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Is there a Relation between Sleep Apnea, Tinnitus, and Hearing Loss?

Uyku Apnesi, Tinnitus ve İşitme Kaybı Arasında Bir İlişki Var Mı?

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Abstract

Aim: Chronic hypoxia may lead to auditory dysfunction in patients with obstructive sleep apnea (OSA), and this dysfunction may worsen OSA, creating a vicious circle. The aim of this study was to investigate tinnitus and hearing loss in OSA patients.

Material and Method: A total of 147 patients were included in this prospective study. After polysomnography (PSG), the patients with an apnea-hypopnea index (AHI) ≥ 5 were included in OSA group, and the ones with an AHI<5 were included in the simple snoring group. The OSA patients were divided into three OSA severity subgroups as mild, moderate and severe OSA subgroups. Standard pure-tone audiometry (PTA) (0.5, 1, 2, 3 kHz) and high-frequency audiometry (8, 10, 12 kHz) were performed, and Tinnitus Handicap Inventory (THI) was applied to all participants. Audiological results and THI scores were compared among the study groups.

Results: The OSA group consisted of 46 (36.5%) female, 80 (63.5%) male, and a total of 126 patients. The simple snoring group included 13 (61.9%) female, 8 (38.1%) male, and a total of 21 patients. The mean body mass index, hearing thresholds in all tested frequencies and THI scores were significantly higher in OSA group (p=0.024, p=0.001, p=0.015, p=0.017, p=0.039, p=0.002 and p=0.001, respectively). THI score showed a statistically significant and positive correlation with the AHI (p=0.004; r=0.252). The mean THI score was significantly lower in mild OSAS subgroup compared to moderate and severe OSA subgroups (p=0.019).

Conclusion: OSA, hearing impairment and tinnitus are either comorbidities or related etiologically. Higher prevalence of hearing impairment in OSA patients compared to simple snorers suggests that intermittent nocturnal hypoxia, rather than sound of snoring plays a role in hearing impairment.

Keywords: Hearing loss, obstructive sleep apnea, polysomnography, tinnitus

Öz

Amaç: Kronik hipoksi, tıkayıcı uyku apnesi (TUA) olan hastalarda işitme sisteminde işlev bozukluğuna yol açabileceği gibi, işitsel işlev bozukluğu da TUA'yı kötüleştirerek bir kısır döngü oluşturabilir. Bu çalışmanın amacı TUA'da tinnitus ve işitme kaybını araştırmaktı.

Gereç ve Yöntem: Bu prospektif çalışmaya toplam 147 hasta dahil edildi. Polisomnografi (PSG) sonrası apne-hipopne indeksi (AHİ) ≥5 olan hastalar TUA grubuna, AHI<5 olanlar ise basit horlama grubuna dahil edildi. TUA hastaları hafif, orta ve şiddetli TUA alt grubu olarak üç alt gruba ayrıldı. Tüm katılımcılara standart saf ses odyometri (SSO) (0,5, 1, 2, 3 kHz), yüksek frekans odyometri (8, 10, 12 kHz) ve Tinnitus Handikap Envanteri (THE) anketi uygulandı. Çalışma grupları arasında odyolojik sonuçlar ve THE skorları karşılaştırıldı.

Bulgular: TUA grubu 46 (%36,5) kadın, 80 (%63,5) erkek olmak üzere toplam 126 hastadan oluşmaktaydı. Basit horlama grubuna 13 (%61,9) kadın, 8 (%38,1) erkek olmak üzere toplam 21 hasta dahil edildi. Ortalama vücut kitle indeksi, test edilen tüm frekanslarda işitme eşikleri ve THE skorları TUA grubunda anlamlı olarak yüksekti (sırasıyla, p=0,024, p=0,001, p=0,015, p=0,017, p=0,039, p=0,002 ve p=0,001). THE skoru, AHİ ile istatistiksel olarak anlamlı ve pozitif korelasyon gösterdi (p=0,004; r=0,252). Ortalama THE skoru hafif TUA alt grubunda orta ve şiddetli TUA alt gruplarına göre anlamlı olarak düşüktü (p=0,019).

