Original Article

Clinical case control study analysis of vestibular function in patients with obstructive sleep apnea-hypopnea syndrome

Xin Li, Wenjing Chen, Sichao Liang, Zhenping Guo, Manlin Lu, Yuhuan Zhang, Xuemei Yuan, Yu Sun, Lifen Qu, Qiang Chen, Jingying Ye

School of Clinical Medicine, Beijing Tsinghua Changgung Hospital, Tsinghua University, Beijing, China

Contributions: (I) Conception and design: X Li, J Ye; (II) Administrative support: J Ye; (III) Provision of study materials or patients: X Li, W Chen; (IV) Collection and assembly of data: S Liang, Z Guo, M Lu, Y Zhang, X Yuan, Y Sun, L Qu, Q Chen; (V) Data analysis and interpretation: X Li, W Chen; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Jingying Ye. School of Clinical Medicine, Beijing Tsinghua Changgung Hospital, Tsinghua University, Beijing, China.
Email: yejingying@yeah.net.

Background: To investigate the effects of hypoxia degree and sleep duration on vestibular function in obstructive sleep apnea-hypopnea syndrome (OSAHS) patients. We made further study of the low oxygen levels of OSAHS and hypoxic duration on the impact of vestibular function, and further studied the OSAHS the longest apnea time and Vestibular Evoked Myogenic Potential (VEMP) abnormal rate and the relationship between the vestibular function of canal paralysis (CP).

Methods: A total of 87 OSAHS patients and 47 healthy individuals were enrolled in this study. There was no difference in gender, age and body mass index (BMI) values in matched experimental groups. Other diseases of other systems were excluded. All the participants completed sleepiness questionnaires (i.e., the Epworth sleepiness scale and the STOP-BANG questionnaire) and the Dizziness Handicap Inventory (DHI). Additionally, a caloric test, positional test, electrocochleogram, and VEMP test were administered to evaluate the vestibular function of all the participants. A polysomnography (PSG) was also performed.

Results: The current investigation generated the following three major findings: (I) there was a significant correlation between body mass index and canal paresis [CP; P=0.014, odds ratio (OR) =1.791, 95% confidence interval (CI): 1.125–2.851] and a significant positive correlation between the DHI score and VEMP results (P=0.0061, OR =3.667, 95% CI: 1.449–9.276); (II) the CP abnormality rate of the OSAHS group was significantly higher than that of the control group (P<0.05); (III) there was a significant correlation between the longest apnea duration and the DHI score (r=–0.191, P<0.05).

Conclusions: The abnormality rate of the vestibular function of OSAHS patients is higher than that of healthy people. OSAHS intermittent hypoxia can affect vestibular function in the inner ear, and the longer the duration of prolonged hypoxia, the more serious the vestibular function damage.

Keywords: Obstructive sleep apnea-hypopnea syndrome (OSAHS); vestibular function; vertigo; inner ear

Submitted May 20, 2022. Accepted for publication Jul 26, 2022.
doi: 10.21037/apm-22-718
View this article at: https://dx.doi.org/10.21037/apm-22-718

Introduction

Obstructive sleep apnea-hypopnea syndrome (OSAHS) is a common disease during sleep. OSAHS is characterized by recurrent episodes of partial or complete upper airway collapse during sleep that is highlighted by a reduction in or complete cessation of airflow despite documented ongoing inspiratory efforts. Due to the lack of adequate alveolar ventilation that results from the upper airway narrowing, oxygen saturation may decrease, and the partial pressure of carbon dioxide may occasionally increase. The events are

mostly terminated by arousals. The clinical consequences of OSAHS include excessive daytime sleepiness related to sleep disruption (1). The complications include cardiovascular and cerebrovascular diseases, neuro mental disorders, pulmonary hypertension or right heart failure, type II diabetes, and non-alcoholic fatty liver disease (2-4). OSAHS itself may be an independent risk factor for stroke.

Studies have shown that cerebral infarction patients with OSAHS usually have metabolic disorders, such as blood lipid and blood glucose, which can lead to the recurrence of cerebral infarction, which has a negative effect on the prognosis of patients, and eventually creates a vicious circle (5,6). Additionally, chronic intermittent hypoxia leads to mitochondrial dysfunction in inner ear hair cells. Researchers have found that continuous positive airway pressure (CPAP) therapy can improve the hypoxia of patients with Meniere's disease and effectively regulate the central oxygenation and blood flow and thus restore cochlear microcirculation to normal (7).

