Evaluation of auditory system in obstructive sleep apnea patients

Chee Chean Lim1,2, Tengku Ezulia Binti Tengku Nun Ahmad1, Halimuddin Bin Sawali2, Ahmad Nordin Bin Afandi2, Vinota Paniselvam2, Merlinda W. Bernard2, Prepageran Narayanan1, Mohd Zukiflee Bin Abu Bakar1

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Abstract
Objectives Obstructive sleep apnea (OSA) has been associated with auditory dysfunction both to the cochlear and higher auditory pathways. However, available literatures presented conflicting results. We aimed to study the impact of OSA severity and their polysomnography parameters on hearing function.

Materials and methods A total of 44 patients were included after evaluation for sleep disorders and were divided into four groups in accordance with apnea–hypopnea index (AHI). Pure tone audiometry (PTA), distortion product otoacoustic emission (DPOAE) and auditory brainstem response (ABR) were compared in commensurate with the severity of AHI. Polysomnography oximetry parameters of oxygen desaturation index, mean SPO2, minimum SPO2 and percent SPO2 < 90% were correlated with their respective PTA, DPOAE and ABR results.

Results There was no significant change in the PTA, DPOAE and ABR results in connection with AHI severity. However, we found significant correlations between mean SPO2 and percent SPO2 < 90% with ABR wave I, III and V absolute latencies. Minimum SPO2 was also significantly correlated with wave III peak latency changes.

Conclusions Mean SPO2, percent SPO2 < 90% and minimum SPO2 could be key prognostic indicators of central auditory dysfunction in OSA patients. These parameters should be explored further as indicators of OSA severity rather than utilizing AHI alone. The hypoxic burden derived could be a better predictor of auditory function abnormalities rather than one derived from AHI.

Keywords Obstructive sleep apnea · Sensorineural hearing loss · Sleep study · Oximetry

Background

Obstructive sleep apnea (OSA) is among the most common respiratory disorder characterized by intermittent obstruction of the upper airways during sleep resulting in episodes of apnea and/or hypopnea and respiratory event-related arousal (RERA). Senaratna et al. [1] documented in a systematic review that the prevalence of OSA ranged from 9% to 38%, higher in men and with increasing age. Many studies have linked OSA with major cardiovascular, neurocognitive and endocrine disorders which led to increased morbidity and mortality. Intermittent hypoxia and reoxygenation events in OSA resulted in a cascade of oxidative stress, endothelial dysfunction, systematic inflammation, platelet activation and plasma hyperviscosity causing reduced perfusion to the central and peripheral end organs [2, 3].

The cochlea is sensitive to chronic events of intermittent hypoxemia in OSA patients as it is supplied by a terminal end artery with inadequate collateral circulation. It was also shown that chronic hypoxia during apnea and hypopnea can impair transmission of nerve impulses of the auditory nerve as it is highly sensitive to oxygen concentrations, giving rise to central auditory pathways abnormalities [4, 5]. Most studies utilized the apnea hypopnea index (AHI) to grade the severity of OSA, while other sleep study parameters were seldom being used to correlate with auditory function. The goals of this study were to investigate the impact of OSA severity (AHI) and to evaluate the polysomnography (PSG) parameters affecting hearing function.
Materials and methods

This is a prospective cross-sectional study conducted on patients with symptoms of obstructive sleep apnea in Queen Elizabeth Hospital, Sabah from June 2019 to May 2021. Approval for the study was obtained from the Medical Research and Ethics Committee (NMRR-19-714-46840). Patients underwent sleep study overnight in the hospital followed by a series of audiological tests. They ranged from 18 to 55 years old without existing pathology of the middle or inner ear, medical illnesses, such as diabetes mellitus, untreated hypertension, dyslipidemia, stroke, heart failure and myocardial infarction. They should neither be on continuous positive sleep pressure devices and oral appliances nor have history of chronic noise exposure, ototoxic drugs and psychiatric diseases.

Overnight PSG was performed based on standard criteria for patients suspected with OSA (Somnmedics, Germany). Age, sex, ethnic group, epworth sleepiness scale, previous medical and drug history, occupation, exposure to noise, smoking history, neck circumference, height, weight and body mass index were documented. All patients recruited underwent thorough physical examination including endoscopy of the ears and a complete audiological evaluation. Sleep study machine consisted of channels including nasal airflow sensor, snore sensor, abdominal and thoracic belts, pulse oximetry, leg electromyography and body position. Sleep stages were scored in 30-s epochs according to standard criteria.

