

HİPOTİROİDİ VE HİPERTİROİDİ HUZURSUZ BACAK SENDROMUNU VE ONUN UYKU KALİTESİ İLİŞKİSİNİ ETKİLİYOR MU?

DO HYPOTHYROIDISM AND HYPERTHYROIDISM AFFECT RESTLESS LEG SYNDROME, SLEEP AND ITS QUALITY?

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ÖZET

Tiroid disfonksiyonlu hastalarda huzursuz bacak sendromu ve bu sendromun uyku bozuklukları üzerine olan etkisini araştırmayı hedefledik.

31 hipotiroidi, 31 hipertiroidi tanılı hasta çalışma grubu ve bu hastalarla yaş ve cinsiyet uygun 30 gönüllü kontrol grubu olarak çalışmaya dahil edildi. Huzursuz Bacak Sendromu (HBS) tanısı Uluslararası kriterlere uygun olarak konuldu. Güniçi uykululuk, uyku kalitesi ve insomni değerlendirmesi skalalara göre değerlendirildi.

Çalışma yaş ortalaması 41.50 (min-max = 20-72) idi. Hipotiroidili 4 hasta ve hipertiroidili 7 hasta kadın cinsiyette idi. HBS tanısı alan hastalar hipotiroidili grupta hipertiroidili gruba göre sayıca fazla idi. Gruplar arasında; uyku kalitesi ve uyku latansı değerlendirilmesi için istatistiksel olarak anlamlı fark olmasa da sübjektif farklılıklar saptandı. Beck depresyon sklası gruplar arasında istatistiksel olarak farklı idi (p=0.010). Beck depresyon skorları hipertrioidili grupta yüksek iken, gönüllü katılan kontrol grubunda düşük olarak saptandı. Hamilton anksiyete skorları arasında anlamlı fark saptanmadı (p=0.486).

Hipotiroid grubunda HBS sıklığı yüksek saptandı. HBS tanılı hastaların Depresyon değerlendirme puanları hipertiroidili grupta yüksek saptandı.

Anahtar Kelimeler: Tiroid Bozuklukları, Huzursuz bacak sendromu, Uyku kalitesi

ABSTRACT

We aimed to evaluate the frequency of restless legs syndrome (RLS) and its sleep disturbance in patients with thyroid dysfunction.

31 patients with hypothyroidism and 31 patients with hyperthyroidisim as study groups and 30 age and gender-matched healthy volunteers as a control group were enrolled in the study. The diagnosis of RLS was made according to the criteria of the International RLS Study Group. Extreme daytime sleepiness, sleep quality and insomnia estimated by assessment tools

Among our study population, the median age was 41.50 (min-max = 20-72). 4 patients in the hypothyroid group and 7 patients in the hyperthyroid group were female. The RLS-diagnosed patients



were significantly higher in the hypothyroid group than the hyperthyroid group. While subjective sleep quality and sleep latency were significantly different in the study population, there was no correlation between all groups in sleep quality according to PSQI. ESS and ISI scores were not significantly different in all groups. When the subsequent categorization of BDI into mild, moderate and severe was made, a significant difference was found between the three groups (p=0.010). Among the study groups although the percentage of low-BDI patients in the control group was higher (70%), the percentage of the severe-BDI was higher in the hyperthyroid group (16.13%). The severity of anxiety scores was not measured significantly between all groups according to the HAS (p=0.486).

The frequency of RLS was significantly higher in the hypothyroid group. Those who had more severe depression scores according to the depression assessment scales were higher in the hyperthyroid group.

Keywords: Thyroid disorders, restless legs syndrome, sleep quality

1. INTRODUCTION

Thyroid diseases are frequent and significant endocrine diseases affected many populations. Thyroid hormones play a regulatory role in the production of enzymes, vitamins, and minerals, which are mediators of many metabolic events. Thyroid dysfunction can cause a variety of metabolic malfunctions mostly including intolerance to heat, irritability, sleep disturbances, and headaches.