Gallina *et al.* evaluated the effects of sleep apnea and its associated hypoxia on the peripheral, principal, and central vestibular systems. The peripheral vestibular system may become asymmetric or hyporeflexic due to hypoxic damage, while the central vestibular system corrects this disequilibrium (8). The latency of I and V waves and the electrocochleogram (ECochG) results of patients with moderate and severe OSAHS disease are altered (9). Han *et al.* (10) found that the positive rate of caloric test in OSA patients was 67.5%. Additionally, the caloric test showed characteristic changes due to the decline of vestibular function. Kayabasi *et al.* found that the chronic hypoxic condition in patients with severe OSA negatively affects their vestibular functions (11). Thus, moderate and severe OSAHS causes changes in inner ear hearing and vestibular function.

The limitation of previous studies was that only the changes of vestibular function in OSAHS patients were analyzed, and the relationship between OSAHS hypoxia time and vestibular function impairment was not analyzed. This study not only started with vestibular function, but also added the abnormal rate of vestibular myogenic evoked potential as an objective indicator, and combined the degree of hypoxia, apnea time and abnormal rate to analyze the correlation.

To further verify the functional vestibular alterations of OSAHS patients, patients with OSAHS and healthy volunteers (as the control) were enrolled in the current study. Patients in both groups completed sleepiness questionnaires [i.e., the Epworth sleepiness scale (ESS) and the STOP-BANG questionnaire (SBQ)] and the Dizziness Handicap Inventory (DHI), and their vestibular function was evaluated by various tests. Polysomnography (PSG) was performed, and the relationship between sleeping ventilatory time and vestibular function was analyzed to reveal the functional vestibular alterations in OSAHS patients. We present the following article in accordance with the STROBE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-718/rc).

Methods

Subjects

Patients diagnosed with OSAHS at the Beijing Tsinghua Changgung Hospital from January 2019 to June 2020 were enrolled in the OSAHS group. Healthy normal individuals were selected and enrolled in the control group. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Institutional Review Board of the Beijing Tsinghua Changgung Hospital (Ethics Number: 20150911-05), and informed consent forms were signed by all participants before the study began. Before the onset of the sleep study, data were collected for each participant individually, including data on gender, age, medical history, and weight and height to calculate body mass index [BMI = weight (in kg)/height^2 (in m^2)]. Neck circumference was measured using the following standard: the tape measure was placed at the upper edge of the 7th cervical vertebra at the back of the neck to the lower part of the laryngeal node at the front.

All the participants underwent a full-night PSG study with at least 7 hours of recording time (Grael HD PSG System, Compumedics, Australia). Sleep staging was scored according to the criteria of the American Academy of Sleep Medicine (AASM) published in 2007 (12). Apnea was defined as the cessation of airflow for more than 10 seconds. Hypopnea was defined as a reduction of airflow of more than 30% lasting more than 10 seconds and associated with a higher than 4% decrease in oxyhemoglobin saturation. The number of apneas and hypopneas per hour of sleep was recorded and calculated to obtain the apnea-hypopnea index (AHI). OSAHS was diagnosed according to the following criteria: the PSG showed that apnea and hypopnea recurred more than 30 times during 7 hours of sleep every night, or an AHI score ≥5. Under the diagnostic scoring system, an AHI score ≥5 indicated OSAHS, an AHI score ≥15 indicated moderate-to-severe OSAHS, and an AHI score

≥30 indicated severe OSAHS.

To be eligible for inclusion in the OSAHS group, patients had to meet the following inclusion criteria: (I) be aged 30–60 years old; (II) have no history of vertigo, hearing loss, tinnitus, ear abscess, or otological surgery; (III) have no family history of vertigo; (IV) have type A tympanogram; (V) have no disease of the nervous system, cardiovascular system, endocrine system, blood system, renal system, digestive system, and no other otorhinolaryngology disease; (VI) have an AHI ≥ score 5.

To be eligible for inclusion in the control group, patients had to meet the following inclusion criteria: (I) be aged 30–60 years old (there was no difference in the gender, age, and BMI between the control group and the experiment group); (II) have no history of vertigo, hearing loss, tinnitus, ear abscess, or otological surgery; (III) have no family history of vertigo; (IV) have type A tympanogram; (V) have no disease of the nervous system, cardiovascular system, endocrine system, blood system, renal system, digestive system, and no other otorhinolaryngology disease; (VI) have an AHI ≤ score 5.