Sonuçlar: TUA, işitme kaybı ve kulak çınlaması ya komorbiditelerdir ya da etiyolojik olarak ilişkilidir. Basit horlayanlara kıyasla TUA hastalarında işitme bozukluğu prevalansının daha yüksek olması, horlama sesinden ziyade aralıklı gece hipoksisinin işitme bozukluğunda daha fazla rol oynadığını düşündürmektedir.

Anahtar Kelimeler: İşitme kaybı, obstrüktif uyku apnesi, polisomnografi, tinnitus

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INTRODUCTION

Obstructive sleep apnea (OSA) is an important health problem affecting 15-30% of men and 10-15% of women in North America. Hypoxia due to repetitive upper airway obstructions during sleep cause systemic inflammation and vascular endothelial damage through several proinflammatory cytokines and mediators, leading to various comorbidities.[1-4]

Tinnitus impairs quality of life and has been defined as perception of sound in absence of an external acoustic stimulus.[5] Tinnitus and OSA may interact in a negative way. Most of the patients with tinnitus have insomnia, however tinnitus is more frequent in OSA patients.[6] OSA may also be associated with a higher risk of hearing impairment.[7] Several studies that investigated the relation of OSA with auditory dysfunction reported that the patients with sleep apnea had a higher risk of developing both tinnitus and hearing loss.[7-9] Tinnitus Handicap Inventory (THI) is the most widely used measure to determine perceived tinnitus handicap severity.[10]

The aim of this study was to investigate the tinnitus and hearing impairment in OSA patients through THI, standard pure tone audiometry (PTA) and high frequency audiometry.

MATERIAL AND METHOD

A total of 291 consecutive patients who admitted to the sleep laboratory of a tertiary referral center with complaints of snoring and/or daytime sleepiness and witnessed sleep apnea between the July 2017 August 2018 were included in this prospective study. The patients with any mental or neurological disorders (18 patients), diabetes mellitus (15 patients), hypertension (18 patients), middle/inner ear disorders/significant air-bone gap in standard PTA or results other than a Type A tympanogram (8 patients), age ≥65 years (10 patients), history of otological surgery (1 patient), hyperlipidemia (9 patients) and the ones who did not accept to participate in the study and/or left without completing the study (65 patients) were excluded. A total of 147 patients were included in the study.

All patients had full-night standard polysomnography (PSG) during spontaneous sleep under the supervision of a sleep technician. PSG was recorded with Alice 5 PSG device (Philips Respironics, The Netherlands). Recorded data were electrooculogram (EOG), electroencephalogram (EEG), nasal airflow, thoracic and abdominal respiratory efforts, blood oxygen saturation, body position and submental and bilateral tibialis anterior electromyograms (EMG). A PSG and sleep disorders-certified ENT physician scored the PSG data manually according to the standard criteria of American Academy of Sleep Medicine. Complete interruption of airflow for at least 10 sec was regarded as apnea. At least 30% decrease in airflow amplitude accompanied by 3% oxygen desaturation and a reduction in chest/abdominal respiratory effort amplitude and/or related arousal was considered as hypopnea. The number of apneas and hypopneas per hour of sleep was used to calculate the apnea-hypopnea index (AHI).[11]

In relation with their AHI, the patients were divided into following groups: The patients with an AHI ≥ 5 were included in OSA group, and the ones with an AHI < 5 were included in the simple snoring group. Moreover, the patients with OSA were divided into three subgroups in relation with the severity of OSA as "Mild OSA" (5 ≤ AHI < 15), "moderate OSA" (15 ≤ AHI < 30) and "severe OSA" (AHI ≥ 30) subgroups.

The standard PTA (0.5, 1, 2, and 4 kHz) and high-frequency audiometry (8, 10 and 12 kHz) were performed using Interacoustic AC-40 (Assens, Denmark) clinical audiometer. The air and bone conduction thresholds were measured at four frequencies (0.5, 1, 2, and 3 kHz).The hearing threshold at 3 kHz was calculated by obtaining the mean of the hearing thresholds at 2 and 4 kHz.

