatment follow-up is often performed biochemically. While it is aimed to keep thyroid stimulating hormone (TSH) levels between 0.5-2.5 mIU/L in healthy individuals under treatment, this range and threshold values vary in pregnant women, the elderly and individuals with cardiovascular risk factors(2). In some studies conducted, it was stated that more than half of the patients under thyroid hormone replacement therapy were treated with underdose or overdose(3, 4). Conditions such as poor patient compliance, wrong dose timing, drug interactions and comorbid diseases are effective in treatment failures. If treatment failure is not noticed, of patients symptoms due to hypothyroidism or hyperthyroidism will continue and conditions such as increased cardiovascular risk, osteoporosis, deterioration in lipid profile and decreased quality of life may be added.

In this study, it was aimed to determine the frequency of treatment with underdose or overdose in primary hypothyroidism patients under levothyroxine sodium treatment, to investigate the factors that may be effective in treatment failure, to examine the characteristics of the patients treated with the wrong dose.

MATERIAL AND METHODS

This retrospective study was carried out on 500 patients diagnosed with primary hypothyroidism who were followed up at Necmettin Erbakan University Meram Faculty of Medicine Endocrinology and Metabolism Diseases Service and Polyclinics and Internal Diseases Polyclinics, are over 18 years of age, without thyroid malignancy and who had been receiving fixed dose LT4 replacement therapy for the last 6 months between January 2015 and December 2016. Sociodemographic information of the patients, anthropometric characteristics (height, weight, body mass index [BMI]), pregnancy information, hypothyroidism cause, treatment indications, thyroid hormones, lipid profiles, LT4 doses, comorbid diseases, hypothyroidism symptoms were obtained from hospital archive, ENLIL automation system and PATIENT-PRO system records. Ethics committee approval was obtained for the study from the Scientific Research Ethics Committee of Necmettin Erbakan University Meram Medical Faculty with the decree dated 16.12.2016 and numbered 2016/765. Our study was carried out in accordance with the Declaration of Helsinki.

In our study, TSH levels were taken as the treatment target. Based on the Turkish Society of Endocrinology and Metabolism (TEMD) 2016 guidelines, TSH target levels of LT4 replacement therapy were in the range of 0.5-2.5mIU/L in the normal population, 0.5-6 mIU/L in patients aged 70-79 years, and 0.5-7.5 mIU/L in patients aged >80 years(5). Normal or risk-free patients were defined as patients aged between 18 and 70 who were not pregnant. In pregnant women, the target of 0.5-2.5 mIU/L for the first trimester, 0.5-3.0 mIU/L for the second and third trimesters, which is the joint decision of the "American Thyroid Association" and the "Endocrine Society" and TEMD 2016 guidelines. However, since pregnant women did not have trimester information, the treatment target was 0.5-2.5 mIU/L in pregnant patients. If TSH levels were above the desired range, it was accepted that the patients were treated with an insufficient dose, if they were below the desired range, they were treated with a high dose and those whose TSH levels were within the desired range were considered to be treated with the correct (normal) dose. BMI values were calculated from the height and weight values of the patients. BMI values were analyzed in 6 categories according to the classification of the World Health Organization(WHO). Patients with a BMI ≥30 kg/m² were considered obese.

Statistical Analysis

Statistical analyzes were performed using the SPSS version 20.0 (IBM®Inc, Chicago, USA) package program. Descriptive statistics are summarized as numbers, percentages, mean and standard deviation. The conformity of the variables to the normal distribution was examined using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov, Shapiro-Wilk tests). Numerical variables (age, BMI, low density lipoprotein (LDL), high density lipoprotein (HDL), very low density lipoprotein (VLDL), triglyceride (TG), total cholesterol (TC)) determined according to the normal distribution status were compared between the two groups using the T test in Independent Groups, and the One-Way ANOVA test between the three groups. Homogeneity of variances was evaluated with Levene's test. In cases where there was a significant difference, post-hoc analyzes were performed with the Bonferonni test. Pearson and Spearman correlation tests were used in the correlation analysis. Chi-square analysis was used to compare ordinal data. In the statistical analyzes in the study, comparisons with a p value below 0.05 were considered statistically significant.

