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ORIGINAL ARTICLE

Association Between the Severity of Obstructive Sleep Apnea Syndrome and Free Thyroid Hormone Levels

Obstrüktif Uyku Apne Sendromu Şiddeti ile Serbest Tiroid Hormonları Arasındaki İlişki

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Abstract

Introduction: To analyze the relationship between obstructive sleep apnea syndrome (OSAS) severity and hypothyroidism. The association between apnea–hypopnea index and thyroid hormone levels has also been evaluated.

Methods: This study was conducted retrospectively on 255 patients who underwent a polysomnography test and were diagnosed with OSAS between January 2018 and March 2019. Patients who had chronic diseases and who were using drugs that affected thyroid hormone levels and sleep patterns were not included in the study. Patients' age and gender; thyroid-stimulating hormone (TSH), T4, and T3 levels; and T3/T4 ratios were compared with OSAS severity.

Results: There was a significant association between advancing patient age and OSAS severity ($p<0.001$). There was a negative association between OSAS severity and free T4 ($p=0.007$), free T3 levels ($p=0.001$), and T3/T4 ratio ($p=0.011$). Of the 255 patients enrolled in this study, 47 (18.4%) had mild OSAS, 71 (27.8%) had moderate OSAS, and 137 (53.8%) had severe OSAS. OSAS was more common in males. The prevalence of hypothyroidism was two times more common in females. Hypothyroidism frequency was 6% in the study group. Nevertheless, there was no significant association between OSAS severity and gender and TSH levels.

Discussion and Conclusion: Lower free T3 and free T4 levels will escalate OSAS severity. It is recommended to evaluate thyroid hormone status especially in elder patients with OSAS.

Keywords: Obstructive sleep apnea syndrome, thyroid hormones, thyroxine, triiodothyronine

Obstructive sleep apnea syndrome (OSAS) is characterized by partial or total obstruction of the upper respiratory tract and recurrence of these obstructions during sleep. Snoring, daytime sleepiness, fatigue, low adaptation to surrounding events, gaining weight, apathy, and lethargy are symptoms related to OSAS.[1] The prevalence of OSAS in the general population was reported to be 3%–7% in males and 2%–5% in females.[2] In patients with OSAS, hypothyroidism was more frequent.[3]

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Thyroid hormones have an important role in the regulation of growth, heart rate, motility of the gastrointestinal system, body temperature and energy usage, and the maintenance of body weight. In the case of hypothyroidism, one is expected to have fatigue, constipation, weight gain, difficulties in concentration and learning, and cold feeling. The prevalence of hypothyroidism in the general population is 0.3%–9.2%.[4] Clinical findings in OSAS resemble hypothyroidism. Hypothyroidism contributes to the accumulation of mucopolysaccharides and proteins in the pharynx and results in restriction of the airway. In hypothyroidism, reduced control in pharyngeal dilator muscles due to neuropathy is also expected. These factors aggravate the risk for OSAS development.[5] The prevalence of OSAS prominently increases in people with advancing age of up to 50 years, but this increase rate, decreases after 50 years.[6]

To eliminate the negative effects of advancing age on the risk of developing OSAS, a study with participants over 50 years was conducted. This study aims to examine the relationship between OSAS and hypothyroidism. Additionally, the relationship between apnea–hypopnea index (AHI) and thyroid hormones was also examined.

Materials and Methods

Study Design, Place, Duration, and Setting

This single-center study was conducted in a tertiary hospital located in Ankara, between January 2018 and March 2019, retrospectively, after acquiring approval from the local ethics committee (App. No: 2019/49). This study was conducted in compliance with the Helsinki declaration and good clinical practices guidelines; written informed consent was obtained from each participant.

Inclusion Criteria

Of the 561 patients who underwent a polysomnography test, 255 who were diagnosed with OSAS and whose complete records could be obtained were enrolled in the study.

Exclusion Criteria

Patients who had malignancy, neuromuscular diseases, and cerebrovascular diseases were excluded since those diseases could affect sleep order. Patients who were having medications that affect the respiratory system and thyroid hormone levels such as amiodarone, lithium, and drugs affecting dopamine levels were also excluded.