Questionnaires

Each subject completed sleeping questionnaires and a balance questionnaire. The sleeping questionnaires included the ESS (13) and the SBQ (14). The DHI was developed by Jacobson and Newman and was used as the balance questionnaire (15). Validated Chinese versions of the questionnaires were adopted. All the questionnaires were administered in accordance with the principle of informed consent. The ESS is widely used to assess daytime sleepiness. Participants rate their susceptibility to falling asleep using a scale from 0 to 3 in relation to 8 real-life scenarios (16). Scores are totaled, and a score ≥6 indicates sleepiness, a score ≥12 indicates excessive daytime sleepiness, and a score ≥16 indicates dangerous sleepiness. For the SBQ, a score of 5–8 is categorized as being at high risk of moderate-to-severe OSAHS (14). Under the DHI, the total score can range from 0–100, and a score of 16–34 points indicates a mild handicap, a score of 36–52 points indicates a moderate handicap, and a score of ≥54 points indicates a severe handicap.

Rank correlation coefficient method, application of case-control matching, because apnea has certain direction, namely the subjects in the process of 7 hours of sleep, and record the average apnea duration, the longest apnea duration, average duration of the longest duration, low ventilation, and the longer you sleep, the more into deep sleep, hypoxia, the more obvious. Correlation Kendall test was used for statistical analysis because of its directivity and vestibular function.

The evaluation of vestibular function

The following inner ear vestibular function tests included: a videonystagmography (VNG), positional test, caloric test, ECochG, and vestibular evoked myogenic potential (VEMP) test. The tests were performed using the ICSchartr 200 system (GN OTOMETRICS A/S, Auditory Evoked Potentioal System, ICS Chartr EP 200). The whole measurement of vestibular function was based on the guidelines of the AASM (17).

Statistical analysis

SPSS software (version 23.0; IBM, Armonk, NY, USA) and the chi-square test were used for the statistical analysis. The differences of age and BMI were analyzed by an independent sample *t*-test, and Kendall's tau test was used to test the correlation between 2 indexes.

Results

The demographic data of the OSAHS group and the control group

Participants' demographic data are set out in *Table 1*. There was no significant difference in the gender or age between the 87 OSAHS patients (male 56, female 31) and the 47 (male 28, female 19) healthy volunteers (P>0.05; see *Table 1*). According to the AHI score, there were 30 mild, 27 moderate and 30 severe OSAHS patients in the OSAHS group, and according to the lowest oxygen saturation, there were 28 mild, 30 moderate and 29 severe OSAHS cases in the OSAHS group.

The univariate logistic analysis of canal paralysis (CP) showed that there was a correlation between BMI and CP (P=0.014; see *Table 2*), and the probability of abnormal CP increased 1.791 times with each increase in BMI (OR =1.791, 95% CI: 1.125–2.851); Patients in the OSAHS group were more likely to have abnormal CP than those in the control group (P=0.0291, OR =2.490, 95% CI: 1.097–5.652); Patients with an abnormal ESS score were more likely to have abnormal CP (P=0.0216, OR =2.880, 95% CI: 1.168–7.099). The results of the univariate logistic analysis of the VEMP test revealed a significant positive correlation

Table 1 The demographic data of the OSAHS group and the control group

Variables	Group		P value
	OSAHS	Control	
Sex			0.859[a]
Male	56	28	
Female	31	19	
Age (year)	48.95±13.31	47.68±7.28	0.137[b]
BMI (kg/m^2)	23.72±2.98	23.38±2.04	0.064[b]
AHI score			
Mild	30	–	
Moderate	27	–	
Severe	30	–	
Lowest oxygen saturation			
Mild	28	–	
Moderate	30	–	
Severe	29	–	

Data are presented as No. and mean ± standard deviation. [a], Chi-square test; [b], non-parametric Mann-Whitney U test. OSAHS, obstructive sleep apnea-hypopnea syndrome; BMI, body mass index; AHI, apnea/hypopnea index.

between the DHI score and VEMP (P=0.0061, OR =3.667, 95% CI: 1.449–9.276; see *Table 3*). No statistically significant correlation was found between VEMP and the other variables (P>0.05).

