Original Research

Evaluation of the Association between Obstructive Sleep Apnea and Hearing Loss

Amir Hossein Mohammadi[1], Amir Houshang Mehrparvar[1], Raziyeh Soltani-Gerdfaramarzi[2]*, Ehsan Samimi[1], Mehrdad Mostaghaci[3]

[1.] *Department of Occupational Medicine, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*
[2.] *Industrial Diseases Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*
[3.] *Occupational Medicine Specialist, Isfahan University of Medical Sciences, Isfahan, Iran*

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Abstract

Background and Objective: Obstructive sleep apnea (OSA) through hypoxia and re-oxygenation periods leads to oxidative stress, endothelial dysfunction, and activation of inflammatory cycles, which eventually may cause disorder in vasa nervorum, and peripheral neuropathy in hearing pathway. In this study, we aimed to evaluate the effect of severe sleep apnea on hearing function.

Materials and Methods: In this study, 91 individuals were evaluated and categorized in two groups of patients suffering from severe obstructive sleep apnea [Apnea/Hypopnea index (AHI) > 30], and controls (AHI < 5). Pure tone audiometry (PTA) was performed for all the subjects.

Results: Mean hearing threshold at 250-8000 Hz was 24.44 ± 6.80 dB, and 15.75 ± 5.10 dB in case and control groups, respectively ($P < 0.01$). Evaluation of each frequency showed that hearing threshold was significantly higher at 4000 Hz in the group with severe obstructive apnea. The only effective factor among all variances of sensorineural hearing loss in obstructive sleep apnea was the oxygen desaturation index, which predicted 18% of hearing loss variances. The frequency of hearing loss in patients with obstructive sleep apnea was higher than those without it. The severity of obstructive sleep apnea had significant relationship with hearing loss.

Conclusion: The frequency of hearing loss in patients with obstructive sleep apnea was estimated to be more than subjects without it. The severity of obstructive sleep apnea was associated with hearing loss. Obstructive sleep apnea may be a risk factor for hearing loss due to hypoxia. Thus, treatment of it may reduce risk of hearing loss. Further studies are required to evaluate the influence of treatment of obstructive sleep apnea on hearing loss.

Keywords: Obstructive sleep apnea; Pure tone audiometry; Apnea/hypopnea index; Hearing loss

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Introduction

Obstructive sleep apnea (OSA) is among the most common respiratory disorders during sleep affecting about 5% of general population (1). Similar to smoking, OSA has become a significant concern for population health (2). OSA could lead to complications such as daytime sleepiness (3), hypertension and cardiovascular disorders (4), increased vehicle accidents (5), and reduction of quality of life (6).

OSA was known as a disease usually for men (7). However, recent studies among general population have shown that OSA is not rare in women; its relative prevalence in men to women is 3:1 to 2:1, and 6% of middle-aged women suffer from OSA (8). Patients suffering from OSA are at a greater risk of hypertension, nighttime arrhythmia, pulmonary hypertension, heart failure, myocardial infarction, and stroke (9). Increased sympathetic tone is the reason for daytime hypertension among patients with OSA (10).

***Corresponding author**: R Soltani-Gerdfaramarzi, Industrial Diseases Research Center, Shahid Rahnamoun Hospital, Farrokhi Ave., Yazd, Iran*
Tel: +9835162713393, Fax: +983516229194
Email: raziyeh_soltani@yahoo.com

The causes of sleepiness, fatigue, irritability, and personality changes are due to oxygen desaturation during sleep, and chronic sleep deprivation (11). Intermittent hypoxia and reoxygenation during OSA, and subsequent oxidative stress, impairment of endothelial function, and activation of inflammatory cascade activate the sympathetic nervous system, suppress parasympathetic activity, stimulate oxidative stress and systemic inflammation and activate platelets (12).

Hypoxia causes damage to peripheral nerves due to vasa nervorum injury, which may cause irreversible damage after long-term disease (13). Change in the production of the atrial natriuretic peptide changes plasma volume; subsequent intermittent hypoxia due to OSA leads to permanent hyperviscosity (14).

Sleep disorder secondary to OSA may increase interleukin 6 (IL6), leading to sleepiness and tiredness (15). In addition to IL6, other inflammatory and immune factors such as natural killer (NK) cells and lymphocytes increase in sleep disorders as well (16). CRP is also reported to increase in sleep apnea (17).