Hypothyroidism is more frequently seen rather than hyperthyroidism in thyroid disorders (Braverman et al., 2000). Thyroid hormones are closely in relationship between cerebral functions and mental state. Thyroid gland abnormalities are closely related to neurocognition and emotional impairment (Dugbartey,1998). Behavioral changes, persistent neurophysiological disorders have been reported (Bossowskiet al., 2007).Indeed, patients with thyroid gland abnormalities have difficulties falling asleep and maintaining sleep. The researches reported that patients with hypothyroidisim feel commonly fatigued in daytime and short-time sleep at night whereas patients with hyperthyroidisim feel more anxious and irritable in daytime and insomnia at night (Sridhar et al., 2011).

Restless Legs Syndrome (RLS) is a disease characterized by an abnormal sensation, some sort of dysesthesia that cannot be described in the extremities, especially in the legs. Symptoms begin at rest and at night when sleep begins, and disappear during the day. It is claimed that the most important factor that causes this situation the circadian rhythm of dopamine circulation in the central nervous system (Doran et al., 1990).

RLS may be seen alone or may occur secondary to the course of several diseases such as peripheral polyneuropathy, diabetes, multiple sclerosis, rheumatoid arthritis. In reported studies, the prevalence of RLS varies between 0.25% and 15.3%, is more common in women and its prevalence increases with age (Van de Vijver et al. 2004; Nichols et al., 2003; Ghorayeb et al., 2009). However, there was no study on the presence of RLS in patients with thyroid dysfunction.

The first classification of sleep diseases was made in 1979, then this classification had undergone serious revisions, and in conclusion, the definition re-organized under 7 main headings and published as "AASM International Classification of Sleep Disorders ICSD 3" in February 2014. Insomnia, which is one of the sleep disorders, is a clinical condition which courses with difficulty in starting or maintaining sleep and related daytime dysfunctions despite the availability of environment and conditions suitable for sleep. Insomnia is a common symptom and disease in various diseases since it is a common problem.

Excessive daytime sleepiness is a quite common problem affecting a large part of the population. According to epidemiological studies, 4-5% of the population has excessive daytime sleepiness. Adequate wakefulness is essential for social and occupational life performance. State of sleep can cause workforce loss and serious accidents (Ursavaş, 2014).



It is known that all endocrinological diseases are accompanied by sleep disorders. Although the hypothalamus is the basic organ in the regulation of the endocrine system, it also participates in the formation of sleep.

In the study, our goal is to determine the incidence of RLS in cases with hypothyroidism and hyperthyroidism, and to assess sleep disorder and sleep quality combined with emotional screening tests (Beck Depression Inventory (BDI) and Hamilton Anxiety Scale (HAS)) matched with healthy volunteers. Therefore, we could analyze patients with RLS in thyroid abnormalities during daytime and night-time.

2. MATERIAL and METHODS

In this cross-sectional prospective study, we evaluated 92 cases at three groups including 31 patients with hyperthyroidism, 31 patients with hypothyroidism and 30 healthy volunteers at Endocrinology follow-up clinic, Bursa Yüksek İhtisas Training and Research Hospital, Sağlık Bilimleri University during a-year period. Clinical diagnosis of restless leg syndrome, excessive daytime sleepiness, sleep quality and insomnia were blindly evaluated by sleep disorder Neurology Specialist. The emotional screening tests including The Hamilton Anxiety Scale (HAS) and the Beck Depression Inventory were assessed. The mood states of the patients were assessed by BDI and HAS.

The Restless Leg Syndrome diagnosis was made according to the criteria of the International RLS Study Group (Allen et al., 2014).

Epworth Sleepiness Scale (ESS) is a practical, easy to score and use, and widely used scale (Murray, 1991). The severity of sleepiness is scored by asking the patient questions about 8 different conditions. It is scored as 0-3 and the higher score shows sleepiness. According to this scale, scores taken below 10 are considered normal while values between 10-15 are considered as increased sleepiness. However, scores at 16 and above show a very serious and dangerous level of pathological sleepiness.