Comparison of inner ear vestibular function between the OSAHS group and control group

The results of the vestibular function examination in 87 cases of the OSAHS group and 47 cases of the control group are set out in *Table 4*. The positive rate of the caloric test of the OSAHS group was significantly higher than that of the control group (P<0.05). The abnormality rates of the positional test, VEMP test, and ECochG of the OSAHS group were higher than those of the control group, but the differences were not statistically significant (P>0.05).

Correlation between the PSG parameters and vestibular function in the OSAHS patients

A 7-hour PSG was performed to monitor the ventilation of the OSAHS patients during sleep. The mean apnea duration, the longest apnea duration, the mean hypopnea duration, and the longest hypopnea duration were all recorded. The correlation of these PSG parameters with inner ear vestibular function was analyzed using the Kendall's tau test. The results are set out in *Table 5*. The results showed that only the longest apnea duration was significantly negatively correlated with the DHI score (r=–0.191, P<0.05).

Discussion

OSAHS is a disease characterized by obstructive apnea and/or respiratory dyspnea-related arousal caused by the repeated collapse of the upper respiratory tract during sleep. Long-term intermittent hypoxia in OSAHS patients may involve the vestibular organs of the inner ear, which may lead to a decline of semicircular canal function that is often bilateral dysfunction. The more severe the hypoxemia, the more obvious the decline of semicircular canal function. With the aggravation of hypoxemia, the chance of bilateral horizontal semicircular canal involvement is also higher. Such patients have semicircular canal dysfunction; however, they lack the typical symptoms of acute vestibular injury, such as vertigo and balance disorder. Han *et al.* found that the positive rate of the caloric test in OSAHS patients was 67.5% (10). Tabuchi *et al.* conducted animal experiments in this field and found that all kinds of internal ear injury could be caused under different degrees of ischemia; for example, squeezing the labyrinthine artery in white guinea pigs caused transient internal ear ischemia. When CAP perfusion was performed, continuous ischemia occurred, and reperfusion after half an hour did not enable recovery to pre-ischemia levels (18).

In this study, in the OSAHS group, the longest apnea duration was correlated with the vertigo index. Among the vertigo indexes, the positional test, VEMP test, and ECochG all reflect changes of semicircular canal function and membranous labyrinth function. However, the average apnea duration, average hypopnea duration, and the longest hypopnea duration had no significant correlation with the balance system. This may be because hypoxia only affects the balance system when the apnea has a long duration.

Olaithe *et al.* performed a meta-analysis and found that OSA studies were accompanied by deficits in attention and memory, suggesting that short-term sleep disturbance in OSA may contribute to deficits in these domains (19). Nocturnal hypoxia and sleep disorder are the main factors of cognitive dysfunction in patients with OSAHS. EL-Gharib

Table 2 Univariate logistic analysis of CP

Variables	CP normal	CP abnormal	P	OR (95% CI)
Vertigo			0.558	1.304 (0.537, 3.165)
≤30	73 (67.59)	35 (32.41)		
>30	16 (61.54)	10 (38.46)		
STOP-BANG			0.1627	1.684 (0.810, 3.502)
Normal	45 (72.58)	17 (27.42)		
Abnormal	44 (61.11)	28 (38.89)		
BMI (kg/m^2)			0.014*	1.791 (1.125, 2.851)
<24	43 (75.44)	14 (24.56)		
24–28	31 (67.39)	15 (32.61)		
≥28	15 (48.39)	16 (51.61)		
Sex			0.0607	0.496 (0.238, 1.032)
Male	40 (58.82)	28 (41.18)		
Female	49 (74.24)	17 (25.76)		
Group			0.0291*	2.490 (1.097, 5.652)
Control	37 (78.72)	10 (21.28)		
OSA	52 (59.77)	35 (40.23)		
Hypnosia			0.0216*	2.880 (1.168, 7.099)
Normal	78 (70.91)	32 (29.09)		
Abnormal	11 (45.83)	13 (54.17)		
Age (year)	47.66±12.59	51.89±12.36	0.0696	1.028 (0.998, 1.058)

Data are presented as n (%) and mean ± standard deviation. *, P<0.05. CP, canal paresis; BMI, body mass index; OSA, obstructive sleep apnea.

et al. applied CPAP to improve the nocturnal hypoxia state and the time of nocturnal apnea in patients with OSAHS (20). As a result, the severity of OSAHS was reduced and the cognitive function of patients with moderate-to-severe OSAHS was improved, but it did not recover to the normal level. This may be related to the irreversible brain damage caused by hypoxia. In the current study, the DHI score increased with the increase of the longest apnea duration in patients with OSAHS, which indicated that the behavior score, body score, and emotion score of the balance system increased, which suggests a certain correlation with cognitive function.

