Comparison of Polysomnography Variables in Obstructive Sleep Apnea Patients with or without Excessive Daytime Sleepiness

Gündüz Aşırı Uykululuğu Olan ve Olmayan Obstrüktif Uyku Apneli Hastalarda Polisomnografik Değişkenlerin Karşılaştırılması

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Geliş Tarihi/*Received:* 20.06.2013
Kabul Tarihi/*Accepted:* 29.01.2014

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ABSTRACT Objective: Excessive daytime sleepiness (EDS) is a common symptom in patients with obstructive sleep apnea (OSA), and the reason for this could not be fully elucidated. The aim of this study was to compare polysomnographic and demographic features of patients with OSA with or without EDS according to Epworth Sleepiness Scale (ESS). **Material and Methods:** A total of 82 adult patients who were diagnosed with OSA with polysomnography were retrospectively divided into 2 groups in terms of having EDS (ESS>10) or not (ESS≤10) according to ESS score. **Results:** Forty six patients had an ESS score >10. Patients with OSA suffering from sleepiness were younger (p=0.010), more obese (p=0.039), had higher arousal index (p=0.051) and apnea hypopnea index (AHI) (p=0.036) on polysomnography. There was no gender difference between two groups (p=0.423). Polysomnographic findings revealed that there were no differences in total sleep time, sleep efficiency or overall distribution of sleep stages (N1,N2, N3, REM), or nocturnal mean and minimum saturation (p=0.516, p=0.790, p=0.674, p=0.852, p=0.677, p=0.137, p=0.286, p=0.353, respectively). On multivariate regression analysis, arousal index, total AHI, and age were effective in determination of ESS score (p<0.001). **Conclusion:** OSA patients with EDS were younger and more obese when compared to OSA patients with no EDS. No single factor was effective for detection of EDS with ESS score. Rather, factors such as severity of OSA, arousal index, and age were collectively decisive.

Key Words: Sleep apnea, obstructive; polysomnography

ÖZET Amaç: Gündüz uykululuk, obstrüktif uyku apneli (OSA) hastalarda sık görülen, ancak nedeni tam olarak aydınlatılamamış bir semptomdur. Çalışmada Epworth uykulukluk skalası (ESS) sonucuna göre aşırı uykululuğu olan ve olmayan OSA'lı hastaların polisomnografik ve demografik özelliklerinin karşılaştırılması amaçlandı. **Gereç ve Yöntemler:** Polisomnografi ile OSA tanısı konmuş 82 [Apne hipopne indeksi (AHİ)>15/sa] erişkin hasta (28 kadın/54 erkek), ESS sonucuna göre gündüz aşırı uykululuğu (GAU) olan (ESS>10) ve olmayan (ESS≤10) şeklinde 2 grupta retrospektif olarak incelendi. **Bulgular:** Hastalardan 46'sında ESS>10 idi. Gündüz uykululuğu olan OSA'lı hastalar daha genç (p=0,010) ve obezdi (0,039). Bu grubun polisomnografilerinde arousal indeksi (p=0,051) ve apne hipopne indeksi (AHİ) daha yüksekti (p=0,036). İki grup arasında cinsiyet farklılığı görülmedi (p=0,423). Polisomnografilerinde total uyku süresi, uyku etkinliği ya da uyku evrelerinin dağılımı (N1,N2,N3,REM), nokturnal ortalama saturasyon ve en düşük saturasyon değerleri açısından, iki grup arasında anlamlı fark yoktu (sırasıyla p=0,516, p=0,790, p=0,674, p=0,852, p=0,677, p=0,137, p=0,286, p=0,353). Çoklu regresyon analizinde ESS skorunun belirlenmesinde, arousal indeksi, total AHİ, yaş ve vücut kitle indeksi (VKİ) değişkenlerinin birlikte etkili olduğu saptandı (p<0,001). **Sonuç:** Aşırı uykululuk tarif etmeyen OSA'lılara göre, uykululuğu olanların daha genç ve daha obez olduğu saptanmıştır. GAU'nun varlığını göstermede kullanılan ESS skorunda, sorumlu tek bir faktörün bulunmadığı; OSA'nın ağırlığı, arousal indeksi, yaş ve VKİ gibi faktörlerin hep birlikte ESS skorunda belirleyici olduğu gösterilmiştir.

