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Original Article

Hypertension in patients with sleep disordered breathing: cause or result? a cross-sectional analysis

Murat Kayabekir[1], Omercan Topaloglu[2]

[1]Regional Training and Research Hospital, Sleep Disorder Center, Electrophysiology Laboratory, Erzurum, Turkey
[2]Inonu University Faculty of Medicine, Department of Internal Medicine Division of Endocrinology, Malatya, Turkey

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Abstract

Aim: Sleep disordered breathing and its most frequent presentations, cardiovascular complications of OSAS, are important, frequent and not well known causes of mortality and morbidity. When considering physiological hemodynamic processes during sleep, togetherness of HT and OSAS become an important clinical picture. To investigate the frequency of hypertension in 'Obstructive Sleep Apnea Syndrome' (OSAS) patients applied to sleep laboratory.
Study Design: Retrospective clinical study.
Material and Methods: The test protocol consisted of the PSG recording and diagnosis. Sleep stages and respiratory events observed during sleep were evaluated according to "American Academy of Sleep Medicine" (AASM). The blood pressure measured manually by a sphygmomanometer and the measurements occur 3 times on the left arm. Data analysis was performed using IBM SPSS 23.0 statistical software package. Data were analyzed using descriptive statistical methods (frequency, percentage, mean, standard deviation, median, min-max).
Results: Blood pressure measurements of 336 patients were evaluated. 98 (48 male, 50 female) of 336 OSAS patients were diagnosed as hypertension (29%). Hypertensive male patients had 3.3 times increased risk to be diagnosed as severe OSAS than female patients (OR=3,30; 95% CI=1,436-7,585). Together with this, hypertension frequency was found as 29% in patients with sleep disordered breathing.
Conclusion: Finally; although hypertension and OSAS seem to be distinct clinical pictures, co-existence of these two disorders has been increased. Frequency of hypertension increases with increasing severity of OSAS. Hypertensive patients have increased risk for developing OSAS.

Keywords: Hypertension; Risk For OSAS; Coronary Risk.

INTRODUCTION

Maintenance of sleep health is as important as awakening to protect and sustain body health. Cardiovascular and respiratory systems continue to work in sleep by the rules of sleep physiology as all the other body systems. In general aspect, blood pressure and heart rate decrease during sleep. Hemodynamic changes occurred during normal physiological sleep is under the effect of autonomic nervous system (1). Two different stages of sleep lead different effects on cardiovascular system: a) NREM (non-rapid eye movement; calm and synchronized sleep, deep wave sleep). B) REM (rapid eye movement; dynamic, asynchronous, paradoxical sleep) (2). Sympathetic nervous system activity, heart rate, blood pressure and blood pressure fluctuations decrease in NREM sleep, and are lower than in awakening. Blood pressure increase and its regulation is disturbed during REM sleep; but still levels are lower than those of awaken period (3,4).

Sleep disordered breathing consists of simple snoring, upper airway resistance syndrome, obstructive sleep apnea syndrome (OSAS), central sleep apnea syndrome, Cheyne-Stokes breathing, obesity hypoventilation syndrome (5).

Most of the subjects referred to sleep clinics and laboratory experience sleep disordered breathing. Each one subject of four has the risk of development of OSAS. The most important risk factor for OSAS is age (40-60) and male sex. After 65 years old, it is known that the risk of disease decreases (6,7).

OSAS is a disease affecting personal life by extensive complications and so crucial to be treated. It is a syndrome

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Corresponding Author: Murat Kayabekir, Regional Training and Research Hospital, Sleep Disorder Center, Electrophysiology Laboratory, Erzurum, Turkey, E-mail: kayabekirmurat@gmail.com

characterized by recurrent sleep arrest or decrease during sleep, interrupted sleep, increased blood pressure, impaired glucose tolerance and daytime sleepiness (8-10). The other factors predisposing OSAS consist of race, obesity, neck circumference, cigarette-alcohol-sedative usage, genetic factors, comorbid disorders (acromegaly, hypothyroidism, Down syndrome, storage disorders like amyloidosis and mucopolysaccharidosis), posture and gravity, anatomic factors, and hormones (11).