Polysomnography Test

All participants underwent a polysomnography test lasting for one night with Embla N7000 (Natus Neurology, Embla Systems, Ontario, Canada) under video monitorization and supervision of a technician in a room with a single bed and in which optimal sound and light levels and temperature were maintained. During the test course, respiratory patterns of patients, data obtained from electromyography of legs, electrocardiographs, nasal air flows, thorax and abdominal respiratory movements, and oxygen saturation data gathered via a pulse oximeter from fingers were recorded. Polysomnography records were evaluated according to the criteria declared by the Academy of American Sleep Medicine in 2012.

Definitions

Apnea was defined as a 90% reduction in amplitude of airflow from the nose or mouth, lasting for at least 10 s. Hypopnea was defined as a 30% reduction in amplitude of airflow and a drop in oxygen saturation of more than 3%, lasting for at least 10 s. AHI was calculated using the observance of total apnea and hypopnea incidences in 1 h period.

Participants

Apnea and hypopnea periods during sleep time were detected, and AHI was calculated. Patients who had AHI lower than 5 were accepted as normal and did not have OSAS. Participants were grouped into three according to AHI scores: mild (AHI between 5 and 15), moderate (AHI between 15 and 30), and severe OSAS (AHI over 30) groups.

After the polysomnography test, fasting blood samples for thyroid-stimulating hormone (TSH), free thyroxine (T4), and free triiodothyronine (T3) levels were obtained from every patient in the morning. TSH, free T4, and free T3 hormone levels were examined using Roche Hitachi Cobas 601 (Switzerland) instrument. The normal range for TSH was 0.4–4.3 mIU/L; for free T4, 10.30–21.88 pmol/L; and for free T3, 3.53–6.45 pmol/L.

Age, gender, and TSH, free T4, and free T3 levels of all participants were recorded, and T3 to T4 ratio (T3/T4) were calculated for each.

Statistical Analysis

Data were examined with statistical analysis software SPSS version 25 (SPSS Inc., Armonk, NY, USA). All variables were analyzed using the Kolmogorov–Smirnov test, and data distribution was found to be normal. Data were reported as

Table 1. Age, gender, mean thyroxine, triiodothyronine, and thyroid-stimulating hormone values according to OSAS severity

	Mild OSAS (n=47)	Moderate OSAS (n=71)	Severe OSAS (n=137)	p
Age (years)	46.09±11.31	50.49±610.41	55.08±11.81	<**0.001**†
Gender (male/female)	29/18	46/25	92/45	0.788‡
Free T3§ (pmol/L)	5.11±0.90	4.76±1.72	4.20±0.98	**0.001***
Free T4‖ (pmol/L)	16.09±3.34	17.63±5.79	15.31±2.83	**0.007**††
TSH¶ (mIU/L)	1.54±0.93	2.10±1.91	2.23±1.90	0.070†
T3/T4 ratio	2.74±0.57	2.33±0.57	2.37±0.67	**0.011**†

OSAS: Obstructive sleep apnea syndrome; †: ANOVA test; ‡: Chi-square test; §: Triiodothyronine; ‖: Thyroxine; ¶: Thyroid-stimulating hormone; *: ANOVA test, post hoc: Group 1–2: p=0.218, group 1–3: p<0.001, and group 2–3: p=0.017; ††: ANOVA test, post hoc: Group 1–2: p=0.082, group 1–3: p=0.364, and group 2–3: p=0.002.

mean±standard deviation. Data of groups were compared via one-way ANOVA test and chi-square tests, where applicable. A p-value of <0.05 was accepted to be significant.

Results

There was a significant association between advancing patient age and OSAS severity (p<0.001) and a negative association between OSAS severity and free T4 level (p=0.007), free T3 level (p=0.001), and T3/T4 ratio (p=0.011). OSAS severity was found to increase with advancing age and low free T4 and free T3 levels.