Subjective tinnitus severity was assessed using a validated Turkish version of a standardized outcome measure, the THI.[12] THI consists of 25 items answered as yes (4 points), sometimes (2 points), or no (0 point). The total score may range between 0 and 100.[13] The THI and audiometric tests were completed within two days after PSG. The THI scores and audiology test results were evaluated and compared among the study groups.

All participants provided their informed consents, and the study protocol was approved by the local ethics committee (Date: 05.10.2017, Decree no: E17-1411).

IBM-SPSS for Windows v.21.0 software (IBM Corporation, Armonk, NY, USA) was used for statistical analysis of the data. The normality of the distribution of data was analyzed with Kolmogorov-Smirnov test. The descriptive data were presented as mean±standard deviation, median, minimum and maximum. Categorical variables were expressed in numbers and percentages. One-way ANOVA test was used to compare three or more groups with normal distributions, while Student t test was employed for the two-group comparisons of data with normal distributions. The comparison of quantitative data among three or more groups without normal distributions was done with Kruskal Wallis test, and Mann Whitney U test was used to detect the group that caused the difference. Spearman's Correlation Analysis was used for analysis of the correlations among the study parameters. The significance level was set at $p<0.05$.

RESULTS

A total of 147 patients were included in the study. The OSA group consisted of 46 (36.5%) female, 80 (63.5%) male and a total of 126 patients. The simple snoring group consisted of 13 (61.9%) female, 8 (38.1%) male and a total of 21 patients. The mean ages of OSA and control groups were 47.26±6.93 and 43.47±6.40 years, respectively. There was a statistically significant difference between the groups in terms of age ($p=0.019$). On PSG, it was evident that both simple snoring and OSA patients snored during the study in the sleep

laboratory.

Comparisons of THI scores, audiometry and polysomnography (PSG) findings between the OSA and simple snoring groups

Table 1 shows THI scores and audiometry and polysomnography (PSG) results of the OSA and the simple snoring groups. The mean body mass index (BMI), AHI, mean hearing thresholds at standard PTA (0.5, 1, 2 and 3 kHz), 8, 10 and 12 kHz as well as THI scores were significantly higher in OSA group compared to the simple snoring group (p=0.024, p=0.001, p=0.015, p=0.017, p=0.039, p=0.002 and p=0.001, respectively) (**Table 1**).

Table 1. The demographic characteristics and the audiometric, THI, polysomnography (PSG) findings among the groups.

Variables	AHI < 5 (n=21) Mean±SD	AHI ≥ 5 (n=126) Mean±SD	p
Age (years)	43.47±6.40	47.26±6.93	[a]p=0.019
Female Male	13 (61.9%) 8 (38.1%)	46 (36.5%) 80 (63.5%)	[b]p=0.028
BMI (kg/m²)	28.42±1.99	30.38±3.68	[a]p=0.024
AHI (ev/hr)	2.98±1.13	22.58±14.87	[a]p=0.001
PTA	10.57±2.78	12.83±4.30	[a]p=0.015
8 kHz	24.76±8.13	30.55±10.22	[a]p=0.017
10 kHz	27.85±7.51	33.37±10.95	[a]p=0.039
12 kHz	31.66±8.26	40.75±12.44	[a]p=0.002
THI	32.38±9.02	40.07±7.68	[c]p=0.001

aMann Whitney U Test bPearson's chi-squared Test cStudent T Test
AHI: Apnea-hypopnea index, PTA: Pure-tone audiometry, THI: Tinnitus Handicap Inventory, BMI: Body mass index, kHz: Kilohertz.

Comparisons of THI scores, audiometry and polysomnography (PSG) findings among the subgroups determined by OSA severity

Table 2 shows THI scores, audiometry and polysomnography (PSG) findings of the subgroups determined by the severity of OSA. In relation with the AHI scores of the OSA group, 47 patients had mild OSA, 46 patients had moderate OSA, and 33 patients had severe OSA (**Table 2**).