Major symptoms consisting snoring, respiratory arrest during sleep determined by relatives of patients, and excessive daytime sleepiness are so important criteria for diagnosis of the disease. Polysomnography (PSG) is the gold standard method for diagnosis of OSAS. Characteristic PSG findings in OSAS may be as followings: a) increase in superficial sleep, decrease in deep sleep and REM b)apnea and hypopnea repeat frequently c) oxygen desaturation repeat frequently d)REM sleep causes increasing apnea frequency and duration, and severity and duration of oxygen desaturation. Recumbent position also contributes to these increments. e) it is typical to observe paradoxical chest and abdominal movements f) heart rate generally slows down during apnea, and fastens after apnea; arrhythmia may be seen. g) irregular snoring interrupted with frequent apnea is heard in respiratory voice recording (Figure1) (12).

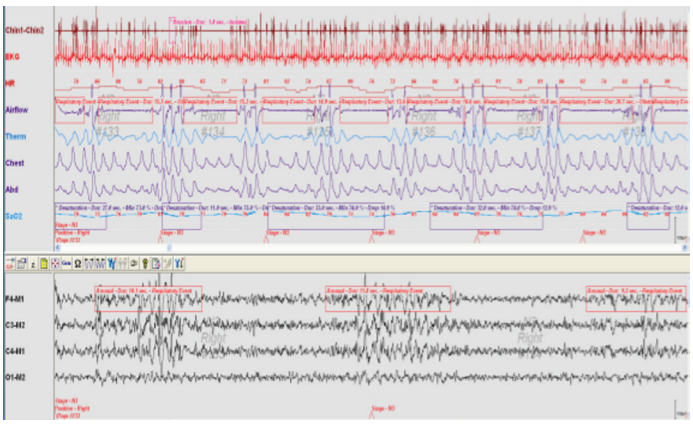

Figure 1. Characteristic findings of PSG in OSAS (frequently recurrent apnea, paradoxical chest-abdomen movements, decrease in oxygen saturation, arousal). (The Center of Sleep Disorders, Archive of Electrophysiology Laboratory, 2016, Erzurum, Turkey).

Degree of the disease is determined by AHI (apnea-hypopnea index; it is achieved by dividing sum of number of apnea and hypopnea to sleep duration in terms of hours) value established according to PSG results (Table 1).

Table 1. Classification of OSAS.

AHI	Severity of OSAS
5<	Normal
5-15	Slight
16-30	Moderate
>30	Severe

Sleep apnea syndrome could be mentioned if the index is higher than 5, but the values of clinical importance are 15 or higher. Clinical signs and complications respecting a lot of systems may develop in OSAS. Complications related to cardiovascular system are frequently seen. Hypertension (systemic, pulmonary), coronary artery disease (myocardial infarction, angina pectoris), ventricular hypertrophy and dysfunction (congestive heart failure), cardiac arrhythmia (bradycardia, sinus tachycardia, atrioventricular block, ventricular and atrial ectopic contraction) are frequently encountered cardiovascular events in OSAS.

The association between OSAS and hypertension (HT) has been shown in a lot of epidemiological studies. In cases with OSAS, increased blood pressure response against progressive hypoxemia ensues; recurrent OSA initiates hypertension by causing continuous increments in sympathetic tone. In OSAS patients, risk of development of hypertension increases proportionally with the disease severity. Pulmonary vasoconstriction resulting from alveolar hypoxia developed during apnea may cause sudden increase in pulmonary arterial pressure and pulmonary hypertension (13,14). Co-existence of OSAS with diseases which endothelial dysfunction has an important role in its physiopathological basis is seen frequently. Endothelial dysfunction and atherosclerosis take important roles in development of cardiovascular events in OSAS. The risk factors for OSAS (age, male sex, obesity, cigarette and alcohol use) are also well known risk factors for hypertension and coronary artery disease. In subjects with coronary artery disease, OSAS has been determined more frequently (30%). In OSAS patients, it has been shown that the risk of development of coronary artery disease was 5 times higher, independent of other risk factors (15-17).