Of the 255 patients were enrolled in the study; 167 were males (65.5%) and 88 were females (34.5%). The mean patient age was 52.15±11.83 (50.35±11.55 in males, 55.55±11.66 in females, p=0.001). Forty-seven (18.4%) patients had mild OSAS, 71 (27.8%) had moderate OSAS, and 137 (53.8%) had severe OSAS. OSAS was more common in males. The prevalence of hypothyroidism was two times more common in females. Hypothyroidism frequency was 6% in the study group; five (33%) were males, and 10 (67%) were females. Table 1 shows age, gender, mean thyroxine, triiodothyronine, and TSH values according to OSAS severity.

There was no significant association between OSAS severity and gender and TSH levels.

Discussion

The prevalence of OSAS increases with advancing age between 18 and 45 years but remains stable between ages 55 and 65 years.[6] The prevalence of OSAS in males is two times more than in females.[7] This study also reveals similar results in the male-to-female ratio and increased OSAS severity with advancing age. Huang et al.[8] reported a study with 2006 males and 339 females concluding that OSAS was more severe in males than in females. This presented study did not reveal any association between gender and OSAS severity.

The prevalence of hypothyroidism change according to gender. In a study with the general population, it was reported that hypothyroidism was more frequent in females than in males (5.9%–2.3%).[9] This study has compliant results, females more frequently had hypothyroidism; the female-to-male ratio was 2.

There were inconsistent results in the studies inspecting the prevalence of hypothyroidism in OSAS. Ayık et al.[10] reported hypothyroidism prevalence as high as 10.6% in their study. Contrary to this, a study with 336 patients who had a polysomnography test reported no difference between groups for the prevalence of hypothyroidism.[11] A study from the United States inspecting 118 female participants reported that there was no difference in hypothyroidism prevalence.[12] This presented study reports a 6% prevalence of hypothyroidism in OSAS patients. This presented result is similar to the prevalence of hypothyroidism in the general population.[4] These inconsistent results were explained by racial, environmental, economic factors, and differences in methods used in diagnosis.[13]

When considering the association between thyroid hormones and OSAS severity, a study from Turkey with 150 patients with OSAS and a control group of 32 patients reported no significant association.[14] Takeuchi et al.[15] reported that there was a significant negative association between free T3 levels and OSAS severity. This presented study reports a negative association between free T3 and OSAS severity, concordantly; which was explained by the effect of inflammation in OSAS development.[16] Systemic inflammatory markers such as C-reactive protein, interleukin-6, and tumor necrosis factor-alpha are reported to be increased in OSAS.[17] As OSAS severity increases and hypoxia becomes more prominent, the severity of inflammation becomes more evident.[18] The result shows that the peripheral conversion of T4 to T3 becomes disrupted[19] and T3 levels decrease. In the present study, both free T3 and T3/T4 ratios were found to be associated with OSAS severity.

A study from Denmark reported a 3- to 4-fold increase in the prevalence of hypothyroidism in young patients when compared with elder patients.[20] This presented study, which was conducted with participants aged over 50 years, reveals a negative association between free T3 and free T4 and OSAS severity. However, there was no association between TSH and OSAS severity. This condition may be explained by the effectiveness of free T4 in evaluating thyroid functions in elder patients when compared with TSH.[20]

Limitations

The retrospective design of the study, exclusion of patients who did not have OSAS after polysomnography because they were very few in numbers is limitations of this study. Although polysomnography tests include other parameters such as mean oxygen stauration leves, minimum oxygen saturation during sleep, existence of Cheyne Stokes respiration pattern besides AHI, only AHI data were recorded in hospital data base. Thus, other variables could not be used to evaluate OSAS severity.

Conclusion

The results of this study show that lower free T3 and free T4 levels will escalate OSAS severity; patients having these levels must be monitored, and euthyroidism must be achieved with appropriate medication. It is recommended to regularly evaluate thyroid hormone status eespecially in elder patients with OSAS. Examination of TSH only may not be sufficient to evaluate thyroid hormone status in these patients. Also, examinations of free T3 and free T4 must be considered.

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