The mean standard PTA, 8 kHz and 12 kHz thresholds did not significantly differ among the OSA subgroups (p=0.179, p=0.600 and p=0.155, respectively). The mean 10 kHz value differed significantly among the subgroups (p=0.024). The paired comparisons performed to determine the subgroup that caused the difference indicated a significantly higher mean 10 kHz hearing threshold in the patients with severe OSA (p=0.007). The paired comparisons of other subgroups did not yield any significant differences (**Table 2**).

The mean THI scores differed significantly among the subgroups (p=0.019). Mild OSA subgroup had significantly lower THI scores compared to moderate and severe OSA subgroups (p=0.014 and p=0.027, respectively) (**Figure 1, Table 2**).

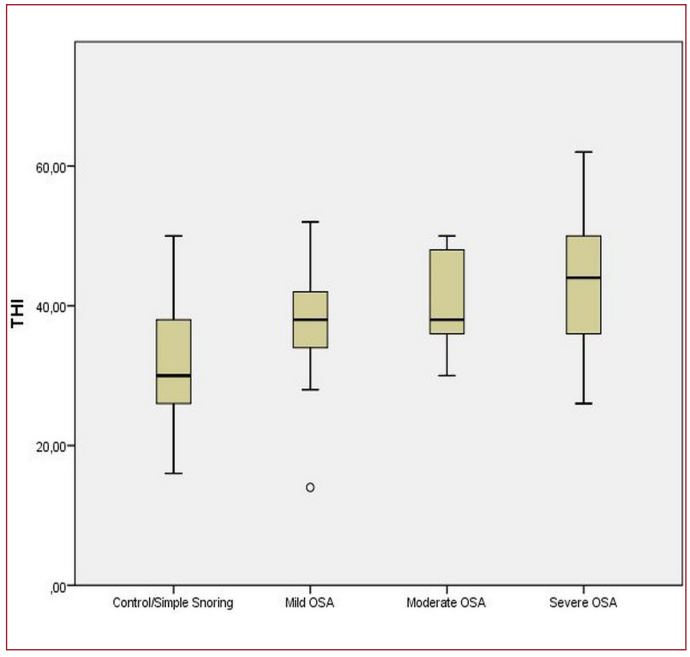

Figure 1. The mean tinnitus handicap inventory scores in control and OSA subgroups

Table 2. Comparisons of the audiometric and THI scores according to degree of OSA.

Variables	15 ≤ AHI < 15 (n=47) Mean±SD	215 ≤ AHI < 30 (n=46) Mean±SD	3AHI ≥ 30 (n=33) Mean±SD	p	Binary Comparisons dp
Age (years)	43.29±5.95	48.36±6.01	51.36±6.64	[c]p=0.001*	
Female Male	14 (29.8%) 33 (70.2%)	18 (39.2%) 28 (60.8%)	14 (42.5%) 19 (57.5%)	[b]p=0.017*	
BMI (kg/m²)	28.43±2.15	31.03±3.75	32.25±4.09	[a]p=0.001*	
AHI (ev/hr)	10.48±2.31	19.94±2.83	43.49±13.10	[a]p=0.001*	
PTA (dB)	12.19±3.76	12.30±3.30	14.48±5.72	[a]p=0.179	
8 kHz (dB)	31.06±11.88	28.91±7.21	32.12±11.18	[a]p=0.600	
10 kHz (dB)	32.55±10.26	31.30±11.51	37.42±10.31	[a]p=0.024*	[1-2]p=0.368 [1-3]p=0.062 [2-3]p=0.007*
12 kHz (dB)	38.82±12.47	40.65±13.60	43.63±10.32	[a]p=0.155	
THI	37.70±6.35	40.91±6.06	42.30±10.32	[c]p=0.019*	[1-2d]p=0.014* [1-3d]p=0.027* [2-3d]p=0.492

aKruskal Wallis Test, bPearson's chi-squared Test, c One Way ANOVA Test, dStudent T Test, *p<0,05
AHI: Apnea-hypopnea index, PTA: Pure-tone audiometry, THI: Tinnitus Handicap Inventory, BMI: Body mass index, kHz: Kilohertz