Some studies reported the frequency of hypertension as 30-60% in OSAS patients (18). We aimed to detect the frequency of hypertension in severe or moderate degree OSAS patients referred to.

MATERIAL and METHODS

Between 2013 and 2014, 910 patients consulted to our laboratory with snoring, witnessed apneas, excessive daytime sleepiness were examined with PSG. Of total 336 patients (diagnosed with sleep disordered breathing), 98 patients having both moderate (15<AHI≤30) or severe (AHI>30) OSAS and hypertension were included in the study. The group of the patients who are candidates for future hypertension (the group with a diastolic pressure of 85-89 mmHg and a systolic pressure of 130-139 mmHg) was excluded from this study. Moderate or severe OSAS patients who were hypertensive or had systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥90 mmHg measured after 5 minutes rest in subsequent three follow-up visits were accepted as hypertensive. The blood presure manually measurements occur 3 times on the left arm by a sphygmomanometer that the measurements occur as twice early in the morning and for once at night just before the PSG. Data analysis was performed using

IBM SPSS 23.0 statistical software package. Data were analyzed using descriptive statistical methods (frequency, percentage, mean, standard deviation, median, and min-max). We used multivariate linear regression model to analyze the effects of AHI on hypertension. Regression model explained AHI change with a rate of 56% (R2 = 0,556) (Diastolic Arterial Pressure-DAP), with a rate of 70% (R2 = 0,698) (Systolic Arterial Pressure-SAP). This model was found as statistically significant [DAP= 89,2+0,38 x AHİ, SAP = 134,9 + 0,40 x AHİ] (Figure 2).

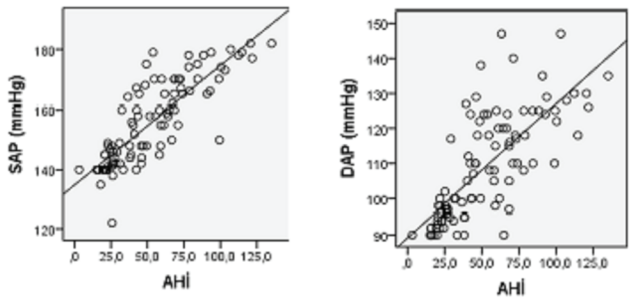

Figure 2. Multivariate linear regression model to analyze the effects of AHI on hypertension (SAP. Systolic Arterial Pressure; DAP. Diastolic Arterial Pressure).

PSG includes six electroencephalography (EEG) channels, two electrooculography (EOG) channels, one submental muscle electromyography (EMG) channel, two EMG channels fixed on both anterior tibial mucles, one channel nasal cannula to measure oro-nasal air flow, one channel oro-nasal thermal sensor, two channels inductive plethysmography to show respiratory effort of thorax and abdomen, one channel "body position" sensor to determine body position, one channel finger probe pulse oximeter measuring arterial oxyhemoglobin saturation (SpO2), and simultaneous video recording.

Sleep stages and respiratory events observed during sleep were evaluated according to "American Academy of Sleep Medicine" (AASM) guideline published in 2007. Apnea was defined as interruption of oronasal airflow at least 10 seconds. Hypopnea was defined as decreased oronasal airflow and oxygen saturation by at least 50% and 3%, respectively, together with arousal. Arousal was defined as waking up or passing to superficial sleep stage during sleep.

RESULTS

336 moderate or severe OSAS patients were selected from 910 sleep disordered patients. Blood pressure measurements of 336 patients were evaluated. 98 (48 male) of 336 OSAS patients were diagnosed as hypertension (29%).

