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Incidence of hypothyroidism and its correlation with polysomnography findings in obstructive sleep apnea

K. Murat Ozcan · Adin Selcuk · Ibrahim Ozcan · Talih Ozdas · Fatih Ozdogan · Mustafa Acar · Huseyin Dere

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Abstract The aim of this study is to investigate the thyroid functions and its correlation with polysomnography findings in obstructive sleep apnea patients. This study was conducted on 203 patients evaluated with the complaints of snoring, witnessed apnea and daytime sleepiness and established polysomnography (PSG) indication between May 2008 and August 2011. All patients' nocturnal PSG recordings were carried out. The thyroid function was classified as euthyroid, subclinical hypothyroidism and clinical hypothyroidism after analyzing serum TSH and free T4 values. The correlation between the data obtained from PSG records and thyroid function values was statistically compared. Apnea hypopnea index obtained from PSG was in the range of 5.4–132.9/h, and mean value was 32.7/h. The lowest oxygen saturation level was in the range of 20–92 %, and the mean value was 76.4 %. According to PSG results, 55 patients (27.09 %) had mild obstructive sleep apnea syndrome (OSAS), 48 patients (23.65 %) had moderate OSAS and 100 patients (49.26 %) had severe OSAS. On evaluation of the thyroid function test results, 10.8 % ($n = 22$) of the patients were defined to have subclinical hypothyroidism and 1.97 % ($n = 4$) clinical hypothyroidism. We found a total of 12.77 % subclinical and clinical hypothyroidism in patients with OSAS. Though the incidence of hypothyroidism was pretty high in patients with OSA, there was no statistically significant correlation between thyroid functions and polysomnography findings. We suggest that evaluation of the thyroid functions is important and necessary in patients with OSAS. Polysomnography findings do not correlate statistically with thyroid function tests, addressing the need for thyroid screening for all OSAS patients.

Keywords Hypothyroidism · Obstructive sleep apnea

Introduction

Sleep disordered breathing is known to be associated with systemic disorders [1]. Hypertension, cardiovascular diseases, neurological disorders and endocrine disorders are some of them. lots of laboratory tests are used together with polysomnography (PSG), which is the most significant standard to diagnose sleep breathing disorders. As a result of these tests, medical problems with concomitant sleep breathing disorders are diagnosed, and thus, therapy for these diseases with intensifying symptoms becomes possible [2]. In this study, we investigated the incidence of hypothyroidism by means of evaluating serum thyroid hormone levels in patients with sleep disordered breathing, and correlated them with polysomnography findings.

K. M. Ozcan · H. Dere
ENT Clinic, Ankara Numune Education and Research Hospital, Ankara, Turkey

A. Selcuk (✉) · F. Ozdogan
ENT Clinic, Derince Education and Research Hospital, Ibn-i Sina Street No: 35, Derince, Kocaeli, Turkey
e-mail: sadin27@yahoo.com

I. Ozcan
ENT Clinic, Kayseri Education and Research Hospital, Kayseri, Turkey

T. Ozdas
ENT Clinic, Yenimahalle State Hospital, Ankara, Turkey

M. Acar
ENT Clinic, Yunus Emre State Hospital, Eskisehir, Turkey

Materials and methods

A total of 203 patients consisting of 120 male and 83 female between the ages of 20 and 75 (average 49.95 ± 10.02), who were performed polysomnographic evaluation for snoring, witness apnea and daytime sleepiness, were included in this study.

Consent was obtained from all patients enrolled in the study via consent forms, which explained their inclusion in the study and their participation according to the following conditions.

The medical history of all patients was obtained. All cases were analyzed for the presence of witness apnea and recorded.

The existence of hypertension, asthma, diabetes and other systemic diseases was ascertained and then recorded. Patients with a previous history of thyroid gland pathology and medical treatment were not included in this study.

The height and weight of each patient were recorded, and body mass index (BMI) was calculated as body weight (kg)/height $(m)^2$.

Polysomnography was performed on all patients during spontaneous sleep under technician control in a single room at Ankara Numune Education and Research Hospital Sleep Center. The Alice 5 Diagnostic Sleep System and Alice® Sleepware software program were used (Alice® 5 Sleep System, Model No: AC02109, Philips, Respironics, PA, USA). The diagnostic system has following features: Fully integrated sleep laboratory system over a network cable; expanded channel capability to 55 total channels; high-quality ECG with 6 channels and pulse transit time, and real time impedance display. Sound and imagery recordings were performed throughout the night. Electroencephalogram (EEG) at PSG, electromyogram (EMG-sub mental, right–left tibialis), electrooculogram (right–left EOG), electrocardiograph (ECG), nasal airflow, thorax and abdominal respiratory efforts, pulse oxymetry with blood oxygen saturation and body position parameters were recorded throughout the night.

Data obtained for all patients were scored manually by the same specialist. The distribution of sleep stages obtained by scoring PSG data, total sleep time, REM period, non-REM period, the number and maximum period of respiratory events happening at this period, all night Apnea hypopnea index (AHI), AHI of REM and non-REM, lowest oxygen saturation, sleep time with oxygen saturation below 90 %, arousal index, AHI for right, left, supine and prone lying positions were recorded.

