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Polyneuropathy in obstructive sleep apnea patients

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Abstract

Aim: Hypoxemia due to obstructive sleep apnea (OSA) is thought to cause peripheral nerve damage. A case-control study was conducted to test the accuracy of this phenomenon.

Materials and Methods: The patient group consisted of 45 patients with OSA who had an apnea-hypopnea index (AHI) score of >10 and were newly diagnosed with OSA and control group consisted of 37 individuals who did not have OSA. Sensory and motor nerve conduction investigations were performed on both the upper and right lower extremity Mann-Whitney U, chi square and independent sample T tests were carried out.

Results: Both groups had the same average age of 46. The mean body mass index (BMI) in patients with OSA was 31.81; the average AHI was 55.17; the periodic leg movements in sleep (PLMS) was 30.71; the T90 value was 74.23; the lowest saturation was 37; the average saturation value was 72.97. The other nerves' sensory and motor distal latency lengths were more prolonged than the control group, except the ulnar nerve. The averages of the left median, ulnar, and right peroneal motor nerves' compound motor action potential (CMAP) amplitude were lower in individuals with OSA than in the control group. Compared to the control group, patients with OSA had slower right tibial nerve motor conduction velocity. The mean snap amplitude of bilateral median and left ulnar sensory nerve were higher in patients with OSA.

Conclusion: OSA-induced hypoxia may have an impact on peripheral nerve damage.

Introduction

Repetitive apnea-hypopnea episodes, loud snoring, and intermittent hypoxia-hypercapnia are all symptoms of obstructive sleep apnea (OSA) caused by a partial or total obstruction of the upper airway during sleep [1,2]. Excessive daytime sleepiness and associated neuropsychological disturbances are seen due to non-restful sleep. By various pathophysiological mechanisms, OSA is associated with pre-diabetes, arterial hypertension, hypercoagulability, stroke, arteriosclerosis, severe cardiac arrhythmias, and peripheral neuropathy, all of which lead to increased mortality and cerebrocardiovascular morbidity [3,4]. The impact of OSA on peripheral nerves is not completely understood. It affects 3-10% of the adult population and is associated with age and BMI [5]. Due to the increase in obesity in recent years, it is seen more frequently and is an important public health problem [5,6]. OSA severity is determined by the apnea/hypopnea index (AHI).

The gold standard for diagnosing respiratory illnesses noticed during sleep is polysomnography. It calculates the number of apnea and hypopnea episodes (AHI) that occur per hour of sleep, as well as the oxygen saturation level of hemoglobin (oxygen saturation index, ODI) and a variety of other sleep factors [7].

Nerve conduction studies are the most sensitive and repeatable test in evaluating peripheral nerve functioning, and electroneurography is commonly used for the standard neurophysiological procedure [8,9]. Many disorders have been linked to peripheral nerve damage, including chronic obstructive pulmonary disease (COPD), characterized by persistent hypoxia, polystemia vera, and atherosclerotic peripheral vascular disease [10-12]. In most of these disorders, nerve loss begins in the lower limbs, with sensory nerves being the first to be impacted [6]. There is a link between persistent hypoxia and peripheral nerve injury, frequency, and severity [13].

In the literature, few investigations examine persistent in-

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termittent hypoxia, peripheral nerve injury, and entrapment neuropathies in OSA patients. The sural sensory nerve action potential (SNAP) was lower in the OSA group than in the control group in two experiments on the lower limbs, indicating axonal nerve injury. Continuous positive airway pressure (CPAP) treatment helped alleviate some of the symptoms [3,14]. Carpal tunnel syndrome (CTS) was substantially more common in patients with OSA than in the control group in a study investigating the condition [1]. Another study discovered that ulnar nerve entrapment at the elbow level was more common in OSA patients and that the prevalence increased with positional OSA [15]. Finally, although the upper extremities and motor nerves are less impacted in OSA patients, axonal damage occurs in motor-sensory neurons in the upper and lower limbs, according to a recent study that included upper extremity nerve conduction investigations [6].