The age was significantly and positively correlated with all mean standard PTA hearing thresholds, 8 kHz, 10 kHz, 12 kHz hearing thresholds and THI scores (p=0.001; r=0.291, p=0.011; r=0.226, p=0.001; r=0.482, p=0.001; r=0.488 and p=0.001; r=0.395, respectively). In addition, the mean THI score showed a statistically significant and positive correlation with the AHI and BMI (p=0.004; r=0.252 and p=0.001; r=0.290, respectively) (**Table 3**).

Table 3. The correlation coefficients and p values among demographic characteristics and the audiometric, THI, polysomnography (PSG) findings in patients with OSA.

N=126	AHI (ev/hr)	BMI (kg/m²)	Age
THI Correlation Coefficient	0.252	0.290	0.395
P value	0.004*	0.001*	0.001*
PTA Correlation Coefficient	0.162	0.152	0.291
P value	0.069	0.090	0.001*
8 kHz Correlation Coefficient	0.051	0.030	0.226
P value	0.567	0.738	0.011*
10 kHz Correlation Coefficient	0.105	0.161	0.482
P value	0.242	0.071	0.001*
12 kHz Correlation Coefficient	0.106	0.172	0.488
P value	0.238	0.054	0.001*

Spearman's Correlation test, p < 0.05 AHI: Apnea-hypopnea index, BMI: Body mass index, PTA: Pure-tone audiometry, THI: Tinnitus Handicap Inventory, kHz: Kilohertz.

The audiometry findings (standard PTA, 8 kHz, 10 kHz and 12 kHz hearing thresholds) did not show any statistically significant correlations either with AHI or BMI (p>0.05) (**Table 3**).

DISCUSSION

In our study, we found that both THI scores and hearing thresholds were higher in OSA patients compared to simple snorers. Tinnitus scores were positively correlated with AHI.

OSA is a syndrome that affects almost every cell of human body, and it may cause various comorbidities such as cardiovascular and neurological disorders.[14] Hypoxia caused by recurrent upper airway obstruction results in systemic inflammation and activation of sympathetic nervous system, and vascular endothelial damage follows oxidative stress and systemic inflammation.[15,16]

The exact pathophysiology of hearing loss in OSA is not yet clearly put forward, however several possible mechanisms have been proposed. Small cerebral blood vessels maintain blood to the arterioles of cochlea.[17] The arterioles of cochlea are terminal blood vessels, and cochlea does not have any collateral blood supply. Cerebral blood flow velocity decreases and blood viscosity increases in patients with OSA leading to hypercoagulability.[18] Moreover, cochlear and brainstem microcirculations may be impaired due to autonomic nervous system dysfunction, hypoxia and inflammation, resulting in hearing impairment.[8] Hearing loss may also lead to tinnitus.[19]

Vorlova et al. investigated the effect OSA on hearing, and reported that OSA resulted in hearing impairment possibly due to hypoxia, heart rate variations, decreased brain perfusion and changes in intracranial pressure. The authors also reported that high-frequency auditory thresholds were higher in patients with severe OSA, and this was correlated with the severity of OSA.[20]