Hypoxic OSAHS not only leads to hearing loss, but also affects the vestibular system. The blood supply to the inner ear comes from the labyrinthine artery. From the labyrinthine artery to the inner ear, the labyrinthine artery can be divided into the anterior vestibular artery and the common cochlear artery. The common cochlear artery branches into the vestibular cochlear artery and cochlear aorta (20). The main control range of the cochlear aorta includes three quarters of the cochlear and the cochlear axis. The vestibular cochlear artery further branches into the ramus cochleae and posterior vestibular artery; the former supplies one quarter of the base and the surrounding cochlear axis. The vestibular anterior artery dominates the upper semicircular canal, horizontal semicircular canal, oval cyst spot, and some balloon spots. Thus, pathological changes in these vessels, alterations in the blood flow, and changes in the blood components would affect the blood supply cochlea and vestibular system, which would cause hearing loss to different degrees and changes in vestibular function. The blood supply to the horizontal semicircular

Table 3 Univariate logistic analysis of VEMP

Variables	Normal VEMP	Abnormal VEMP	P	OR (95% CI)
Vertigo			0.0061*	3.667 (1.449, 9.276)
≤30	90 (83.33)	18 (16.67)		
>30	15 (57.69)	11 (42.31)		
STOP-BANG			0.5063	0.756 (0.332, 1.724)
Normal	47 (75.81)	15 (24.19)		
Abnormal	58 (80.56)	14 (19.44)		
BMI (kg/m^2)			0.9209	0.974 (0.557, 1.644)
<24	44 (77.19)	13 (22.81)		
24–28	37 (80.43)	9 (19.57)		
≥28	24 (77.42)	7 (22.58)		
Sex			0.7638	1.134 (0.498, 2.583)
Male	54 (79.41)	14 (20.59)		
Female	51 (77.27)	15 (22.73)		
Group			0.94	1.034 (0.436, 2.453)
Control	37 (78.72)	10 (21.28)		
OSAHS	68 (78.16)	19 (21.84)		
Hypnosia			0.9155	0.943 (0.319, 2.788)
Normal	86 (78.18)	24 (21.82)		
Abnormal	19 (79.17)	5 (20.83)		
Age (year)	48.02±11.84	52.93±14.74	0.0665	1.032 (0.998, 1.068)

Data are presented as n (%) and mean ± standard deviation. *, P<0.05. VEMP, vestibular evoked myogenic potential; BMI, body mass index; OSAHS, obstructive sleep apnea-hypopnea syndrome.

Table 4 Comparison of inner ear vestibular function between the OSAHS group and the control group

Tests	Group	Cases	Abnormal (%)	Normal (%)	χ^2	P value
Positional test	OSAHS	87	3 (3.45)	84 (96.55)	0.055	1.000
	Control	47	2 (4.26)	45 (95.74)		
Caloric test	OSAHS	87	36 (41.38)	51 (58.62)	4.330	0.040*
	Control	47	11 (23.40)	36 (76.60)		
VEMP	OSAHS	87	17 (19.54)	70 (80.46)	0.276	0.658
	Control	47	11 (23.40)	36 (76.60)		
ECochG	OSAHS	87	9 (10.34)	78 (89.66)	0.003	1.000
	Control	47	5 (10.64)	42 (89.36)		

*, P<0.05. OSAHS, obstructive sleep apnea-hypopnea syndrome; VEMP, vestibular evoked myogenic potential; EcochG, electrocochleogram.