Sleep quality was evaluated by Pittsburgh Sleep Quality Index (PSQI) (Daniel et al., 1991). 7 subscales such as subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disorder, sleep medication use, daytime dysfunction are evaluated with 19 questions answered by the study cases. The answers to 19 questions were scored between 0-3 according to symptom frequency. Scoring is as follows; 0 point if never during the past month 0, 1 point if less than one week, 2 points if once or twice a week, and 3 points if three or more times a week. The 7 subscales asked in the questionnaire are scored as very good 0, fairly good 1, fairly bad 2, very bad 3. While the total score obtained is between 0-21, higher values indicate poor sleep quality and a high level of sleep disorder. A total score above 5 indicates clinically that sleep quality is significantly poor. 7 sub-component 3: Sleep duration, Component 4: Sleep efficiency, Component 5: Sleep disorder, Component 6: Medication use, Component 7: Day functions.

Insomnia was evaluated with Insomnia Severity Index (ISI) (Bastien et al. 2001). As scores increase, the level of insomnia is categorized; it corresponds to categories such as insignificant, subsidiary, moderate, severe insomnia.

While assessing sleepiness, insomnia and sleep quality in the study population, Beck Depression Inventory (BDI) and Hamilton Anxiety Scale (HAS) were applied to all participants in order to avoid mood-related confusion. BDI assesses physical, emotional and cognitive symptoms which are seen in depression (Beck et al., 1961). It is a self-assessment scale that includes 21 symptom categories. The highest score to get is 63. The higher total score indicates a higher severity of depression. 0-9: Indicates the normal level. 10-18: Indicates a milder level of depression. 19-29: Indicates a moderate level of depression. 30-63: Indicates a sign of severe depression. HAS has been designed to measure the level of anxiety and symptom distribution for the person and to determine the change in severity



(Maier et al., 1988)The patient's status in the last 72 hours is analyzed and the patient is asked to explain her/his condition with her/his own words. The scale is filled in by the interviewer and is based on the interviewer's momentary convictions. The score of each item is between 0-4 and the total score of the scale is between 0-56. Scaled as 0-5: no anxiety, 6-14: minor anxiety, > 15: major anxiety. The taken score of the patient was assessed according to the belonging range of the score.

SPSS 23 packaged software, Pearson's Chi-Square, Fisher-Freeman-Halton, Shapiro-Wilk, Kruskal-Wallis H tests were used for statistical analysis.

3. RESULTS

Among our study population, the median age was 41.50 (min-max = 20-72). 4 (12.90 %) patients in the hypothyroid group and 7 (22.58%) patients in the hyperthyroid group were female. When the three groups were compared, there was a statistical difference in cases with and without RLS (p= .042). We evaluated 16 patients with RLS in our study. The RLS-diagnosed patients were higher in the hypothyroid group than the hyperthyroid group (p= .730) (Table 1).

	Hypothyroid group	Hyperthyroid group	Control Group	p-value	
Gender [*] n(%)					
Male	4 (12,90)	7 (22,58)	5 (16,67)	- 0,598	
Female	27 (87,10)	24 (77,42)	25 (83,33)		
Age [#]	40 (25-72)	45 (22-66)	38 (20-72)	0,716	
RLS * n(%)	12 (38,71)	4 (12,90)	-	0,042	

Table 1: Characteristics of the hypothyroid group, hyperthyroid group and control group

*Data given in *frequency (percentage)* values. *Data given as median (min-max). **RLS:** Restless Legs Syndrome.

When the subsequent categorization of BDI into mild, moderate and severe was made, a significant difference was found between the three groups (p=0.010). Milder level of depression scores was higher seen in the hypothyroidism group (83.87 %), whereas the severe level of depression scores was higher seen in the hyperthyroidism group (16.13%) among the study population. No significant correlation was found between ESS, HAS, and ISI scoring systems and the presence of RLS (p=0.486) (Table 2).

Table 2: Insomnia Severity Index, Beck Depression Inventory and Hamilton Anxiety Scale Status

 in the hypothyroid group, hyperthyroid group and control group

		GROUPS			
		Hypothyroid group	Hyperthyroid group	Control Group	p-value
ESS n(%)	>=10	4 (12,90)	3 (10,00)	4 (13,33)	
	<10	27 (87,10)	27 (90,00)	26 (86,67)	
	1,0	4 (12,90)	3 (9,68)	11 (36,67)	1,000
	2,0	0 (0,00)	0 (0,00)	4 (13,33)	
	3,0	0 (0,00)	0 (0,00)	1 (3,33)	
HAS n(%)	non-existent	14 (45,15)	10 (32,26)	7 (23,33)	
	minor	15 (48,39)	12 (38,71)	13 (43,33)	0,087
	major	2 (6,45)	9 (29,03)	10 (33,33)	