As a result, this experimental study examined neurography properties and the existence of entrapment neuropathy (CTS, ulnar entrapment at the elbow level) in both the upper and lower extremities more detailed. The study hypothesizes whether motor-sensory peripheral nerve evoked potentials are lower in patients with OSA, or the frequency of entrapment neuropathy is higher in both the upper and lower limbs than in the control group.

Materials and Methods

Study design

54 patients with an AHI score of >10 and newly diagnosed OSA by all-night polysomnography (PSG) and 37 healthy control groups without clinical signs and symptoms of OSA were involved in the study at the Inonu University Chest Diseases Sleep Center. Exclusion criteria meant that nine patients were ruled out of the research. In the neurophysiology lab at Inonu University, nerve conduction studies were conducted on 45 OSA patients and a control group. The patient and control groups were perfectly matched in age, gender, and BMI.

All of the tests were carried out per the institution's policies. The study received approval from Inonu University's Local Ethics Committee (ID number:2016/217) and followed the Declaration of Helsinki's ethical norms. Each participant in the study was asked to sign a written informed consent form.

Clinical examination

All individuals were subjected to a thorough neurological examination. Peripheral motor weakness, sensory loss, and hyporeflexia-areflexia were recorded on examination. Two of these findings were called as probable, if there is any, it is concluded as possible polyneuropathy. Double blind evaluation was used in the study.

Exclusion criteria

Diabetes mellitus, chronic kidney disease, alcoholism, cancer, using of neurotoxic drug, hematological disease, peripheral vascular disease, thyroid dysfunction, vitamin B12-folic acid deficiency, cervical radiculopathy, and rheumatic disease may cause polyneuropathy and entrapment neuropathy were excluded in all groups. Those with compressive mononeuropathies, radicular-brachial-lumbosacral plexus lesions, peripheral nerve damage, and other extra vertebral causes were excluded. The probable or suspected polyneuropathy on neurological examination was eliminated from the control group.

Polysomnography

Polysomnographic examinations were performed overnight concerning multichannel monitoring, including electroencephalography electrodes, chest wall movement, abdominal movement, arterial oxygen saturation, and electrocardiography electrodes. It was accepted that an apnea period when the airflow declined by at least 90% below baseline for 10 seconds or longer [16]. Hypopnea was considered when the airflow decreased by at least 30% for 10 seconds or more, and the associated oxygen saturation (SaO_2) was decreased by 3% or more [16]. The average number of apneas and hypopneas per hour during sleep determined the AHI. OSA was defined as having an AHI of more than 10. The scoring criteria were taken as reference in the research of Mario et al. [6].

Nerve conduction studies

The keypoint electroneurographic system (Dantec, Denmark) was utilized to perform nerve conduction experiments, which were carried out using generally used standard methodologies. The motor and sensory nerve conduction velocities (m/s), the size of the amplitude compound motor action potentials (CMAP) (mV), the SNAP amplitude (V), and the distal motor and sensory latency (ms/cm) were all recorded. All nerve conduction amplitudes and velocities were measured orthodromically with reference values derived using previously established standards [17]. Blind evaluation was performed. Triple stimulation from the wrist, and both distal - proximal elbow was used to treat ulnar entrapment neuropathy.

Nerve conduction investigations were performed on all individuals in three extremities: both of upper and right lower extremity. The motor and sensory conductions of the bilateral median and ulnar nerves and the motor conductions of the right peroneal and tibial nerves and the sensory conduction of right sural nerve were studied. Blind evaluation was performed.