Table 5 Correlation coefficients and significance levels between the PSG parameters and vertigo-related indexes in the OSAHS group

Vertigo-related indexes	Mean apnea duration	Longest apnea duration	Mean hypopnea duration	Longest hypopnea duration
DHI				
r	–0.164	–0.191	0.128	0.076
P	0.079	0.04*	0.169	0.415
Positional test				
r	–0.041	–0.076	0.138	0.061
P	0.655	0.405	0.133	0.507
CP				
r	0.100	0.115	0.018	0.022
P	0.461	0.394	0.896	0.874
VEMP				
r	–0.086	–0.119	0.062	–0.106
P	0.461	0.303	0.599	0.363
ECochG				
r	–0.144	–0.188	0.099	–0.014
P	0.308	0.180	0.484	0.920

*, P<0.05. PSG, polysomnography; OSAHS, obstructive sleep apnea-hypopnea syndrome; DHI, Dizziness Handicap Inventory; CP, canal paresis; VEMP, vestibular evoked myogenic potential; ECochG, electrocochleogram.

canal comes from the anterior vestibular artery, which is a branch of the internal auditory artery. The diameter of the vestibular artery is small, and the collateral circulation is lacking, which make it an energy-consuming organ (11). Thus, due to the special anatomy and function of vestibular organs, OSAHS causes ischemia and hypoxia, which in turn affect vestibular function. Seo *et al.* used hypoxic mice as an OSAHS model and found that the number of mitochondria in the hair cells decreased and the morphology was abnormal in hypoxic mice. VDAC expression increased in the tectum and basement membrane, especially in the hair cells of the mice with chronic hypoxia. This provides evidence of the relationship between OSAHS and the changes of inner ear function and the relationship between mitochondria as a part of pathophysiology (21).

The examination of vestibular dysfunction in this study considered 4 parts: (I) unilateral semicircular CP, which could indicate the lesion of the lateral semicircular canal or afferent nerve conduction pathway on the side of the weakened reaction, and could also be observed in the static compensatory period of vestibular injury; (II) abnormal directional preponderance, which suggests peripheral or central vestibular lesions, but suggests no exact location; (III) bilateral semicircular CP, which mostly suggests bilateral peripheral vestibular lesions or central vestibular lesions; (IV) an enhanced bilateral caloric test response, which was a complaint of some patients, and which also indicates central lesions or unilateral tympanic membrane perforation.

As tympanic membrane perforation was ruled out by otoscope before the examination, the static compensation of central vestibular lesion or vestibular injury was considered. Most of the OHAHS patients had intermittent hypoxia, and their vestibular dysfunction proved that there was some vestibular or central damage. In this study, both groups were examined with the positional test and their rotational nystagmus was recorded. The typical characteristics of rotational nystagmus are rotational nystagmus in a certain direction, often with latency and fatigue, and subjective vertigo. In this study, there was no significant difference between the OSAHS group and the control group, as OSAHS was an intermittent and chronic hypoxic process, and few patients were in the acute stage of vertigo attack when tested; thus, the positive rates of the two groups were low, and there was no difference between the two groups.

In the current study, we found that there was no significant difference in the VEMP and ECochG results between the two groups. There are several possible reasons why CP was affected but VEMP was not in the OSAHS patients. First, repeated apnea leads to a continuous decrease of hemoglobin oxygen saturation, which could further lead to hypoxia during sleep. Additionally, the negative intrathoracic pressure in the OSAHS patients could lead to the slowdown of cerebral blood flow velocity and intermittent hypoxia. During severe ischemia and hypoxia, this kind of chronic hypoxia during sleep affects the vestibular labyrinth. The diameter of the vestibular artery is small, the collateral circulation is lacking, and the inner ear is an organ with high energy consumption. Thus, OSAHS causes ischemia and hypoxia, which in turn affects vestibular function. Second, the pathophysiological examination showed that in the chronic hypoxic mice, the expression in the tectorial membrane and basement membrane, especially in the hair cells, increased, the number of mitochondria in the hair cells decreased, and the morphology was abnormal. Third, VEMP is the response

of sternocleidomastoid muscle to intense short tone stimulation. VEMP originates from the balloon, and its conduction pathway is as follows: inferior vestibular nerve, vestibular nucleus, accessory nucleus and accessory nerve, which are transmitted to the ipsilateral sternocleidomastoid muscle. Additionally, VEMP is a short latency response induced by strong sound, which depends on the tension of muscle activity. Thus, the reflex is suitable for correcting or fine-tuning the autonomic movement of the cervical muscle, stimulating the balloon nerve, and at the same time, excitatory and inhibitory postsynaptic potentials can be recorded in the motor neurons of the cervical muscle. The results provided evidence that the balloon participated in the head motor reflex. As VEMP mainly reflects the head neck muscle movement and balloon nerve function, there was no significant correlation between VEMP and intermittent hypoxia.