RESULTS

In the study, the results of 500 patients were obtained retrospectively. Treatment indication was Hashimoto's disease in 50.0% (n=250) of the patients, after thyroidectomy in 22.6%

Table 1. Demographic and anthropometric characteristics of the participants

	Mean ± SD	Median	Min-Max
AgeGeneral	45.0 ± 15.0	45.0	18-79
BMIGeneral	28.4 ± 4.6	27.8	16.5-52.3
	Percentage (%)	**n(number)**	
Female	86.2	431	
Male	13.8	69	
Age 18-50	59.6	298	
Age 50-65	29.6	148	
Age >65	10.8	54	
BMI<18.5	0.2	1	
BMI 18.5-24.9	20.6	103	
BMI 25.0-29.9	49.2	246	
BMI 30.0-34.9	21.0	105	
BMI 35.0-39.9	6.4	32	
BMI >40	2.6	13	

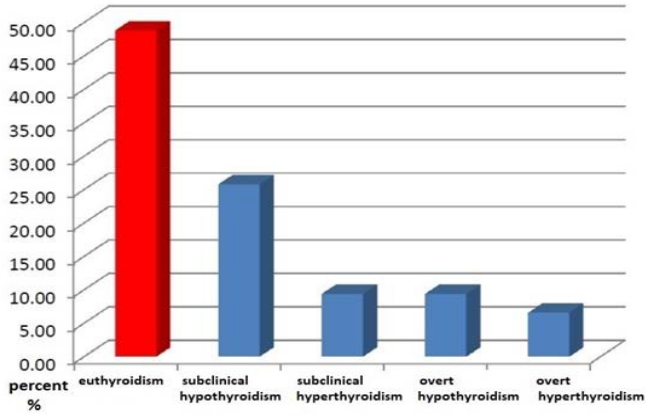

Figure 1. Classification of patients under LT4 therapy according to TSH levels

(n=113), after radioactive iodine (RAI) treatment in 4.2% (n=20) and 23.2% (n=113) were other reasons. Among the other causes, the most common were 10% (n=50) uninodular goiter, 5.8% (n=29) pregnancy, 1.2% (n=6) lithium treatment, 0.6% (n=3) multinodular goiter. While 11.1% (n=48) of the patients were pregnant, 88.9% (n=385) were not.

The mean age of the patients was 45 ± 15 years. 59.6% of the patients were between the ages of 18-50, 29.6% were between the ages of 50-65 and 10.8% were >65 years old. While 95.4% of the patients were between the ages of 18-70, 4.6% were between the ages of 70-79. 86.2% of the patients were female and 13.8% were male. The mean BMI of the patients was 28.4±4.6. When patients were grouped according to BMI, 30% of patients with hypothyroidism were obese (Table 1).

TSH levels were not within the desired target range in 66.8% (n=334) of patients under LT4 replacement therapy. This rate was 70.4% (n=298) in non-pregnant patients between the ages of 18-70, 37.9% (n=11) in patients between the ages of 70-79, and 52.1% in pregnant women (n=25). While the TSH level was higher than the desired target range in 50.8% of the patients (treated with insufficient dose), the TSH level was lower than the desired target range in 16.0% of the patients (treated with high dose) (Table 2).

The mean levothyroxine sodium dose received by the patients was 81.2 ± 52.9 mcg. The mean TSH level of the patients was 5.21 ± 10.59 mIU/L and free triiodothyronine (fT3) values of the 107 participants, free thyroxine (fT4) values of the 234 participants were accessed. The mean fT3 level of these patients was 2.79 ± 0.55 pg/ml and the fT4 level was 1.23 ± 0.33 ng/dl.