Mostly, male patients between 50 and 60 years old or 40 and 50 years old were referred to laboratory. Female patients were mostly between 50 and 60 years old. Two third of the patients were male. It was found that statistically significant differences between genders according to distribution of age groups were present (p<0,05) (Table 2). 71% of moderate or severe OSAS patients were male, 29% were female. There were no statistically significant differences between genders according to being diagnosed as moderate or severe OSAS in laboratory (p>0,05) (Table 3).

There was statistically significant difference between genders according to being diagnosed as moderate and severe OSAS in laboratory for hypertensive patients(p<0,05). Risk of hypertensive male patients to be diagnosed as severe OSAS was 3,3 times higher than the risk of hypertensive female patients (OR=3,30, %95 CI=1,436 -7,585) (Table 4).

Hypertension or co-existent vascular disorders were not found in OSAS patients of between 20 and 30 years old or between 30 and 40 years old. Co-existence of diabetes mellitus (DM) is frequently seen in moderate or severe OSAS patients ≥60 years old. There were no significant differences between DM and congestive heart failure groups according to the age of the patients (p>0,05) (Table 5).

Table 2. Distribution of patients according to age and gender (P<0,0001, χ^2=33,977, DF=4)

Age (years)	Male	Female	Total
		n (%)	
20-30	47 (7,8)	33 (10,7)	80 (8,8)
30-40	89 (14,8)	23 (7,4)	112 (12,3)
40-50	170 (28,3)	64 (20,7)	234 (25,7)
50-60	247 (41,1)	133 (43,0)	380 (41,8)
≥60	48 (8,0)	56 (18,1)	104 (11,4)
Total	601 (100,0)	309 (100,0)	910 (100,0)

Table 3. Distribution of moderate and severe OSAS patients (p=0,308, χ^2=1,038, DF=1)

	Male	Female	Total
		n (%)	
Moderate	119 (49,6)	41 (42,7)	160 (47,6)
Severe	121 (50,4)	55 (57,3)	176 (52,4)
Total	240 (100,0)	96 (100,0)	336 (100,0)

Table 4. Distribution of moderate and severe OSAS patients having also hypertension (p=0,008, χ^2=7,035, DF=1, OR=3,30, %95 CI=1,4357-7,5851, Z=2,812, P=0,005)

	Male	Female	Total
		n (%)	
Moderate	15 (31,3)	30 (60,0)	45 (45,9)
Severe	33 (68,8)	20 (40,0)	53 (54,1)
Total	48 (100,0)	50 (100,0)	98 (100,0)

Table 5. Distribution of co-existent vascular disorders of the patients with moderate or severe OSAS and hypertension (p=0,296, χ^2=1,094, DF=1)

Age (years)	Diabetes Mellitus	Congestive Heart Failure
	n (%)	
40-50	8 (14,3)	--
50-60	18 (32,1)	6 (40,0)
≥60	30 (53,6)	9 (60,0)
Total	56 (100,0)	15 (100,0)

Table 6. Distribution of mean systolic and diastolic blood pressure values of OSAS patients

Blood Pressure (mm-Hg)	Male	Female
Systolic	160 ±10.6	145 ±5.9
Diastolic	100 ±5.0	95 ±6.3

DISCUSSION

Sleep disordered breathing and its most frequent presentations, cardiovascular complications of OSAS, are important, frequent and not well known causes of mortality and morbidity. Myocardial infarction, unstable angına pectoris, ventricular tachyarrhythmias, pulmonary embolism, ischemic and hemorrhagic cerebrovascular events, rupture of thoracic aorta and sudden cardiac death are often seen in REM sleep periods detected frequently in the early morning, which autonomic instability (and sudden sympathetic discharge), thrombocyte aggregation, plaque rupture and coronary spasm are triggered in. Sleep disordered breathing, especially OSAS, provokes these clinical pictures.