Reactive nitrogen species (RNS) and reactive oxygen species (ROS) may lead to mitochondrial membrane damage, cytochrome C release, injury due to ischemia and reperfusion, and stimulation of apoptotic cell death in the inner ear (18).

After exposure to noise, free radicals increase in the cochlea and the peak increase will happen 7-12 days later (19). High levels of ROS in cochlea lead to increased activity of antioxidant enzymes and decreased level of glutathione antioxidant (20). Physiologic stressors cause endogenous vasoactive substances (such as endothelin) to release. Four hours after respiratory events in OSA, endothelin level and blood pressure will increase (21). Serum inflammatory level, C-reactive protein (CRP), and amyloid will increase due to intermittent hypoxia during sleep (22).

The release of oxidative stressor substances may lead to decreased parasympathetic activity, activation of platelets, increased sympathetic tone, and impairment of endothelial function including vasa nervorum and subsequently peripheral neuropathy (13). Obstructive apnea and hypopnea impair mechanism of the inner ear and transformation of neural impulses during night (23).

Different causes of sensorineural hearing loss are identified including infections, immune disorders, neurologic diseases, neoplasms, ototoxic drugs, systemic disorders, head trauma, hematologic diseases, and idiopathic ones.

The aim of this study was to assess the effect of OSA on sensorineural hearing loss and to find the parameters recorded during polysomnography of the patients with OSA that have more influence on hearing loss.

Materials and Methods

This study was a cross-sectional study on patients referred to a sleep clinic in Yazd city, Iran, for assessment of respiratory sleep disorders in 2012. Polysomnography was performed for all the patients. Consent forms were obtained from all study participants. Subjects were divided into two groups: first group, those with Apnea/Hypopnea index (AHI) of more than 30, and second group with an AHI of less than 5.

Using a validated questionnaire, medical and drug history, demographic data, patients' reports of occupational exposure to noise and their habits were collected before overnight polysomnography.

Body height and weight were measured. Pure tone audiometry (PTA) was performed on the day after polysomnography. We did not consider patient's job. However, not being exposed to loud noise in the day before polysomnography was considered by the authors. To assess excessive daytime sleepiness, Epworth sleepiness scale (ESS) was used, and score of more than 10 was considered as abnormal. ESS consists of eight items, which evaluate sleepiness in different daily situations (e.g. watching television, sitting in public places, sitting and reading). ESS score ranges from 0 to 24. ESS score of more than 10 shows abnormal sleepiness.

We evaluated the consumption of ototoxic drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, and gentamicin. Some laboratory assessments were performed to exclude diseases affecting hearing system (e.g. diabetes and hyperlipidemia).

Blood pressure was measured in all participants according to international guidelines (European Society of Hypertension) (24). Hypertension was defined as a positive history of high blood pressure or consumption of antihypertensive drugs, or systolic blood pressure of more than 140 mmHg or diastolic blood pressure of more than 90 mmHg.

Body mass index (BMI) was calculated by dividing weight in Kg by the square of height in cm.

An expert physician performed otoscopy for all the patients. Smokers and ex-smokers were

identified. Those with smoking more than 20 pack-years in a recent time were considered as current smokers.

Overnight polysomnography was performed based on standard criteria for the patients suspicious of sleep apnea (device: Somnomedics, Germany). Polysomnography was continued during the night for observation of apnea (11).

Polysomnography device consisted of 12 channels including electroencephalography, electrooculography, chin electromyography, nasal airflow sensor, snore sensor, abdominal and thoracic belts, pulse oximetry, leg electromyography, and body position.

Sleep stages were scored in 30-second epochs according to standard criteria (12). All breath pauses for more than 10 seconds were considered as apnea (obstructive, if the abdominal and thoracic respiratory effort was present and central, if the respiratory efforts were absent). Hypopnea was considered as more than 30% reduction in airflow for at least 10 seconds accompanied by at least 4% reduction in O_2 saturation. AHI > 30 and AHI < 5 were defined as OSA and simple snoring, respectively (13).

Oxygen desaturation index (ODI) was calculated by dividing the number of more than 4% desaturations above the baseline oxyhemoglobin level by sleep time. The percent time that patient had spent with saturation under 90% and minimum O_2 saturation was also measured for the level of hypoxia during sleep.

Audiometry was performed for all subjects by an expert audiologist (device: Interacoustc, AC40, Denmark). Hearing threshold was measured at frequencies of 250 Hz to 8 kHz in sound level between -10 and 120 dB for each ear. Frequency of 1000 Hz was rechecked for evaluation of response reliability, and it was not accepted if test-retest difference was more than 10 dB. The binaural hearing loss was defined as the mean hearing threshold more than 20 dB at 500 Hz to 6 kHz in both ears (25).