Table 2. TSH levels of patients under LT4 replacement therapy

TSH level		Patients between 18-70 years old, non-pregnant patients	Patients between 70-79 years old	Pregnant	Total
Low	Number	75	4	1	80
	%	17.7	13.8	2.1	16.0
Within the range of target	Number	125	18	23	166
	%	29.6	62.1	47.9	33.2
High	Number	223	7	24	254
	%	52.7	24.1	50.0	50.8
Total	Number	423	29	48	500

Table 3. Dyslipidemia frequency of participants according to LT4 dose

		High dose LT4 N (%)	Sufficient dose of LT4 N (%)	Underdose LT4 N (%)	Total N (%)
Dyslipidemia	Yes	23 (65.7)	61 (62.2)	107 (74.3)	191 (69.0)
	No	12 (34.3)	37 (37.8)	37 (25.7)	86 (31.0)

*Chi-square test was used.

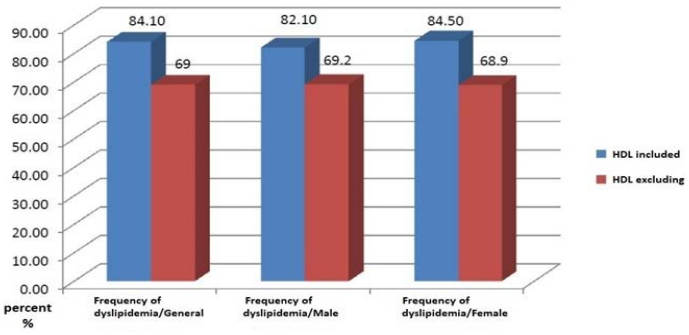

Figure 2. Frequency of dyslipidemia among participants

Of the patients under LT4 replacement therapy, 48.8% (n=244) were euthyroid, 25.8% (n=129) were subclinical hypothyroid, 9.4% (n=47) were subclinical hyperthyroid, 9.4% (n=47) were overt hypothyroid, 6.6% (n=33) were overt hyperthyroid (Figure 1). LDL, HDL, VLDL, TG and TC data were accessed for 277 of the patients (39 males, 238 females). The frequency of dyslipidemia in all patients was 84.1%. The frequency of dyslipidemia was 84.5% in women and 82.1% in men. When HDL values were not included in the dyslipidemia analysis, the frequency of dyslipidemia was 69.0% (69.2% in men, 68.9% in women). While 43.7% of the patients had hypertriglyceridemia, 52.7% had hypercholesterolemia. 30.3% of the patients had both hypertriglyceridemia and hypercholesterolemia. Presence of dyslipidemia did not differ between genders (p=0.968) (Figure 2).

LDL, HDL, TG and TC levels of patients treated with underdose, adequate dose and overdose LT4 were compared. There was no statistically significant difference between the groups in terms of LDL, HDL, TG, and TC levels (respectively; p=0.059, 0.263, 0.224, 0.080) (Figure 3). While 74.3% (n=107) of patients treated with underdose of LT4 had dyslipidemia, 62.2% (n=61) of those treated with adequate dose and 65.7% (n=23) of those treated with overdose had dyslipidemia.

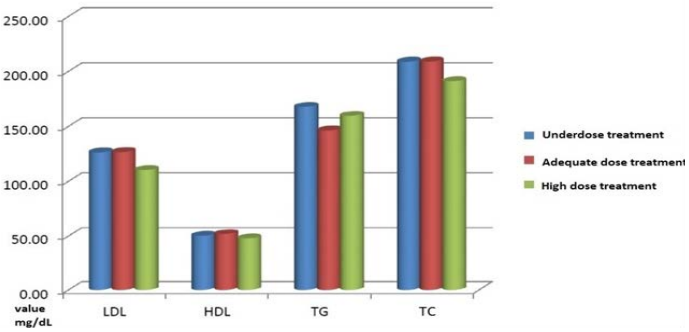

Figure 3. The lipid levels of the participants according to the treatments doses

Table 4. Comorbid diseases of patients

Comorbidity	Percentage	n
*DM	19.2	96
**HT	15.6	78
Hyperlipidemia	6.0	30
Asthma	3.6	18
Coronary artery disease	3.0	15
Bipolar disorder	1.6	8
Anemia	1.4	7
Rheumatoid arthritis	1.2	6
Depression	1.0	5
Heart Failure	1.0	5
Osteoporosis	1.0	5
***COPD	0.6	3
Arrhythmia	0.4	2