Audiological assessments included tympanometry and pure tone audiometry (PTA) of frequencies 250 Hz, 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz, 8000 Hz and 1000 Hz, 1500 Hz, 2000 Hz, 3000 Hz, 4000 Hz, 6000 Hz in sound level between −10 and 120 dB for each ear using Interacoustic AA222 device. DPOAE recording the amplitudes (dB SPL) on frequencies 1, 1.5, 2, 3, 4, 6 kHz were done using Interacoustics titan IMP440 machine. ABR recording brain peak latencies and interwave latencies (milliseconds) were achieved using Intelligent Hearing System’s (IHS) device.

Results

A total of 44 subjects were analysed; 19 males (40%) and 25 females (60%) with a mean age of 32.9 ± 8.05. Kadazan-Dusun made up the biggest ethnicity (30%) followed by Malay (20%), Chinese (10%) and others (40%). The participants had a mean body mass index of 33.4, neck circumference of 40.7 cm, epworth sleepiness scale of 9 and snoring duration of 8.18 years. 90% of them were non-smokers with a mean AHI of 34.3. There were 6 patients with mild OSA, 7 patients with moderate OSA, 24 patients with severe OSA and 7 patients for control group with simple snoring. Our patients’ age, snoring duration, ODI, minimum SPO2, percent SPO2 < 90% and mean SPO2 were significantly associated with AHI (Fig. 1).

Comparison of the median values of PTA at frequencies 250 Hz, 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz, 8000 Hz (Table 1) and the median values of DPOAE at frequencies 1000 Hz, 1500 Hz, 2000 Hz, 3000 Hz, 4000 Hz, 6000 Hz (Table 2) between AHI groups for both right and left ears did not reveal significant difference. Similarly, median values of ABR peak latencies and interpeak latencies between AHI groups for both right and left ears did not show statistical difference between the four groups (p > 0.05) (Table 3).

Correlation analysis between PTA thresholds (Table 4), DPOAE amplitudes (Table 5) and ABR latencies (Table 6) with other sleep study parameters were performed using Spearman correlation test. Wave latencies were significantly correlated with percent SPO2 < 90%, mean SPO2 and minimum SPO2. Our patients’ mean ABR latencies at wave I, III and V were positively correlated with percent SPO2 < 90% (p = 0.024; rho = 0.34, p = 0.036; rho = 0.317, p = 0.03; rho = 0.327, respectively) and negatively correlated with the mean SPO2 (p = 0.029; rho = −0.33, p = 0.016; rho = −0.361, p = 0.023; rho = −0.341). Mean ABR latency at wave III was also negatively correlated with minimum SPO2 (p = 0.015; rho = −0.366).

Discussion

We present a comprehensive analysis on auditory function using PTA, DPOAE and ABR with differing severity of OSA. OSA has well-known negative ramifications on multisystemic organs but the effects of OSA on our auditory system remain unclear. There is insufficient literature data about the causal relationship of OSA and hearing function in both the cochlear and higher auditory pathways.

Our study showed no significant association between auditory function in terms of PTA, DPOAE and ABR in relation to differing AHI severity. Our results further elucidate the conflicting findings in the literature regarding

Statistical analysis

Median PTA, median DPOAE, median ABR latencies and ABR interpeak latencies between AHI groups were compared at each frequency using Kruskal–Wallis rank sum test. Factors associated with AHI groups were analysed using Kruskal–Wallis rank sum test and Fisher’s exact test. Spearman correlation was used to analyse any possible correlation between mean PTA, mean DPOAE, mean ABR latencies and mean ABR interpeak latencies vs four other sleep study parameters (oxygen desaturation index (ODI), percent SPO2 < 90%, mean SPO2 and minimum SPO2).
this subject. Proponents for PTA and DPOAE abnormalities demonstrated that patients with moderate and severe OSA have elevated PTA thresholds and reduced DPOAE amplitudes especially over the high frequencies. Martines et al. [6] detected increased PTA thresholds prominently over the extended high frequency regions (9–16 kHz). Outer hair cells in the cochlea basal regions were more susceptible to hypoxia which could possibly explain the above findings [7]. Meanwhile, Baki et al. [8] concluded in their larger sample study that auditory functions were