Statistical analysis

To review data and analyze descriptive statistics, the SPSS 17.0 software package (SPSS Inc., Chicago, IL, USA) was utilized (frequency, mean, SD). Also the power analysis was made by using G*Power 3.1.9.6 program. The Kolmogrov–Smirnov test was performed to evaluate the data distribution. For demographic characteristics, descriptive statistics were deployed. The continuous variables were analyzed using the independent sample T-test (parametric test) and the Mann Whitney U-test (nonparametric test). For comparing clinical data between groups, the chi-square test was also applied for categorical variables. $p<0.05$ was recognized as the level of significance. Probable sampling technique was used in the study The sample size was determined by using G*Power 3.1.9.6 statistical analysis software package. The confidence intervals

and the total margin error were selected as %95 and %5 respectively. The power was selected as %80. The effect size was determined based on the Larissa et al.[18]. So the current sample size was found suitable in accordance with the statistical calculations. Table 1 represents clinical data of the patients.

Results

The average age of both groups were calculated as 46 in the study. In terms of the female-to-male ratio, there was no statistical difference between the two groups. The average BMI of OSA patients was found 31.81. The mean AHI index in OSA patients was 55.17. PLMS was found as 30.71. In patients with OSA, the mean saturation was recorded as 72.97.

In terms of right and left motor median nerve distal latency, there was a statistically significant difference between the two groups (P=0.000, P=0.000). Although the mean distal latency in OSA patients is longer than in the control group, it is still within normal limits. The amplitudes, conduction velocities, and F latency of the right motor median nerve did not change significantly. Although the left motor median nerve's mean CMAP value was lower in OSA patients than in the control group, it was still within normal limits (P=0.041). There was no statistical difference between the two groups regarding left motor median nerve conduction velocity and F latency (Table 2).

There was no significant difference between the two groups regarding right motor ulnar nerve distal latency, CMAP, conduction velocity, and F latency. Even though the mean of left motor ulnar nerve CMAP was higher in the control group than in the OSA group, both groups were within the normal range (P=0.021). There was no statistically significant difference in the left motor ulnar nerve distal latency, conduction velocity and F latency (Table 3). In all groups, the mean distal latency of the right peroneal nerve was within normal limits. However, it was prolonged in OSA patients (P=0.000). The control group's mean CMAP value was higher yet again (P=0.002). There was no significant difference between the two groups regarding

Table 1. Demographic and clinical data of patients.

Variables	OSA Group (n=45)	Control Group (n=37)	P
	Mean±STD	Mean±STD	
Age	46.84±11.73	46.46±13.62	0.891*
BMI	31.81±4.33	-	
AHI	55.17±25.69	-	
PLMS	30.71±37.84	-	
T90	74.23±73.40	-	
Mean Saturation	72.97±12.97	-	
Gender	n(%)	n(%)	
Female	6 (13.3)	7 (18.9)	0.491**
Male	39 (86.7)	30 (81.1)	

* Independent Sample test, ** Chi Square Test.

Table 2. Comparison of right and left motor median nerve characteristics.

Variables		OSA Group (n=45)	Control Group (n=37)	P
		Mean±STD	Mean±STD	
RMMN	Distal latency	3.74±1.11	3.05±0.35	0.000[a]
	Amplitude	8.14±2.52	8.01±2.20	0.803[b]
	Conduction velocity	55.83±6.34	56.48±4.68	0.604[b]
	F latency	21.88±3.23	21.22±2.23	0.253[a]
LMMN	Distal latency	3.60±0.88	3.03±0.35	0.000[a]
	Amplitude	7.19±2.24	8.45±1.65	0.041[a]
	Conduction velocity	56.64±6.03	55.54±4.17	0.349[b]
	F latency	21.09±2.73	20.42±2.54	0.146[a]

a Mann Whitney u Test, b Independent Sample t test, RMMN: Right Motor Median Nerve, LMMN: Left Motor Median Nerve.

Table 3. Comparison of right and left motor ulnar nerve characteristics.