Apnea hypopnea index, which is an index used to assess the severity of obstructive sleep apnea syndrome (OSAS), is based on the total number of complete cessations (apnea) and partial obstructions (hypopnea) of breathing occurring per hour of sleep. These pauses in breathing must last for 10 s and are associated with a decrease in oxygenation of the blood for apnea scoring. Either more than 50 % air flow reduction or a lesser air flow reduction with associated more than 3 % oxygen desaturation or arousal was scored as hypopnea. According to the number of the apnea and hypopnea per hour (AHI), the severity of the disease was classified (mild 5–15/h, moderate 15–30/h, and severe greater than 30/h), [1].

Simple snoring patients were not included into the study since this group is not in the classification of sleep-disordered breathing [1].

Thyroid hormones were tested by Cobas® 6000 Analyzer Series (Cobas® 6000-e 601 module, Roche, Rotkreuz, Switzerland) by electrochemiluminiscence technology. Reference interval for TSH: 0.27–4.2 mIU/L, for T3: 3.1–6.8 pmol/l and for T4: 12–22.0 pmol/l. Thyroid functions were classified as subclinical hypothyroidism (elevated TSH and normal T4), clinical hypothyroidism (elevated TSH and decreased T4) as a result of the examination of serum TSH and free T4 values. Patients for whom thyroid pathology was detected were administered medication by the department of endocrinology and followed up.

The descriptives and correlations between the thyroid functions and polysomnographic data were analyzed. Statistical analysis was performed using SPSS statistical package version 13.0. Spearman rho test was used for statistical analysis. The $p < 0.05$ values were accepted as significant.

Results

The study was performed between May 2008 and August 2013 with 203 patients, 120 (59.1 %) male and 83 (40.9 %) female. Age of the patients included in this study ranged from 20 to 75 with an average of 49.95 ± 10.02. BMI of the cases ranged from 23.8 to 60.6, the average being 30.7 ± 5.6. AHI obtained by PSG ranged from 5.4 to 132.9, the average being 37.22. The lowest oxygen saturation was 20–92 % (average 76.42 %). Table 1 shows the descriptive values of the patients, the ratios of oxygen saturation levels below 90 % and minimum oxygen saturation levels. According to PSG results, 55 patients (27.09 %) were diagnosed as mild OSAS, 48 (23.65 %) as moderate OSAS, and 100 patients (49.26 %) as severe OSAS. Sleep time elapsed with oxygen saturation below 90 % was 0–322.9 min (average 33.11). AHI for right, left, supine and prone lying positions were as follows: 12.45/h, 17.93/h, 43.45/h and 1.52/h. Mean values of arousal index was 20.6. Maximum duration of apnea and hypopnea was 45.4 min. Mean REM AHI was 26.24/h and mean non-REM AHI was 25.30/h.

Table 2 shows the blood test variables for the various severity groups of OSAS. There was no statistically

Table 1 Descriptive values of the patients, the ratios of oxygen saturation levels below 90 % and minimum oxygen saturation levels

	Mild OSAS	Moderate OSAS	Severe OSAS	Mean
Number of patients	55	48	100	
Age	46.98 ± 11.13	48.14 ± 10.25	52.61 ± 8.93	49.95 ± 10.02
Male ratio	0.51	0.59	0.64	0.59
Female ratio	0.49	0.41	0.36	0.40
BMI	28.76 ± 6.26	28.98 ± 4.11	32.33 ± 5.66	30.73 ± 5.65
Ratios of oxygen saturation levels below 90 %	2.69 ± 1.28	6.46 ± 2.08	29.15 ± 3.55	17.19 ± 2.09
Minimum oxygen saturation	84.71 ± 6.97	81.40 ± 8.06	70.30 ± 15.57	76.45 ± 13.82

Table 2 Blood test variables for the various severity groups. For T4 hormone values and TSH levels

	Number of patients	Mean hormone level	Std. Deviation	Minimum hormone level	Maximum hormone level
T4 (pmol/l)					
Mild OSAS	55	1.0355	0.23585	0.71	1.47
Moderate OSAS	48	1.1090	0.18451	0.71	1.47
Severe OSAS	100	1.0950	0.71473	0.24	7.78
Total	203	1.0867	0.52874	0.24	7.78
TSH (mIU/L)					
Mild OSAS	55	2.6361	2.04897	0.29	9.26
Moderate OSAS	48	1.8981	1.02594	0.23	4.98
Severe OSAS	100	4.7123	13.52767	0.14	100.00
Total	203	3.4787	9.75679	0.14	100.00

Table 3 Distribution of patients according to thyroid function status

	Subclinical hypothyroidism	Clinical hypothyroidism	Euthyroid	Total
Mild OSA	9	0	46	55 (27.09 %)
Moderate OSA	2	0	46	48 (23.65 %)
Severe OSA	11	4	85	100 (49.26 %)
Total	22 (10.80 %)	4 (1.97 %)	177 (87.19 %)	203

significant difference between the OSAS groups for T4 and TSH levels ($p > 0.05$).