BDI n(%)	mild	26 (83,87)	15 (48,39)	21 (70,00)	
	moderate	4 (12,90)	11 (35,48)	9 (30,00)	0,010
	severe	1 (3,23)	5 (16,13)	0 (0,00)	
ISI n(%)	insignificant	23 (74,19)	19 (61,29)	20 (66,67)	
	subsidiary	6 (19,35)	6 (19,35)	8 (26,67)	0,486
	moderate	2 (6,45)	6 (19,35)	2 (6,67)	

ESS: Epworth Sleepiness Scale, HAS: Hamilton Anxiety Scale, BDI: Beck Depression

No significant difference was found between the three groups in terms of the total score of PSQI 5 and below and above (p=0.541). Significant differences were found between the three groups in terms of subjective sleep quality, sleep latency and daytime functions in the component evaluations of PSQI (p=0.004, p=0.001, p=0.001) (Table 3). There was no significant difference in terms of others.

Table 3: Sleep quality status in the hypothyroid group, hyperthyroid group and control group

		GROUPS			
		Hypothyroid	Hyperthyroid	Control	p-value
		Group	Group	Group	
Total PSOI score	<5	18 (58,06)	14 (45,16)	14 (46,67)	0,541
	>=5	13 (41,94)	17 (54,84)	16 (53,33)	
	,0	4 (12,90)	1 (3,23)	12 (40,00)	0.004
PSQI Component 1	1,0	19 (61,29)	17 (54,84)	11 (36,67)	
n(%)	2,0	5 (16,13)	10 (32,26)	7 (23,33)	0,004
	3,0	3 (9,68)	3 (9,68)	0 (0,00)	
	,0	15 (48,39)	6 (19,35)	8 (26,67)	
PSQI Component 2	1,0	3 (9,68)	11 (35,48)	13 (43,33)	0 001
n(%)	2,0	9 (29,03)	3 (9,68)	7 (23,33)	0,001
	3,0	4 (12,90)	11 (35,48)	2 (6,67)	
	,0	12 (38,71)	13 (41,94)	16 (53,33)	0,361
PSQI Component 3	1,0	8 (25,81)	11 (35,48)	3 (10,00)	
n(%)	2,0	7 (22,58)	5 (16,13)	7 (23,33)	
	3,0	4 (12,90)	2 (6,45)	4 (13,33)	
	,0	23 (74,19)	23 (74,19)	22 (73,33)	0,285
PSQI Component 4	1,0	6 (19,35)	4 (12,90)	1 (3,33)	
n(%)	2,0	1 (3,23)	1 (3,23)	4 (13,33)	
	3,0	1 (3,23)	3 (9,68)	3 (10,00)	
	,0	2 (6,45)	4 (12,90)	3 (10,34)	0,452
PSQI Component 5	1,0	23 (74,18)	16 (51,61)	17 (58,62)	
n(%)	2,0	6 (19,35)	9 (29,03)	9 (31,03)	
	3,0	0 (0,00)	2 (6,45)	0 (0,00)	
	,0	27 (87,10)	28 (90,32)	14 (46,67)	0,001
PSQI Component 7	1,0	4 (12,90)	3 (9,68)	11 (36,67)	
n(%)	2,0	0 (0,00)	0 (0,00)	4 (13,33)	
	3,0	0 (0,00)	0 (0,00)	1 (3,33)	

PSQI: Pittsburgh Sleep Quality Index. Data given in *frequency (percentage)* values.



4. DISCUSSION

In our study, we examined 92 cases to evaluate the frequency of restless legs syndrome (RLS) and its sleep disturbance in patients with thyroid dysfunction. We found a statically higher frequency of RLS disorder in the hypothyroidism group, whereas we did not found any significant relationship with day-time and night-time sleepiness and sleep quality among the study population.