Subjects were divided into two groups according to the results of polysomnography: the ones with obstructive apnea and controls. For comparison of continuous and qualitative variables between two groups, t and chi-square tests were used, respectively. To assess the association between polysomnographic parameters and hearing loss, multivariate regression analysis was used in which hearing loss was the dependent factor. P values less than 0.050 were considered as statistically significant.

Results

All the 120 enrolled subjects underwent polysomnography and were recruited in the current study. 29 patients were excluded from the study due to ototoxic drug consumption, pulmonary insufficiency, pathologic injury in middle or inner ears, diseases affecting hearing (diabetes, hyperlipidemia, hypertension, and exposure to noise), and those suffering from mild or moderate apnea.

The mean hearing threshold of all frequencies (250 Hz to 8 kHz) was 24.44 ± 6.80 dB and 15.75 ± 5.10 dB in case and control groups, respectively (Table 1), and the difference was statistically significant. Hearing threshold differences in each frequency showed a significant difference at 4 kHz between the two groups (P < 0.010).

According to the polysomnography findings, 60 patients were categorized in the OSA group (mean AHI = 36.0 ± 12.3 events/hour) and 31 patients in the control group (mean AHI = 3.2 ± 2.0 events/hour) (Table 2). The patients in the OSA group had higher BMI (34.6 ± 8.5 vs. 29.3 ± 9.5 kg/m^2, P = 0.490), higher diastolic blood pressure (90.5 ± 4.0 vs. 7.9 ± 7.5 mmHg, P = 0.450), and more smokers (20 vs. 7, P = 0.037).

We did not observe a significant difference in terms of age, systolic blood pressure, and ESS between the two groups. There was a significant difference regarding respiratory parameters during sleep (ODI, AHI, average SPO_2, and T90 percentage) between the two groups. The mean hearing loss was clearly higher in OSA group.

Table 1. Hearing threshold in OSA and control groups

	PTA	**Frequency (Hz)**						
		250	**500**	**1000**	**2000**	**4000**	**6000**	**8000**
OSA group	24.4 ± 6.8	30.0 ± 4.3	35.0 ± 6.2	40.0 ± 5.1	29.0 ± 18.1	15.0 ± 6.5	12.0 ± 7.9	10.1 ± 7.3
Control group	15.7 ± 5.1	20.0 ± 10.1	30.0 ± 8.3	23.0 ± 5.2	10.0 ± 2.1	10.0 ± 7.1	10.0 ± 7.1	7.3 ± 5.1
P value	0.310	0.420	0.051	0.070	0.010	0.060	0.071	0.010

OSA: Obstructive sleep apnea; PTA: Pure tone audiometry

Table 2. Comparison of different variables between control group and severe OSA group

Variable	Control	Severe OSA	P value
Age (Year)	39.3 ± 12.0	38.5 ± 9.0	0.810
Binaural hearing loss (number)	6.5 ± 5.3	14.8 ± 2.8	0.012
BMI (kg/m^2)	29.3 ± 9.5	34.6 ± 8.5	0.049
Systolic blood pressure (mm/Hg)	120.1 ± 8.1	124.0 ± 13.1	0.690
Diastolic blood pressure (mm/Hg)	79.0 ± 7.5	90.5 ± 4.0	0.045
Epworth Sleepiness Scale (ESS)	11.1 ± 5.1	12.9 ± 5.3	0.120
Apnea/hypopnea index	3.2 ± 2.0	36.0 ± 6.3	< 0.001
Oxygen desaturation index (%)	10.12 ± 9.0	65.0 ± 21.0	< 0.001
Percentage time with oxygen saturation < 90% (%)	31.0 ± 20.5	4.0 ± 3.5	< 0.001
Average oxygen saturation (%)	93.0 ± 2.3	85.0 ± 5.1	< 0.001
Current smoking [number (%)]	7(22)	20(32)	0.037

OSA: Obstructive sleep apnea; BMI: Body mass index

About 38% of the cases in control and 10% of the cases in OSA groups had normal hearing. The difference in mean hearing loss remained even after omitting smokers from the study analysis.

Figure 1 shows the association between hearing loss and AHI and average oxygen saturation. Degree of hearing loss had a significant relationship with AHI (r = 0.298, P = 0.001) and with ODI (r = 0.451, P = 0.001). BMI (r = 0.233, P = 0.015) and age (r = 0.263, P = 0.027) also had a significant association with AHI.