| Variable          | Normal AHI | Mild AHI | Moderate AHI | Severe AHI | p-value^b |
|-------------------|------------|----------|--------------|------------|-----------|
| Age (years)       | 25.00      | 28.50    | 32.00        | 35.0       | 0.016     |
| (18.00, 33.00)    | (23.00, 36.00) | (23.00, 45.00) | (23.00, 55.00) |           |           |
| BMI (kg/m2)       | 27.70      | 34.25    | 32.70        | 33.60      | 0.800     |
| (21.50, 43.40)    | (16.40, 52.40) | (28.00, 37.00) | (20.00, 56.00) |           |           |
| Neck circumference (cm) | 37.00 | 39.50    | 40.00        | 41.50      | 0.290     |
| (30.00, 48.00)    | (34.00, 41.00) | (34.00, 47.00) | (32.00, 57.00) |           |           |
| ESS               | 5.00       | 7.50     | 10.00        | 9.50       | 0.608     |
| (2.00, 16.00)     | (2.00, 19.00) | (5.00, 13.00) | (2.00, 17.00) |           |           |
| Snoring duration (years) | 3.00 | 4.00     | 8.00         | 10.00      | 0.026     |
| (1.00, 10.00)     | (1.00, 10.00) | (1.00, 10.00) | (2.00, 20.00) |           |           |
| ODI               | 2.20       | 13.30    | 16.50        | 45.10      | <0.001    |
| (0.10, 5.90)      | (0.20, 21.10) | (3.60, 24.10) | (29.10, 78.7) |           |           |
| Min. SpO2 (%)     | 83.00      | 86.00    | 87.00        | 72.50      | 0.002     |
| (64.00, 93.00)    | (73.00, 90.00) | (78.00, 90.00) | (35.00, 86.00) |           |           |
| Percent SpO2 < 90% (%) | 0.16 | 0.75     | 1.80         | 17.40      | <0.001    |
| (0.00, 1.50)      | (0.00, 17.00) | (0.00, 7.50) | (2.60, 64.10) |           |           |
| Mean SpO2 (%)     | 96.00      | 95.50    | 96.00        | 93.00      | <0.001    |
| (90.00, 98.00)    | (93.00, 97.00) | (95.00, 97.00) | (81.00, 96.00) |           |           |
| Sex               |            |          |              |            | 0.330^b   |
| Female            | 5 (26.3)   | 3 (15.8) | 3 (15.8)     | 8 (42.1)   |           |
| Male              | 2 (8.0)    | 3 (12.0) | 4 (16.0)     | 16 (64.0)  |           |
| Ethnic            |            |          |              |            | 0.511^b   |
| Chinese           | 1 (16.7)   | 2 (0.0)  | 0 (0.0)      | 5 (83.3)   |           |
| Kadaon-Dusun      | 2 (15.4)   | 1 (7.7)  | 3 (23.1)     | 7 (53.8)   |           |
| Malay             | 2 (25.0)   | 3 (37.5) | 0 (0.0)      | 3 (37.5)   |           |
| Others            | 2 (11.8)   | 2 (11.8) | 4 (23.5)     | 9 (52.9)   |           |
| Smoking           |            |          |              |            | 0.482^b   |
| No                | 7 (17.9)   | 6 (15.4) | 5 (12.8)     | 21 (53.8)  |           |
| Yes               | 0 (0.0)    | 0 (0.0)  | 2 (40.0)     | 3 (60.0)   |           |

**Fig. 1** Factors associated with AHI groups. a Kruskal-Wallis rank sum test; b Fisher’s exact test

**Table 1** Comparison of median PTA between AHI groups at different frequencies (right and left ears)
not influenced by OSA but due to advanced age and that further studies are needed to be certain of this association. Hwang et al. [9] and Spinosi et al. [10] also reported that the presence of OSA did not affect hearing thresholds of their patients. Ekin et al. [11] similarly reported no difference in the hearing thresholds of OSA and/or simple snoring compared to the control group except over the extended high frequency regions.

Some studies have shown significant prolongation of ABR peak and interpeak latencies as a result of chronic intermittent hypoxia causing oxidative stress and systemic inflammation to the higher auditory pathways. Casale et al. [4] studied 18 individuals of severe OSA and demonstrated significant prolongation of wave V latency in comparison with the control group. Matsumura et al. [12] similarly showed that moderate OSA patients had significant changes.

| Frequency (Hz) | ODI | Percentage SPO2 <90% | Mean SPO2 | Min SPO2 |
|---------------|-----|----------------------|-----------|----------|
| 250           | 0.140 | 0.364 | 0.019 | 0.905 | 0.027 | 0.860 | 0.014 | 0.925 |
| 500           | 0.165 | 0.285 | 0.069 | 0.658 | −0.061 | 0.693 | −0.002 | 0.990 |
| 1000          | 0.132 | 0.393 | 0.102 | 0.508 | −0.158 | 0.304 | −0.057 | 0.715 |
| 2000          | 0.130 | 0.400 | 0.018 | 0.907 | −0.028 | 0.855 | 0.073 | 0.636 |
| 4000          | 0.155 | 0.314 | 0.032 | 0.835 | −0.008 | 0.960 | 0.014 | 0.928 |
| 8000          | 0.261 | 0.087 | 0.131 | 0.396 | −0.088 | 0.572 | −0.035 | 0.820 |