Most of OSA patients complain of snoring. Persistent and/or loud snoring sound may damage cochlea through acoustic trauma. Hearing impairment in OSA is a multifactorial mechanism that may also involve cochlear ischemia and hypoxia that causes degeneration of hair cells and cochlear spiral organ. Lu et al. investigated the relationship between OSA and auditory dysfunction, and studied the role of snoring sound contributing to the auditory dysfunction, and reported that rather than hearing loss, OSA could result in tinnitus. They also reported that high-frequency snoring sounds transmitted to the ear canal might have contributed development of tinnitus.[21] A recent meta-analysis reported that 4 and 8 kHz hearing thresholds of the OSA patients were significantly higher than those of the control group, and snoring might have caused hearing impairment in those patients.[8] Similarly, Chopra et al. reported that presence of OSA was significantly correlated with hearing impairment, and both presence of OSA and increased OSA severity were correlated with increased likelihood of hearing impairment in both high and low frequencies.[7] Seo et al. indicated that lowest oxygen saturation was the only variable correlated with hearing thresholds, and severe OSA might be a trigger for hearing loss.[22] In another study, it was reported chronic nocturnal intermittent hypoxia, particularly due to severe OSA, played the major role in development of high-frequency hearing impairment and early cochlear damage. The authors revealed that there was no difference in the standard PTA thresholds between OSA and control groups, however the patients with severe OSA had higher thresholds at high (6 –16k kHz) frequencies.[23]

In our study, we found higher hearing thresholds on standard PTA and high frequencies including 8, 10 and 12 kHz in OSA group compared to the simple snoring group. Our results imply that intermittent nocturnal hypoxia related to sleep apnea causes hearing loss rather than snoring sounds. However, the patients in our OSA group were older compared the simple snoring group, and it may be supposed that older age of might have contributed to this result. OSA subgroup comparisons showed that there was no statistically significant difference among the OSA severity subgroups for standard PTA or 8 and 12 kHz hearing thresholds, however severe OSA subgroup had significantly higher hearing thresholds at 10 kHz. Although not statistically significant, hearing thresholds increased as the AHI scores increased. Accordingly, this result may suggest that the level of hearing impairment increases as the AHI score increases.

Hearing loss (particularly at high frequencies) and tinnitus are closely interrelated. Both conditions may be associated

with various factors and disorders including exposure to noise, otologic infections, obesity, hypertension, Meniere's disease, medications and aging.[24] Several studies reported prevalence of tinnitus in a wide range (5.1% to 42.7%) in relation with different demographic criteria.[25,26] OSA has been reported as a risk factor for tinnitus.[21,23] Lu et al. reported the prevalence of tinnitus in OSA patients as 66%, which was higher compared to the general middle-aged population.[21] Similarly, in a large population-based study it was reported that the risk of tinnitus increased 1.36 times in middle-aged patients with OSA.[27] Another study reported a higher prevalence of tinnitus in OSA patients compared to the individuals without OSA.[23] In our study, we found higher THI scores in patients with OSA compared to simple snoring group indicating that OSA patients suffer from tinnitus more frequently compared to the simple snorers. We also found that moderate and severe OSA patients had higher THI scores compared to mild OSA patients. THI sores showed a significant and positive correlation with AHI. We may say that tinnitus is an early sign of auditory impairment in patients with OSA.

Our study has several limitations. First, it is a single-center study. The mean age and BMI were higher in the OSA group and those might have affected hearing thresholds and THI scores. The changes in study parameters after positive airway pressure treatment were not investigated. The duration of OSA and/or snoring was not included as a study parameter into our study. This may be an important factor for hearing loss and tinnitus. Inclusion of the duration of OSA into the study would enable us to obtain more valuable results.

CONCLUSION

The prevalence of both tinnitus and hearing loss is higher in OSA and particularly in severe OSA compared to simple snorers. OSA, hearing impairment and tinnitus are either comorbidities or related etiologically. Higher prevalence of hearing impairment in OSA patients compared to simple snorers suggests that intermittent nocturnal hypoxia, rather than sound of snoring plays role in hearing impairment. THI scores are significantly and positively correlated with AHI, and tinnitus may be an early sign of auditory impairment of patients with OSA. Further multi-center studies including a larger and more homogeneous study population are required to further clarify the correlation of OSA with hearing impairment and tinnitus.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by the ethics committee of Ankara Numune Education and Research Hospital, and conducted in accordance with the ethical principles of Declaration of Helsinki. (Date: 05.10.2017, Decree no: E17-1411).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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