Variables		OSA Group (n=45)	Control Group (n=37)	P
		Mean±STD	Mean±STD	
RMUN	Distal latency	2.89±1.13	2.70±0.34	0.447 [a]
	Amplitude	7.09±2.06	7.63±1.75	0.409 [a]
	Conduction velocity	57.59±7.92	4.70±0.77	0.327[b]
	F latency	21.96±3.02	21.04±3.30	0.072 [a]
LMUN	Distal latency	2.78±0.75	2.73±0.26	0.197 [a]
	Amplitude	7.16±1.87	8.02±1.63	0.021[a]
	Conduction velocity	57.14±7.16	4.89±0.80	0.147 [b]
	F latency	21.93±2.99	21.76±2.71	0.787 [b]

a Mann Whitney u Test, b Independent Sample t test, RMUN: Right Motor Ulnar Nerve, LMUN: Left Motor Ulnar Nerve.

Table 4. Comparison of right peroneal and tibial nerve characteristics.

Variables		OSA Group (n=45)	Control Group (n=37)	P
		Mean±STD	Mean±STD	
RPN	Distal latency	4.64±1.14	3.73±0.65	0.000[a]
	Amplitude	4.38±1.36	5.44±1.20	0.002[b]
	Conduction velocity	48.74±6.86	48.59±3.87	0.908[b]
	F latency	26.09±9.24	23.90±6.28	0.661[a]
RTN	Distal latency	5.09±1.13	4.54±0.50	0.008[a]
	Amplitude	6.33±2.63	6.67±2.67	0.571[b]
	Conduction velocity	46.48±6.90	48.67±4.03	0.022[a]
	F latency	23.72±8.66	20.64±3.69	0.048[b]

a Mann Whitney u Test, b Independent Sample t test, RPN: Right Peroneal Nerve, RTN: Right Tibial Nerve.

Table 5. Comparison of right and left sensorial median nerve characteristics.

Variables		OSA Group (n=45)	Control Group (n=37)	P
		Mean±STD	Mean±STD	
RSMN	Distal latency	3.23±0.75	2.86±0.26	0.010[a]
	Amplitude	27.16±10.85	22.19±10.73	0.006[a]
	Conduction velocity	53.42±9.03	54.07±6.71	0.783[a]
LSMN	Distal latency	3.24±0.76	2.92±0.25	0.034[a]
	Amplitude	27.49±11.61	21.33±9.34	0.003[a]
	Conduction velocity	53.04±8.43	53.98±4.57	0.545[b]

a Mann Whitney u Test, b Independent Sample t test, RSMN: Right Sensorial Median Nerve, LSMN: Left Sensorial Median Nerve.

Table 6. Comparison of right and left sensorial ulnar nerve characteristics.

Variables		OSA Group (n=45)	Control Group (n=37)	P
		Mean±STD	Mean±STD	
RSUN	Distal latency	2.71±0.72	2.71±0.29	0.106[a]
	Amplitude	20.95±6.63	18.52±7.59	0.127[b]
	Conduction velocity	56.46±7.13	54.71±6.16	0.246[b]
LSUN	Distal latency	2.78±0.86	2.65±0.23	0.415[a]
	Amplitude	22.00±7.59	18.71±6.12	0.021[a]
	Conduction velocity	56.50±7.55	55.41±4.96	0.100[a]

a Mann Whitney u Test, b Independent Sample t test, RSUN: Right Sensorial Ulnar Nerve, LSUN: Left Sensorial Ulnar Nerve.

Table 7. Comparison of right sural nerve characteristics.

Variables	OSA Group (n=45)	Control Group (n=37)	P
	Mean±SD	Mean±SD	
Distal latency	3.53±0.96	3.04±0.57	0.026[a]
Amplitude	10.14±5.76	10.18±2.86	0.654[a]
Conduction velocity	47.90±7.50	50.88±7.02	0.102[a]

a Mann Whitney u Test.

conduction velocity and F-latency.