Anahtar Kelimeler: Uyku apnesi, tıkayıcı; polisomnografi

doi: 10.5336/medsci.2013-36830

Turkiye Klinikleri J Med Sci 2014;34(1):87-92

Obstructive sleep apnea (OSA) is a syndrome characterized by recurrent complete or partial upper airway obstruction during sleep, and frequently accompanied by nocturnal hypoxemia and sleep fragmentation. Approximately half of the patients are affected by excessive daytime sleepiness (EDS), which is an important symptom because it affects quality of life negatively and increases risk of workplace and traffic accidents.[1-7] Although EDS usually presents in patients with OSA, and accepted as a cardinal of it, EDS is not observed in all patients for unknown reasons.[8] Some studies showed an association between EDS and apnea/hypopnea and arousal indexes, whereas some other studies have showed a close relation particularly between nocturnal oxygenation and EDS symptoms, and reported relations with various factors rather than a single factor.[9-11]

The aim of the present study was to investigate the demographic and polysomnographic findings that are potentially effective on EDS in patients with clinically significant OSA [apnea hypopnea index (AHI) >15/h], and to compare the differences between our findings and parameters used in similar studies.

MATERIAL AND METHODS

The study retrospectively enrolled 82 patients (28 females, 54 males) who underwent polysomnography between January 2010 and January 2011, and were diagnosed with moderate or clinically significant OSA (AHI>15/h). Demographic and polysomnographic data of the patients were retrieved retrospectively from patients' files. Patients receiving OSA treatment, those having another accompanying sleep disorder such as periodic leg movement disorder, narcolepsy, parasomnia, central sleep apnea syndrome, and obesity hypoventilation syndrome, those with cancer, severe physical disability, mental retardation, major psychiatric disease, or the ones using hypnotics or antidepressant drugs were excluded. In this retrospective study, polysomnography was the only procedure performed to all patients who applied to the hospital with symptoms consistent with sleep apnea, and no additional procedures were performed. All patients signed their informed consents which included the details and information about the possible problems could be met during polysomnography procedure, and stated that the acquired data could be used for scientific studies while their identity information were kept secret.

ASSESSMENT OF EXCESSIVE DAYTIME SLEEPINESS

Information regarding basic patient complaints about sleep and the comorbidities were retrieved from patient files. For description of EDS, total Epworth Sleepiness Scale (ESS) score (0-24) was used which was obtained by scoring the likelihood of dozing or sleeping in each described situation between 0 (would never doze or sleep) and 3 (high chance of dozing or sleeping) in Turkish validated Epworth Sleepiness Scale (ESS). It describes the likelihood of dozing or sleeping of patients in 8 specific situations, showing subjective state of sleepiness.[12] Patients with a total score greater than 10 were accepted EDS positive.[13] Patients were grouped into two groups according to ESS score being EDS positive (ESS>10) and EDS negative (ESS≤10).

POLYSOMNOGRAPHIC RECORDS

Data of standard polysomnographic records of the study population were evaluated. Whole night polysomnographic study (Somno Star Pro, Viasys Healthcare) consisted of electroencephalogram (C4A1, C3A2, O1A2, O2A1), electrooculogram (ROC A1, LOC A2), electromyogram (2 submental and tibialis anterior), thermistor for oronasal air flow, strain gauges for thoracic and abdominal movements, pulse oximetry, and electrocardiographic records. Variables obtained from polysomnography were AHI, mean oxygen saturation (SpO2), total sleep time (TST), respiratory arousal index (ArI), non-rapid eye movement (NREM 1-3) and REM sleep phases and their durations. Whole night sleep records were taken by sleep technicians, and records were manually scored by an experienced sleep physician, based on Rechtschaffen and Kales criteria and in line with the updates of the American Academy of Sleep Medicine.[14,15] Sleep latency (sleep onset) was described as the time from the turning the lights off to the first sleep phase. Sleep efficiency was obtained from the proportion of sle-

ep duration to the time spent in bed. A drop in airflow greater than 90% for at least 10 seconds was described as apnea and a 3% desaturation or presence of arousal accompanying a drop of 50% in airflow was described as hypopnea. "Apnea/hypopnea" index was calculated from the total number of apnea and hypopneas per sleep hour and "arousal index" was obtained from the arousal number per sleep hour.[15]

STATISTICAL ANALYSIS

All parameters were summarized by descriptive statistics. Data were presented as median (minimum-maximum). The effects of categorical independent variables on sleepiness (EDS) were evaluated with Chi-Square test. Comparisons between two groups of patients were performed using Mann-Whitney U tests for abnormally distributed data. This study investigated the degree and importance of influence of both clinical parameters such as age and body mass index (BMI) and polysomnographic variables such as AHI and arousal index on daytime sleepiness via linear regression analysis. Statistical significance was defined using a p value of 0.05. Statistical analyses were performed with SPSS for Windows software (version 15.0).