When considering physiological hemodynamic processes during sleep, togetherness of HT and OSAS become an important clinical picture. In several studies, hypertension was observed by 30-60% in OSAS of which importance and frequency was well known (18-20). In our study, the frequency of systemic hypertension was found as 29% in moderate and severe OSAS patients who had sleep disordered breathing.

In Turkish hypertension consensus report, the prevalence of hypertension was determined as 31,8% (female 36,1%, male 27,5%), 4 years incidence rate was determined as 21,4% (>65 years old 43,3%) in Turkish adults in population based epidemiological studies (21,22). Actually, in our study, prevalence of HT was 29% in patients with sleep disordered breathing.

OSAS is more frequently seen in patients previous hypertension. In the study done by Fletcher et al., PSG was applied to all hypertensive patients regardless of the symptoms, and AHI was determined as >10. Moreover, 2668 patients complaining snoring were followed by 10 years in a study, and the risk of development of hypertension was observed higher in these patients (23).

There was statistically significant difference between genders according to being diagnosed as moderate and severe OSAS in our study group with sleep disordered breathing and hypertension (p<0,05). Male hypertensive patients had 3,3 times higher risk of being diagnosed as severe OSAS in laboratory in our study (OR=3,30, 95% CI=1,436 -7,585).

In community, each one of four patients has risk of development of OSAS. 36% of the patients referred to our center had clinically important (AHI>15) moderate and severe OSAS.

It is known that the risk of development of disease decreases after age of 65. The patients referred to our laboratory were mostly in between 40 and 60 years old. We found that there was no significant difference between genders according to being diagnosed as moderate or severe OSAS (p>0,05).

OSAS is accepted as an independent risk factor for systemic hypertension anymore. Co-existence of OSAS and systemic hypertension increases mortality and morbidity. The features of hypertension in OSAS patients are different from those of essential hypertension. Diurnal variability of blood pressure is lost in OSAS patients. Blood pressure does not decrease at night in these patients, so they are non-dippers. This alteration may be accepted as an indicator of developing hypertension further. Hypertension is often diastolic and non-dipper nocturnal pattern in apneic patients (24-26). In our study, mean diastolic blood pressure in male patients with sleep disordered breathing was 100 mm-Hg, in female patients it was 95 mm-Hg.

Tkacova et al. searched the association between oxygen desaturation index (ODI) and hypertension in their study. As a result they found that both AHI and ODI were associated with hypertension independent of other risk factors such as age, smoking, obesity, dyslipidemia and DM (27).

OSAS is accepted as one of the preventable causes of hypertension in JNC-7 (Joint National Committee) report for protection, diagnosis, evaluation and treatment of hypertension. Blood pressure of hypertensive OSAS patients may be controlled with 'continuous positive airway pressure' (CPAP) (28). Recent studies showed that OSAS was associated with the mediators leading endothelial injury. Disorders of endothelial dysfunction frequently exist with OSAS. In our study, co-existence of DM and congestive heart failure was seen in hypertensive OSAS patients in age groups of 50-60 and >60 years-old.

CONCLUSION

Although hypertension and OSAS may be seen as two distinct clinical entities, the frequency of co-existence of these disorders has been increased. As the severity of OSAS increases, the frequency of hypertension in OSAS patients increases. From a different viewpoint, hypertensive patients have increased risk of developing OSAS. In untreated OSAS patients; it may lead hypertension, myocardial infarction, ventricular tachyarrhythmia, pulmonary embolism, ischemic-hemorrhagic cerebrovascular accidents and sudden cardiac death. Due to the high frequency of sleep disorders in population; sleep physiology and disorders, especially OSAS and its severe clinical complications should be explicated to medical doctors, dentists and to other health care professionals. Correct diagnosis by electrophysiological signaling in sleep laboratories should also be associated with especially internal medicine, cardiology, neurology, pulmonology and psychiatry. It should be kept in mind that blood pressure of hypertensive patients with sleep disordered breathing could be controlled with CPAP therapy.

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