Table 2  Comparison of median DPOAE amplitudes between AHI groups at various frequencies (right and left ears)

Table 3  Median of ABR absolute latencies and interpeak latencies between AHI groups (right and left ears)

Table 4  Correlation between mean PTA vs ODI, percent SPO2 <90%, mean SPO2, min SPO2
in absolute latency of wave V. On another spectrum, Bernáth et al. [13] suggested that plasma hyperviscosity played a significant role in the brainstem electrophysiological abnormalities in OSA patients. They demonstrated ABR wave III latency changes which normalized after 6 months of continuous positive airway pressure treatment concurrent with the normalization of blood viscosity. On the contrary, Vorlová et al. [14] and Fu Q et al. [15] showed no difference in click-ABR between OSA group vs simple snoring/control group. Unexpectedly, Fu Q et al. [15] illustrated that speech-ABR was able to detect early auditory dysfunctions in mild to moderate OSA patients. Moreover, both Iriz et al. [16] and Kayabasi et al. [17] also studied speech discrimination analyses in OSA patients and found significant impairment in their central auditory pathways.

The variable and conflicting results in auditory tests could be attributed to the limitations of AHI as a tool in grading the severity of OSA. Many papers have expressed its imperfections as it merely reports the frequency of respiratory events and did not account for the magnitude of oxygen desaturation. Furthermore, AHI does not consider the duration of apnea and hypopnea events. It is unfair to assume that a patient with apnea/hypopnea of 10 s is identical to another patient with apnea/hypopnea of 30 or 60 s. Besides, the definition of hypopnea poses a major challenge as there is no definitive consensus over the level of airflow reduction and oxygen desaturation necessary to classify a hypopnea event. Importantly, two patients with similar AHI may differ in severity due to their inherent biological differences in terms of age, occupation, obesity, individual tolerance, genetic profile and whether they have major OSA symptoms. In addition, a patient’s oxygen saturation behaviour may not be the same as that of the respiratory flow when the BMI is increased. Due to its failure to commensurate the mechanisms that underlie the pathophysiologic sequels of OSA, the usage of AHI as an indicator to evaluate the consequences of OSA severity and the response to its treatments have led to flimsy correlations.

Accordingly, we would like to emphasize the importance of integrating oximetry indicators such as mean SPO2, percent SPO2 <90%, and minimum SPO2 in grading the severity of OSA. Our study showed correlations between the above sleep study parameters with ABR wave I, III and V absolute latencies. This is in line with Seo et al. [18] which presented significant negative correlations between mean hearing thresholds and minimum oxygen saturation except that they did not look into ABR wave latencies. Oximetry parameters are even more crucial when a partial sleep study is being performed either in a restricted hospital setting or due to a patient’s own preferences. In essence, physicians should not rely on AHI alone in stratifying a patient’s risk of auditory dysfunction.

Our sample size was relatively small due to the stringent entry criteria and recruitment difficulties faced during the
COVID-19 pandemic. This study was also being carried out in a single tertiary centre in Kota Kinabalu, Sabah. The usage of partial sleep study based on total recording time rather than total sleep time may lead to underestimation of AHI severity as it is usually 15% lower than a full polysomnogram. Finally, this is a cross-sectional study which would only be able to demonstrate an association but unable to draw definitive conclusion about a causal effect.

Conclusions

Our results further expound the conflicting associations of auditory dysfunction in OSA patients. Oximetry parameters, namely, mean SPO2, percent SPO2 <90% and minimum SPO2 could be key prognostic indicators of central auditory dysfunction as shown in our study. These parameters should be explored further to gauge the degree of OSA severity rather than utilizing AHI alone. The hypoxic burden derived could be a better predictor of auditory function abnormalities rather than one derived from AHI.

Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by CCL, TE, HbS, ANBA, VP, MwB, MzbAB. The first draft of the manuscript was written by CCL and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflicts of interest The authors declare that they have no competing interests.

Ethical approval and consent to participate Approval for the study was obtained from the Medical Research and Ethics Committee (NMRR-19-714-46840).

Consent for publication Written informed consent were obtained from participants of this study.

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