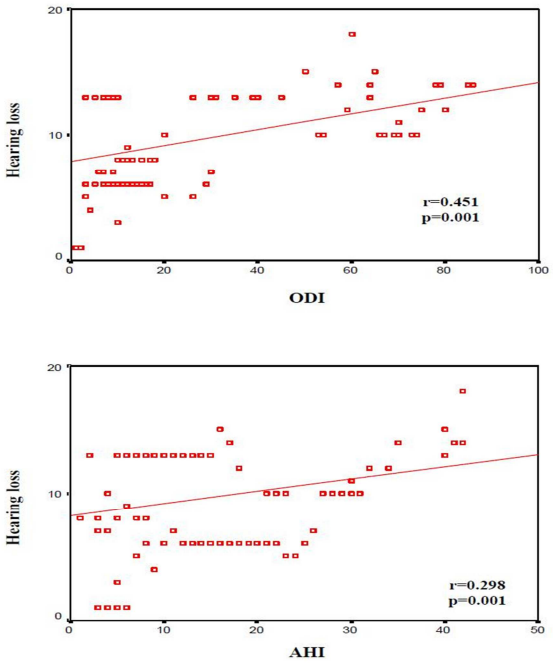

Figure 1. Scatterplots of binaural hearing loss vs. Apnea/Hypopnea index (AHI) (upper) and oxygen desaturation index (ODI) (lower). Binaural hearing loss significantly correlated with AHI (r = 0.298, P = 0.001) and ODI (r = 0.451, P = 0.001) using Pearson's correlation analysis.

Multiple regression analysis was performed. The mean binaural hearing loss was considered as the dependent factor and parameters of sleep disordered breathing and confounding factors as independent factors. This analysis showed that only ODI is the independent factor affecting hearing loss in severe OSA. Partial coefficient determinant (partial R^2) of the ODI for mean hearing loss in both ears after adjusting for confounding factors was 0.18. This means that ODI is 18% of all variances of factors affecting hearing loss in OSA. Table 3 shows the results of regression analysis.

Discussion

In the current study, we found that severe obstructive apnea as an independent factor may damage the function of the auditory system. According to tomotopicity theory, higher frequencies of hearing coded in the basal part of the cochlea and hair cells in the basal part of the cochlea are more susceptible to oxidative stress than the apical part, similar to exposure to noise or ototoxic drugs. This theory explains significant hearing loss in 4 kHz in severe OSA found in current study. Sha et al. theory explains this phenomenon by higher levels of glutathione in the apex and decrease in the level of glutathione in outer hair cells in the basal cochlea (26).

Dziewas et al. have reported that hypoxia caused by OSA is a risk factor for dysfunction of auditory peripheral nerves and treatment of OSA may reverse this effect (27). Chung et al. found similar results in hearing loss at 4 kHz among patients suffering from OSA and their explanation for higher hearing threshold at 4 kHz was vasospasm, thrombosis, and hypercoagulation following OSA (28).

Table 3. Results of regression analysis among cases group for ESS, AHI, ODI, AOS, and PTOS

	Crude				Adjusted*			
	B (β)**	SE	P value	R^2	B (β)	SE	P value	Partial R^2
ESS	0.031 (0.32)	0.005	0.002	0.065	0.025 (0.36)	0.03	0.061	0.064
AHI	0.032 (0.35)	0.006	0.001	0.088	0.027 (0.37)	0.05	0.055	0.078
ODI	0.034 (0.47)	0.007	0.001	0.203	0.030 (0.38)	0.04	0.037	0.181
AOS	-0.070 (-0.17)	0.054	0.006	0.067	-0.040 (-0.09)	0.10	0.450	0.012
PTOS	0.027 (0.21)	0.045	0.008	0.056	0.021 (0.19)	0.07	0.089	0.051

* Body mass index (BMI), current smoking and diastolic blood pressure adjusted.
** B: Unstandardized regression coefficient, β: Standardized regression coefficient
ESS: Epworth sleepiness scale (ESS); AHI: Apnea/Hypopnea index; ODI: Oxygen desaturation index; AOS: Average oxygen saturation (%); PTOS: Percentage time with oxygen saturation of less than 90%

Bernath et al. evaluated the theory that blood hyperviscosity in patients with OSA can change brainstem auditory evoked potentials (BAEPs). In their study, 610 patients with OSA were assessed for BAEP in a prospective study. Patients with hyperviscosity showed BAEPs (24% sensorineural and 76% brainstem changes). After 6 months of treatment with continuous positive airway pressure (CPAP), 66% had normal viscosity and waved three changes of BAEP turned to normal in 70% of the patients (16). The findings of their study are consistent with our results about the effect of OSA on exacerbation of sensorineural hearing loss.