Thyroid function disorders are the most common endocrine disorders in the world and our country. Thyroid hormone has vital importance on the maturation and function of the central nervous system. Although thyroid dysfunction does not cause structural damage to the brain, it can be associated with various psychiatric disorders, sleep disorders and physical diseases (Davis et al., 2007).

According to epidemiological studies, RLS can be seen in 1-15% of the general population (Yüksel et al., 2006). Indeed, in our study, the rate of RLS was 38% in the hypothyroidism group and 13% in the hyperthyroidism group. We did not diagnose RLS in the healthy-volunteers group.

Although it is accepted that there is dysfunction in the central-origin dopamine system in RLS, the etiopathogenesis is not fully clarified (Trenkwalder et al., 2018).

Investigating thyroid dysfunction in RLS could be beneficial to understand underlying pathogenesis in RLS because of the very close and important relationship between thyroid gland activity and the brain. We could think that our study is very valuable that contributes to reveal the thyroid dysfunction in the etiology of RLS in this field.

Sleep disorder symptoms are almost viewed in common health problems. Thyroid gland dysfunction is linked to sleep disturbances and commonly insomnia due to effect irreversible and severe changes in central nervous systems. Firstly, insomnia is frequently seen in hyperthyroidism. Following the literature, in our study, when the assessment was made between three groups according to ISI, the number of patients with moderate ISI scores were higher in the hyperthyroid group than the other groups. Excessive Daytime Sleepiness (EDS) is the most common sleep-related symptom and its estimated prevalence in the community is up to 18%. In our study, EDS (ESS above 10) was found 12.9 % in the hypothyroid group and 10% in the hyperthyroid group.

In our study, we did not find any significant difference in terms of sleep quality between patients with hypothyroidism and hyperthyroidism. However, interestingly, we found only significant differences in sleep latency, daytime functions and subjective sleep quality of the lower components of sleep quality. The rate of prolonged sleep latency was significantly higher in patients with hyperthyroidism than the other groups. This situation might be explained about the symptoms of hyperthyroidism. The rate of those who stated that their subjective sleep quality as poor was 9% and it was significantly higher in both hypothyroidism and hyperthyroidism cases compared to healthy controls.

It is known that abnormal thyroid functions can affect mood and affect the course of mood disorders. In the literature, it is stated that psychiatric symptoms can occur in hypothyroid patients as seen in all chronic diseases (Bauer et al., 2001). Depression, dysmnesia, slowing of thought and concentration disorder are the most common psychiatric symptoms in hypothyroidism, indeed nonspecific symptoms are seen at the beginning (Whybrow et al., 1969). While the depressive mood is the most common psychiatric symptom, anxiety and sleep disorders commonly coexist. The researches reported that 33% of anxiety disorder and 43% depression occurred in hypothyroidism (Jain, 1972). It is known that there is a relationship between thyroid hormones and brain functions affecting receptor systems and biochemical reactions in the brain. Therefore, it is thought that any increase or decrease in thyroid hormone level might be related to the level of psychiatric symptoms. Another study suggested that severe psychiatric symptoms were seen in hypothyroid and subclinical hypothyroid patients compared to healthy controls apart from being affected by thyroid hormone levels (Eren et al., 2006). The most common psychiatric condition in hyperthyroidism (25%) is depression. In approximately 15% of cases, signs of depression can appear before hyperthyroidism symptoms. Anxiety disorders are frequently seen in hyperthyroidism as much as close to depression. Anxiety disorders and depression commonly occur during hyperthyroidism. Numerous hypotheses



have been asserted concerning the mechanism of which thyroid disorders increase the risk of developing psychiatric disorders. Marangell et al. hypotetized that there is a relationship between neurotransmitter activity and thyroid hormones (Marangell et al., 1997). However, in our study, the number of patients who has severe levels according to the BDI was more in hyperthyroidism cases by the studies that have been carried out; whereas there was no significant difference between the groups in Hamilton Anxiety Scale comparisons contrary to common belief.

5. CONCLUSION

In daily polyclinic practice, many physicians routinely require thyroid hormones from patients with sleepiness, insomnia, depressive, anxiety signs and restless legs syndrome symptoms. For this reason, we think that this study of ours is valuable and there is a need for new studies with more number of cases related to the medical conditions.

Disclosures

The authors have no conflicts of interest to disclose.

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