Researchers have used CPAP for the treatment of Meniere's disease and found that the main cause of endolabyrinthine hydrops is abnormal cochlear microcirculation (7). CPAP therapy can improve a patient's hypoxia, effectively regulate the central oxygenation and blood flow, and thereby normalize the cochlear microcirculation and reduce endolymphatic edema. Kayabasi *et al.* found that the decrease in semicircular canal function and the decrease proportion of electronystagmogram in moderate and severe OSAHS were significantly higher than the control group (11). At the same time, the results of the positional test, cerebellar function test, and Romberg test were normal. Thus, it can be concluded that severe OSAHS can cause vestibular dysfunction. Cochlear electrogram is often used in patients with Meniere's disease and hydrolabyrinthine. The increase of the endolymph and asymmetric vibration of the basement membrane are the basis of the production of Single Positive (SP), and a ratio ≥0.4 is abnormal.

Sasaki *et al.* and Martini *et al.* (22,23) studied vestibular end organs in the ischemic model by immunoelectron microscopy and found that if the duration of ischemia was 10 minutes, the glutamate levels in the type I and II hair cells and supporting cells of the vestibular decreased, but the morphological changes in the nerve extension and calyces dendrites were not significant. When the ischemia lasted for 30 minutes, the morphological changes were obvious, and the precondition neurons of the inner ear were irreversibly damaged (23,24). In OSAHS patients with neuro-otological diseases, the occlusion of the anterior inferior cerebellar artery is confirmed by pathology, which leads to labyrinthine artery ischemia and cerebellar ischemia, which can lead to central and peripheral vertigo, acute vestibular syndrome, and unilateral hearing loss. Recurrent vertigo or dizziness accompanied by hearing loss and headache may be caused by common pathogenic factors of Meniere's disease and vestibular migraine. In this study, there was no difference in vestibular function between OSAHS patients and controls. This may be because endolymphatic hydrops was not obvious in the OSAHS patients, and a small number of participants showed poor cooperation due to fear of tympanic membrane perforation caused by cochlear electrogram, resulting in the shallow contact of the silver ball electrode with the tympanic membrane. Thus, the significance of this examination is unclear, and needs to be examined in further studies in the future. The results of this study suggest that the increase of intermittent hypoxia and apnea time associated with OSAHS can lead to the decrease of vestibular function caused by inner ear ischemia and further lead to vertigo.

The major limitation of the current study is the sample size. Due to the limitations in funding and time, only 87 patients who had been diagnosed with OSAHS were enrolled in the study. Further, this was a single-center study performed at 1 hospital, which may affect the representativeness of the samples. Thus, multicenter studies with larger sample sizes still need to be conducted to investigate the effects of OSAHS on vestibular function.

In conclusion, intermittent hypoxia in OSAHS can lead to vestibular dysfunction, decreased semicircular canal function, and an increased abnormal CP rate. The longer the longest apnea time, the higher the DHI score. These findings may help to better identify some of the vertiginous symptoms of which OSAHS patients complain.

Acknowledgments

Funding: The study was supported by General program of National Natural Science Foundation of China (No. 81873696), and Beijing Municipal Administration of Hospitals Incubating (No. PX2016031).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-718/rc

Data Sharing Statement: Available at https://apm.amegroups.com/article/view/10.21037/apm-22-718/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-718/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Institutional Review Board of the Beijing Tsinghua Changgung Hospital (Ethics Number: 20150911-05), and informed consent forms were signed by all participants before the study began.