More studies are required for documentation of changes in the hearing system following vascular dysfunction in vasa nervorum and intermittent hypoxia in OSA.

Severity and duration of OSA are also important factors for causing hearing loss, which should be separately evaluated. The effect of apnea treatment on reversing hearing impairment is also another issue that should be assessed.

This study showed higher hearing impairment in patients with OSA compared to normal ones. The relationship between various parameters, such as SPO_2 percentage, T90 percentage, ODI, AHI, and hearing loss was evaluated, and after adjusting for confounding factors, the most potent relationship was observed to be with ODI.

We measured hearing thresholds at frequencies of 500-6000 Hz, and binaural hearing loss was defined as hearing threshold higher than 20 dBA in both ears.

OSA is a risk factor for hypertension and cardiovascular diseases. OSA is the underlying disease of secondary and resistant hypertension. OSA increases both daytime and nighttime blood pressures via activating various neurohumoral factors such as sympathetic nervous system and the renin-angiotensin-aldosterone system. OSA increases blood pressure during sleep compared with awaking. A characteristic of blood pressure in OSA is increased blood pressure variability, marked midnight blood pressure surges during sleep in patients with OSA. The exaggerated blood pressure surge may trigger OSA-related cardiovascular events occurring during sleep. Understanding the characteristics of OSA-related hypertension is important to achieve blood-pressure control, including the sleep period, for more effective prevention of cardiovascular disease (29).

To the best of our knowledge, few studies have assessed the association between OSA and hearing loss. Sensorineural hearing loss is influenced by many factors such as age, ototoxic drugs, occupational noise exposure, and infections. OSA causes free radicals due to hypoxia and re-oxygenation during sleep, which may lead to hearing impairment.

According to the results of this study, one of the less-known causes of sensorineural hearing loss is OSA; and ODI as an independent factor in OSA causes hearing impairment.

There are many evidences about the relationship of OSA and oxidative stress. Some studies have shown a decrease in the level of oxidative stress after treatment by CPAP (30). Recent studies show the association of oxidative stress (according to lipid peroxidation and antioxidant capacity) and severity of OSA (31).

Although simple regression analysis showed a relationship between AHI and hearing loss, multivariate analysis showed that ODI is the best predictor of hearing loss; as ODI is an indicator of transient episodes of hypoxia and re-oxygenation. The other reason is that ODI is more reproducible than the AHI (32).

Our study had some limitations. The patients referred to our clinic might had more risk factors for hearing loss than normal population. We selected the subjects without apnea as the control group, so we could not consider patients with mild and mod-

erate apneas. The relationship between ODI and hearing loss was not so strong (r = 0.451) which was almost 20 percent of the variance and after considering other confounding risk factors, ODI contributed to 18% of the variance. We have not reached a significant clinical association between hearing loss and ODI in patients with OSA in this study. This was a cross-sectional study; so finding a causal relationship between OSA and hearing loss may be impossible. To find the association between hearing loss and ODI in patients with OSA, a prospective study with clinical intervention is required.

Obesity and OSA were strongly associated with diagnosis of OSA. Obese subjects are highly prone to be sleepy during the day. Their self-reports of OSA symptoms are not reliable. The prevalence of OSA is estimated to be as high as 45% in obese subjects. Obesity predisposes to and potentiates OSA. The prevalence of OSA and its consequences may increase because of current obesity epidemic (33).

Conclusion

In current study, the frequency of hearing loss in patients with OSA was estimated to be more than subjects without it. The severity of OSA has a significant relationship with hearing loss. These results can explain the higher prevalence of hypertension and cardiovascular, cerebral, and vascular diseases among patients with OSA. Hypoxia and intermittent oxygenation during sleep and eventual production of free radicals can cause exacerbation of sensorineural hearing loss.

This is an innovative finding in the field of occupational medicine. The treatment of OSA may reduce risk of noise-induced hearing loss (NIHL), and we need to conduct longitudinal studies to evaluate this hypothesis.

Conflict of Interests

Authors have no conflict of interests.

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