*Diabetes mellitus
**Hypertension
***Chronic obstructive pulmonary disease

There was no difference between the groups in terms of the frequency of dyslipidemia (p=0.125) (Table 3). While 59.0% (n=295) of the patients had no additional disease, 41% (n=205) had comorbid disease. The most common comorbid diseases were diabetes mellitus (DM), hypertension (HT), coronary artery disease, hyperlipidemia and asthma (Table 4).

The most common symptom in the patients was swelling in the body and concentration impairment (45.0%). This was followed by lack of attention (43.8%), constipation (43.4%), chills (42.0%) and irritability (40.6%) (Table 5). 66.8% (n=334) of the patients were taking levothyroxine sodium while fasting in the morning. 20.8% of them (n=104) were taking while fasting at noon, 7.4% of them (n=37) were taking while fasting in the evening. 3.8% of them (n=19) were taking while full in the morning, 1% (n=5) of them were taking while full in the afternoon, 0.2% (n=1) of them were taking while full in the evening. When the patients were grouped as those with and without TSH levels in the normal range, age (p=0.280), gender (p=0.104), presence of comorbid disease (p=0.708) and BMI (p=0.888) were similar in both groups (Table 6).

DISCUSSION

The first striking finding of our study was that although most of the patients used LT4, their TSH levels were not within the desired range and the treatment goals could not be achieved. More than half of the patients had concomitant dyslipidemia. Comorbidity was present in approximately half of the patient group. Despite the use of LT4, the targeted TSH values could not be reached, and a significant proportion of the patients had symptoms related to hypothyroidism.

In the "Colorado Thyroid Disease Prevalence" study conducted in the United States, only 60.1% of 1525 patients under LT4 replacement were reported to be euthyroid(3).

Table 5. Dyslipidemia frequency of participants according to LT4 dose

Symptom	Hyperthyroidsm N=80 Percentage	Euthyroid N=244 Percentage	Hypothyroidism N=176 Percentage	Total N=500 Percentage
Swelling in the body	22.5	36.5	51.1	45.0
Difficulty concentrating	50.0	42.2	46.6	45.0
Attention deficit	51.3	41.8	43.2	43.8
Constipation	42.5	41.4	46.6	43.4
Feeling cold	45.0	41.8	40.9	42.0
Irritability	56.3	41.0	33.0	40.6
Weight gain	22.5	35.2	55.1	40.2
Over-sleeping	26.3	41.4	43.2	39.6
Palpitations	47.5	23.8	33.5	31.0
Itching	23.8	25.4	26.1	25.4
Menstruation disorder*	22.5	22.1	21.0	21.8
Infertility	20.0	11.9	14.2	14.0
Heat intolerance	18.8	7.0	8.0	9.2
Weight loss	22.5	3.7	1.1	5.8

*Menstrual irregularity was analyzed only for female gender, while others were analyzed for both genders.