References

1. De Backer W. Obstructive sleep apnea/hypopnea syndrome. Panminerva Med 2013;55:191-5.
2. Brooks DM, Kelly A, Sorkin JD, et al. The relationship between sleep-disordered breathing, blood pressure, and urinary cortisol and catecholamines in children. J Clin Sleep Med 2020;16:907-16.
3. Edwards S, Bijlani S, Fairley H, et al. Frequency and prevalence of obesity and related comorbidities in West Texas. Proc (Bayl Univ Med Cent) 2019;33:1-4.
4. Castello-Branco RC, Cerqueira-Silva T, Andrade AL, et al. Association Between Risk of Obstructive Sleep Apnea and Cerebrovascular Reactivity in Stroke Patients. J Am Heart Assoc 2020;9:e015313.
5. Lisabeth LD, Sánchez BN, Lim D, et al. Sleep-disordered breathing and poststroke outcomes. Ann Neurol 2019;86:241-50.
6. Hermann DM, Bassetti CL. Role of sleep-disordered breathing and sleep-wake disturbances for stroke and stroke recovery. Neurology 2016;87:1407-16.
7. Nakayama M, Masuda A, Ando KB, et al. A Pilot Study on the Efficacy of Continuous Positive Airway Pressure on the Manifestations of Ménière's Disease in Patients with Concomitant Obstructive Sleep Apnea Syndrome. J Clin Sleep Med 2015;11:1101-7.
8. Gallina S, Dispenza F, Kulamarva G, et al. Obstructive sleep apnoea syndrome (OSAS): effects on the vestibular system. Acta Otorhinolaryngol Ital 2010;30:281-4.
9. Li X, Chen WJ, Zhang XY, et al. Inner ear function in patients with obstructive sleep apnea. Sleep Breath 2020;24:65-9.
10. Han X, Lu H, Chen T, et al. Feature of semicircular canal function in obstructive sleep apnea-hypopnea syndrome. Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi 2015;50:482-7.
11. Kayabasi S, Iriz A, Cayonu M, et al. Vestibular functions were found to be impaired in patients with moderate-to-severe obstructive sleep apnea. Laryngoscope 2015;125:1244-8.
12. Iber C, Ancoli-Israel S, Chesson A, et al. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology, and Technical Specifications. 1st ed. Westchester, IL: American Academy of Sleep Medicine, 2007.
13. Hurlston A, Foster SN, Creamer J, et al. The Epworth Sleepiness Scale in Service Members with Sleep Disorders. Mil Med 2019;184:e701-7.
14. Chung F, Abdullah HR, Liao P. STOP-Bang Questionnaire: A Practical Approach to Screen for Obstructive Sleep Apnea. Chest 2016;149:631-8.
15. Jacobson GP, Newman CW. The development of the Dizziness Handicap Inventory. Arch Otolaryngol Head Neck Surg 1990;116:424-7.
16. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991;14:540-5.
17. Malhotra RK, Kirsch DB, Kristo DA, et al. Polysomnography for Obstructive Sleep Apnea Should Include Arousal-Based Scoring: An American Academy of Sleep Medicine Position Statement. J Clin Sleep Med 2018;14:1245-7.
18. Tabuchi K, Ito Z, Wada T, et al. The effect of mannitol upon cochlear dysfunction induced by transient local anoxia. Hear Res 1998;126:28-36.
19. Olaithe M, Skinner TC, Hillman D, et al. Cognition and nocturnal disturbance in OSA: the importance of

accounting for age and premorbid intelligence. Sleep Breath 2015;19:221-30.
20. EL-Gharib AM, Sharsher RS. Effect of nasal continuous positive airway pressure (CPAP) on auditory P300 in obstructive sleep apnea syndrome (OSAS). Egyptian Journal of Ear, Nose, Throat and Allied Sciences 2016;18:55-9.
21. Seo YJ, Ju HM, Lee SH, et al. Damage of Inner Ear Sensory Hair Cells via Mitochondrial Loss in a Murine Model of Sleep Apnea With Chronic Intermittent Hypoxia. Sleep 2017. doi: 10.1093/sleep/zsx106.
22. Sasaki A, Matsubara A, Tabuchi K, et al. Immunoelectron microscopic analysis of neurotoxic effect of glutamate in the vestibular end organs during ischemia. Acta Otolaryngol 2012;132:686-92.
23. Martini A, Luzzi V, Pietrafesa E, et al. Workers with Obstructive Sleep Apnea Syndrome: Proposal of a Clinical-Anamnestic Tool for the Occupational Health Surveillance. Safety and Health at Work, 2022.
24. Wang B, Yao W, Xue Q, et al. Nomograms for predicting difficult airway based on ultrasound assessment. BMC Anesthesiol 2022;22:23.

(English Language Editor: L. Huleatt)

Cite this article as: Li X, Chen W, Liang S, Guo Z, Lu M, Zhang Y, Yuan X, Sun Y, Qu L, Chen Q, Ye J. Clinical case control study analysis of vestibular function in patients with obstructive sleep apnea-hypopnea syndrome. Ann Palliat Med 2022;11(8):2685-2694. doi: 10.21037/apm-22-718