When numeric data were compared with the Spearman-rho correlation test ($p < 0.05$), there was no statistically significant correlation observed between TSH, free T4 value and age, BMI, AHI, minimum saturation and sleep time elapsed with oxygen saturation below 90 %.

As a result of the thyroid function test results, it was determined that 22 patients (10.8 %) showed subclinical hypothyroidism, and 4 patients (1.97 %) showed clinical hypothyroidism (Table 3).

Discussion

A great number of diseases may be a risk factor for OSAS, and diseases associated with it are encountered very often. These diseases include hypothyroidism, acromegaly, diabetes mellitus, and polycythemia [2].

Hypothyroidism has been associated with obstructive sleep apnea, as some symptoms overlap in both disorders. The overlap between the two disorders may create a problem for the treating physician in differentiating two disorders [3].

Intracellular glycogen storage increases in the muscles in the case of hypothyroidism. Thus, it is observed that perinuclear lipid distribution increases because membrane is framed with glycogen. Mitochondrial irregularity is aroused, and as a result of this, poor muscle tone is observed [4]. Moreover, with impaired sleep structures, apathy, lethargy and lack of attention may be observed. Most of these complaints may be related to sleep disorders dependent on hypothyroidism. Central, mixed or obstructive type apneas and hypopneas may develop in case of hypothyroidism [4, 5].

It is thought that myxedema tissues developed depending on hypothyroidism cause snoring by breaking the normal pharyngeal closure pattern [5]. Orr et al. reported in a study performed in 1981 that recurrent sleep apnea episodes were observed in three patients diagnosed clinically and biochemically as myxedema via polygraphical studies. They stated that sleep apnea episodes with a case of euthyroid developed after L-thyroxin therapy performed on patients were healed substantially [6].

In a study performed by Skjodt et al. [7], obstructive sleep apnea was determined via PSG for 124 of 200 patients having complaints about witness apnea or diagnosed abnormalities at oximetry. In addition hypothyroidism was also observed for 2.4 % (3 patients) of these patients. Thyroxin and CPAP therapy was started for the three patients. It was concluded that thyroid functions should be examined as a biochemical parameter, especially for patients with sleep breathing disorder.

On the other hand, there are studies available indicating that the hypothyroidism prevalence of patients with sleep breathing disorder is not different from the normal population, that thyroid replacement therapy is a little effective or not effective on sleep apnea, that thyroid replacement therapy for patients with clinical hypothyroidism provides a little healing or no healing, and that it is not important to use thyroid function tests for the routine determination of sleep breathing disorder [8–10].

Skjodt et al. [7] determined that free T3 values were correlated as statistically significant with the lowest oxygen saturation values and sleep periods elapsed (below 90 %) ($p < 0.05$, $p < 0.05$). The percentage of total sleep period elapsed (90 %) increased with a decreasing free T3 value.

Misiolek et al. [11] reported in a study performed in 2007 that PSG is performed before and after thyroxin therapy for 15 hypothyroidism patients. It was observed that there is a statistically significant correlation between the snoring level with thyroxin premedication serum T4 and TSH values (the snoring level increases with decreasing free T4 level and increasing TSH level), but the post medication period correlation is the same as before and there is a statistically significant difference between premedication and post medication AHI, desaturation index and lowest oxygen saturation percentage [11].

It was deduced from several studies that thyroxin replacement therapy is effective in the healing of sleep apnea and symptoms [12].

In the study of Resta et al. [13], 118 patients with pure snoring and OSAS were divided into three groups, the first group consisting of 63 patients with normal TSH and thyroid functions, the second group consisting of 30 patients with subclinical hypothyroidism with normal T4 and TSH level due to levothyroxine therapy, and the third group consisting of 15 patients with subclinical hypothyroidism with high TSH level without levothyroxine therapy. It was observed that there is no statistically significant difference between these groups in terms of age, sex, BMI and neck circumference measurement values. When PSG values of all patients were compared, it was observed that there is no statistically significant difference in terms of OUA prevalence, oxygen saturation and percentage of sleep period elapsed below 90 % saturation [13].

Subclinical hypothyroidism has a prevalence of approximately 5–10 in the general population; it is more common in females and in the elderly. The prevalence of primary hypothyroidism in the general population is 0.1–2 % [14]. In the United States, it is present in 4.6 % of population (clinical, 0.3 %, subclinical 4.3 %), [15].

In our study, we found that 10.8 % of the patients had a subclinical hypothyroidism and 1.97 % of the patients had clinical hypothyroidism among OSA patients. This incidence is higher compared to most of the previous reports and the prevalence of the disease in normal population. Polysomnography findings do not correlate statistically with thyroid function tests, addressing the need for thyroid screening for all degree of OSAS patients.

Conclusion

Hypothyroidism appears as one of the factors playing a role in sleep disordered breathing pathogenesis. It is concluded in this study that thyroid functions for patients with sleep disordered breathing should be assessed as a biochemical parameter, regardless of the disease severity. To distinguish hypothyroidism-related snoring and apnea from other sleep breathing disorders and to avoid having to perform further tests and therapy, thyroid function screening should be performed at the beginning of the algorithm.

Conflict of interest None.

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