Table 6. The relationship between the participants' TSH levels and gender, BMI and age

TSH levels	Within the normal range Mean ± SD	Below or above the normal range Mean ± SD	p
Age*	47.1 ± 161	44.0± 14.4	0.280
BMI*	28.3 ± 4.7	28.4 ± 4.6	0.888
Gender**	**Number (%)**	**Number (%)**	
Male	17 (24.6)	52 (75.4)	0.104
Female	149 (34.6)	282 (65.4)	
Comorbidity**			
Yes	70 (34.1)	135 (65.9)	0.708
No	96 (32.5)	199 (67.5)	

*T-test for independent spouses
**Chi-square test

The 12.2% difference in the rate of patients with euthyroidism between the two studies is due to the fact that the definition of euthyroidism was defined separately in our study according to age groups and pregnancy status, and the narrower TSH interval was used. In the "Colorado Thyroid Disease Prevalence" study, euthyroidism was defined in a wider range of 0.3-5.1 mIU-L. Again, in another study (Crilly and Esmail) (6), only 50% of 332 primary hypothyroidism patients were reported to be euthyroid. This rate was reported as 59.7% in the study by Vigario et al.(7), 46.9% by De Whalley et al.(8) and 52% in the study by Parle et al.(9). The results of these studies were similar to the results of our study.

In a multicenter study conducted by Vaisman et al (10) in 2013, it was reported that serum TSH levels were not at the desired level in 42.7% of over 2000 hypothyroid patients. While the treatment dose was insufficient in 28.2% of these patients, the treatment dose was excessive in 14.4%. In our study, 50.8% of the patients were treated with an insufficient dose, while 16% were treated with a high dose. In the study conducted by Vigario et al.(7), 40.3% of the patients were treated with underdose or overdose. While 25.9% of the patients were treated with underdose (21.5% subclinical hypothyroidism, 4.4% overt hypothyroidism), 14.4% of the patients were treated with overdose (13% subclinical hyperthyroidism, 1.4% overt hyperthyroidism). In our study, these rates were similar, with 25.8% subclinical hypothyroidism, 9.4% subclinical hyperthyroidism, 9.4% overt hypothyroidism and 6.6% overt hyperthyroidism. In the study conducted by De Whalley et al.(8), 30% of the patients were treated with underdose and 23% with overdose. In this prospective study, it was reported that the dose of LT4 was increased in only 44% of patients treated with underdose and the dose was reduced in only 11% of those treated with overdose. In the study conducted by Parle et al.(9), 27% of the patients were treated with an insufficient dose and 21% with an overdose. In another study by Sawin et al.(11) in the USA, it was reported that 37% of the patients had TSH levels above 10 mU/L (overt hypothyroidism) despite treatment. These studies carried out by Parle and Sawin were

carried out in the 1990s. Despite this, it is seen that the same problems continue in studies conducted today, and that the desired treatment goal in primary hypothyroidism patients is unsuccessful. Treatment failure will negatively affect the clinical results of the patients and increase the disease burden. In the study conducted by Vaisman et al.(10), it was reported that the quality of life of patients treated with insufficient dose was worse. Similar results were also reported by Vigario et al.(7). On the other hand, complications such as continuation of symptoms, osteoporosis and increased cardiovascular risk will further increase the burden of treatment failure on the patient.

These findings indicate that the desired treatment goals are not achieved in at least half of the patients on LT4 replacement therapy. A number of causes have been identified that are blamed for failure to achieve treatment goals. Although there are differences in activity, stability and bioavailability between different LT4 preparations, differences can be observed even in preparations produced by the same manufacturer(12). Also, poor drug compliance, use of proton pump inhibitors, conditions that impair LT4 absorption by causing hypochlorhydria such as autoimmune atrophic gastritis, diseases that decrease luminal absorption, increased LT4 requirement such as weight gain, pregnancy, and diseases that change TSH levels such as Addison's disease increase treatment failure(13). Supporting these findings, in our study, only 66.8% of the patients took the drug at the right time and while hungry, 41% of the patients had comorbid diseases and 30% of the patients were obese.