RESULTS

Demographic features and clinical characteristics of patients are given on Table 1. Snoring and witnessed apnea were the most common symptoms, and 75.6% (63 patients) described EDS. EDS status of patients was determined by ESS score; patients with an ESS score >10 was considered EDS positive [46 patients (14 F/32 M)] while patients with an ESS score ≤10 were considered EDS negative [36 patients (14 F/ 22 M)]. The most common comorbidity was hypertension, diagnosed in 43.9% of patients (Table 1).

Patients with EDS were significantly younger (p=0.010), and more obese (p=0.039). There was no gender difference between two groups (p=0.423) (Table 2).

Polysomnographic examination revealed that there were no differences in total sleep time, sleep efficiency or overall distribution of sleep stages (p=0.516, p=0.790, p=0.674, p=0.852, p=0.677, p=0.137, respectively) (Table 2).

TABLE 1: Characteristics of patients with obstructive sleep apnea.

Gender (F/M)	28/54
	(Mean ± SD)
Age (years)	53.3±11.8
BMI (kg/m^2)	33.8±8.2
Symptoms	**(n, %)**
Snoring	79 (96.3)
Witnessed apnea	72 (87.8)
EDS	62 (75.6)
Headache	35 (42.7)
Sweating	33 (40.2)
Waking up with a sense of suffocation	20 (24.4)
Comorbidities	
Hypertension	36 (43.9)
Atherosclerotic Heart Disease	13 (15.9)
Diabetes mellitus	18 (21.9)
Gastroesophageal reflux	16 (19.5)

F: Female; M: Male; SD: Standard deviation; BMI: Body mass index; EDS: Excessive daytime sleepiness.

Total AHI was significantly higher (p=0.036) while the arousal index was higher in borderline significance (p=0.051) in OSA patients with daytime sleepiness. However, there was no significant difference between two groups in terms of mean apnea and hypopnea durations, NREM/REM AHI as well as nocturnal oxygenation parameters (p=0.714, p=0.510, p=0.689, p=0.556, p=0.286, p=0.353, respectively) (Table 2).

Linear regression analysis showed that arousal index, total AHI, age and BMI were all effective in determining ESS score (p<0.001) (R Square=0.241).

DISCUSSION

It is widely known that EDS is a frequent symptom in patients with OSA. Our findings indicated that EDS was not the single factor determining the ESS score, but rather factors like severity of OSA, arousal index, age, and BMI were all decisive in ESS score. In our study, we preferred an AHI>15/h instead of AHI>5/h to ensure inclusion of patients

TABLE 2: Clinical and polysomnographic findings of patients with obstructive sleep apnea with or without excessive daytime sleepiness.

	ESS ≤10 n=36	ESS >10 n=46	p
Gender (F/M)	14/22	14/32	0.423
	Median (min-max)	Median (min-max)	
Age (years)	59 (36-74)	49 (31-76)	0.010*
BMI (kg/m^2)	32.1 (17.3-52.50)	34.2 (16.6-68)	0.039*
TST (min)	282.8 (211.5-438.5)	302.5 (235.5-432)	0.516
Sleep onset (min)	19.3 (0.5-77)	10.5 (0- 43.5)	0.067
Sleep efficiency (%)	75.5 (60-90)	78.0 (75-96)	0.790
Arousal Index (./h)	17.5 (5.3-50.6)	26.6 (3.9-109.1)	0.051**
N1 (% TST)	13.8 (1.8-28.7)	15.2 (3.1-52.3)	0.674
N2 (% TST)	65.8 (0.0-76.4)	59.9 (36.0-89.5)	0.852
N3 (% TST)	9.4 (0.0-25.5)	12.1 (0.0-32.0)	0.677
REM (% TST)	11.9 (0.3-29.8)	8.8 (0.0-25.9)	0.137
Mean total duration of obstructive apnea (sec)	17.5 (12.0-30.0)	17 (10.0- 42.0)	0.714
Mean total duration of hypopnea (sec)	16.0 (13.0-27.0)	16.0 (11.0-23.0)	0.510
AHI total (./h)	30.8 (15.8-122.2)	52.6 (15.7- 109.0)	0.036*
AHI NREM (./h)	26.0 (0.0-123.0)	21.8 (0.0-129.0)	0.689
AHI REM (./h)	24.4 (0.0- 124.0)	48.8 (0.0-120.0)	0.556
Mean SpO_2	89.5 (70.0-95.0)	88.0 (56.0- 97.0)	0.286
Minimum SpO_2	78.0 (70.0-90.0)	89.5 (69.0-89.0)	0.353

F: Female; M: Male; ESS: Excessive daytime sleepiness; BMI: Body mass index; TST: Total sleep time; REM: Rapid eye movement; AHI: Apnea hypopnea index; SpO2: Oxygen saturation.