Although both groups' right tibial nerve distal latency was within normal limits, the OSA patient group was longer (P=0.008). In terms of CMAP, there was no significant difference between the two groups. Although the control group's mean conduction velocity was higher, both groups' mean conduction velocity was within the normal range (P=0.022). Although it was still within the usual range, the OSA group had a longer mean F latency than the control group (P=0.048, Table 4).

Although the OSA patient group had a longer mean right sensory median nerve distal latency, it was still within the normal range (P= 0.010). The OSA patient group's mean SNAP value was higher than the control group's (P=0.006). In terms of conduction velocity, there was no significant difference between the two groups. The OSA patients had a prolonged left sensory median nerve distal latency. On the other hand, the mean value is within the usual range (P=0.034). The OSA group had a greater mean SNAP value (P=0.003). In terms of mean conduction velocity, there was no significant difference between the two groups (Table 5).

No statistically significant differences were identified regarding right sensory ulnar nerve distal latency, SNAP value, and conduction velocity. The left sensory ulnar nerve SNAP value was greater in OSA patients (P=0.021). No significant differences were discovered between mean distal latency and conduction velocity (Table 6).

Although both groups' right sural nerve distal latency was within normal limits, the OSA patient group was longer (P=0.026). No significant differences were discovered in terms of SNAP and conduction velocity (Table 7).

Discussion

The mean AHI index was found as 55.17 in this investigation. The mean saturation was 72.97 percent. Similar cases have been found in the literature [19].

OSA is associated with proinflammatory mediators in the literature [2,18], which is hypothesized to play a role in the pathophysiology of carpal tunnel syndrome. Carpal tunnel syndrome was detected in 27.5 percent of OSA patients in a research [1]. The study discovered that OSA patients have a longer motor and sensory median nerve distal latency. Although the left motor CMAP's mean value is within acceptable limits, it is lower in OSA patients than in the control group. According to the research, recurren intermittent hypoxemia in OSA is an independent risk factor for peripheral nerve injury [19].

Ulnar nerve entrapment neuropathy among upper extremity neuropathies is the second most frequent after CTS [20]. Topcuoglu et al. [15] frequently detected ulnar nerve entrapment neuropathy in OSA patients. OSA patients had lower mixed and sensory nerve amplitudes, according to Mayer et al., [21]. According to Ludeman et al., recurrent intermittent hypoxemia contributes to peripheral nerve damage in OSA patients [19]. Topcuoglu et al. [19] found that the left ulnar nerve CMAP value was lower in patients with OSA than in the control group. This situation may indicate peripheral nerve damage caused by recurrent hypoxemia.

The average distal latency of the peroneal and tibial nerves was found to be longer in OSA patients comparison to control group. Peripheral nerve injury is usually caused by a lower peroneal CMAP amplitude and a lower tibial nerve conduction velocity.

Although the mean sural nerve distal latency was within normal limits, it was longer in the OSA group than in the control group in the study. As previously stated, this could lead to peripheral neuropathy in the future. In their study, Rainer et al. [3] found a decrease in the sural nerve SNAP value in OSA patients comparison to the control group.

The literature contains findings that show parallelism with this situation [22]. Prolongation in distal latency, low amplitude, and deceleration in nerve conduction velocity are the indicators of polyneuropathy. Examples of this subject are a similar trend in the statistical results of the current study. The limitations of the current studies are expressed as follows: the number of patients could be more. The results of the post-treatment effect could be more beneficial. A nerve conduction study that can be done after hypoxia treatment may give more concrete information.

Conclusion

In this study, patients with OSA had their peripheral nerve distal latency, amplitude, conduction velocity, and F latency length compared to a control group. The evidence supporting peripheral neuropathy in OSA patients versus the control group is determined (Prolongation in distal latency, low amplitude, and deceleration in nerve conduction velocity).

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Conflict of interest

The authors declare that they have no competing interest.

Financial disclosure

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Ethics approval

The study received approval from Inonu University's Local Ethics Committee (ID number:2016/217) and followed the Declaration of Helsinki's ethical norms.

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