Another striking finding of our study was the high frequency of dyslipidemia. While the frequency of dyslipidemia was 69%, the frequency of hypercholesterolemia was 52.7%, the frequency of hypertriglyceridemia was 43.7%, the frequency of hypercholesterolemia + hypertriglyceridemia was 30.3%. In the study of O'Brien et al.(14), it was reported that 56% of 295 hypothyroid patients had hypercholesterolemia,1.5% had only hypertriglyceridemia, 34% had hypercholesterolemia and hypertriglyceridemia. These findings were consistent with our study. In light of these findings, it can be said that hypothyroidism is a common cause of dyslipidemia. Several possible reasons have been suggested for the association between hypothyroidism and dyslipidemia. Cholesterol and LDL levels increase in hypothyroidism because thyroid hormone stimulates the HMG-CoA reductase enzyme, which is responsible for the first step of cholesterol synthesis and activates LDL receptors (increased LDL oxidation).

However, in hypothyroidism, lipoprotein lipase activity decreases and TG level increases. As a result, there is an increased risk of cardiovascular disease(15). Conflicting results have been reported for HDL values. While HDL is found at high or normal levels in some studies, it has been reported that it tends to decrease in hypothyroidism in some studies(16).

Although the frequency of dyslipidemia is found to be high in hypothyroid patients, it was reported that it can regress with LT4 replacement therapy. In the study conducted by Tanis et al.(17), it was reported that there was a significant decrease in TC values (mean 131 mg/dl decrease from 310 mg/dl) with LT4 replacement therapy. In our study, the high rate of dyslipidemia in patients despite LT4 replacement therapy confirms treatment failure. In our study, the most common symptoms of hypothyroidism were swelling in the body (45%), impaired concentration (45%), lack of attention (43.8%), constipation (43.4%), and chills (42.0%). Similarly, in the study conducted by Georgiou et al.(18), these symptoms were reported among the most common symptoms. On the other hand, irritability (56.3%), palpitation (47.5%), weight loss (22.5%) were prominent in those whose TSH levels are in the hyperthyroid range, while swelling in the body (51.1%), weight gain (55.1%), excessive sleepiness (43.2%) were prominent in patients with hypothyroidism. In a review by McAninch et al.(19), supporting our findings, they stated that hyperthyroidism symptoms become more pronounced as LT4 dose increases and hypothyroidism symptoms become more pronounced as LT4 dose decreases. Therefore, questioning the symptoms of the patients in the evaluation of treatment failure will help to normalize the treatment. Change or exacerbation of symptoms associated with hyperthyroidism or hypothyroidism should be a warning for treatment failure.

Since our study is a retrospective study, it includes all the limitations of a retrospective study. In our study, LT4 replacement therapy was evaluated with TSH levels, which are frequently preferred biochemically. However, it was reported that even if TSH levels are within normal reference values in hypothyroidism, the well-being of patients may decrease and cognitive disorders may persist(20). Therefore, it can be said that TSH alone is not sufficient in the follow-up of the treatment. The results obtained are descriptive due to the design of the study and a cause-effect relationship cannot be reached. Our study does not illuminate the underlying reasons why the treatment target could not be achieved in a large number of patients. More comprehensive prospective and controlled studies can shed light on this issue.

CONCLUSION

Treatment failure in patients with hypothyroidism is higher than expected. In our study, TSH levels were not in the therapeutic range in 66.8% of the patients. Most of the patients were treated with underdose or overdose of LT4. Similarly, two-thirds of the patients were accompanied by dyslipidemia. When hypothyroidism cannot be treated, it leads to serious consequences and significantly affects

the quality of life of patients. To prevent treatment failure, patients should be followed closely, conditions such as patient non-compliance associated with treatment failure, incorrect posology and timing of the drug, malabsorption, multiple drug use, comorbid diseases should be identified, controlled and corrected appropriately for each patient. Since there are so many factors affecting LT4 replacement therapy failure, overcoming this problem requires a multidisciplinary approach. On the other hand, the high frequency of dyslipidemia in patients who cannot achieve the desired treatment goal increases the risk of cardiovascular disease. The well-being of the patients will be improved by regulating the treatment doses, informing the patients about the correct use of the drug, evaluating and normalizing the lipid profile in hypothyroid patients whose patient follow-ups are made with TSH levels.

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