* p< 0.05

** Marginal significance.

with more severe disease. In contrast to many other studies, we chose this AHI value because we think it is clinically more significant.

The exact cause of EDS has not been fully elucidated. In our study, 56% (n=46) of patients with OSA were detected to have subjective sleepiness, and in line with literature, ESS score increased as severity of OSA increased in our study. In agreement with the literature, we detected that AHI and respiratory-related arousals were more important in explaining presence of EDS.[9,10,16,17]

Similar to other studies, we showed that the OSA patients with EDS were younger and there was a negative relationship between ESS score and age.[16,18] One study indicated a decrease in nighttime sleep efficiency and daytime sleep density in older compared to younger patients as a result of the shift of the hemostatic sleep mechanism towards wakefulness.[19] In addition, Bixler et al. attributed this association to depression that is more common in young people, or metabolic factors instead of thinking that this relationship simply stems from unmet sleep needs.[18] Since our study was retrospective, presence of depression in patients was not questioned, and only patients with the diagnosis of major depression were excluded.

Although some studies showed that sleepiness was more common in females, no significant relationship between sex and EDS was shown in our study, similar to findings of Bixler et al.[18,20]

Some studies reported an association between EDS and obesity.[18,21,22] In agreement with certain studies suggested that sleepiness might be a symptom of metabolic syndrome, our study revealed that obese OSA patients had more prominent EDS. Hence, regression analysis showed that BMI was one of the determinants of EDS. Previous studies showed that proinflammatory cytokines such as in-

terleukin-6 and tumor necrosis factor alpha (TNF-α) increased in patients with EDS.[23] Kritikou et al. also stressed the concurrence of OSA with EDS and inflammation.[24] All these results are consistent with recent studies which suggested OSA was a systemic inflammatory disease rather than a local anatomical disorder.[23,25-27]

Unlike Roure et al. who demonstrated sleep time was long and sleep efficiency was sufficient in OSA patients with EDS, we showed that there was no differences for total sleep time and sleep efficiency.[16] In line with the literature, we showed no relation between distribution of sleep phases and EDS. Furthermore, it has been shown in literature that there is no relationship between distribution of sleep phases and EDS.[18] REM sleep restriction is considered to be effective on sleepiness because of a decrease in total sleep time. However, studies showed that frequent arousals were more important.[28] We also did not detect any isolated association between isolated NREM and REM AHI separately and ESS, although there was a significant relationship between ESS score and total AHI which indicated the severity of OSA. Chami et al. reported that there was not any independent effect of REM-dominant sleep disordered breathing (SDB) on EDS and quality of life.[25]

Some studies showed a baseline association between EDS and parameters showing sleep disturbance, such as AHI and ArI whereas some other studies found that nocturnal hypoxemia causing neural damage in cerebral centers maintaining wakefulness was the main determinant in EDS.[9-11,16] Molecular mechanism linking nocturnal oxygen desaturation and EDS has not been fully elucidated. Animal studies showed neural cell loss in regions responsible from wakefulness, caused by oxidative and inflammatory events resulting from chronic intermittent hypoxemia during sleep.[29] Similar studies have suggested that minimum SpO2 level is effective on the state of sleepiness.[9,10,16] On the other hand, we found that parameters of nocturnal oxygenation in EDS were not as determinative as they were in other studies in OSA patients with sleepiness,. We suggest that this is the possible result of the fact that OSA is a considerably heterogeneous disorder with respect to both its causes and consequences. Indeed, not all OSA patients with different phenotypes have similar results.[30] This, in turn, leads to non-homogenous levels of oxygen desaturation in patients with similar AHI values.

We did not find any significant difference between durations of respiratory events apart from AHI, such as apnea and hypopnea. Mediano et al. reported longer apnea durations in patients with OSA suffering from excessive sleepiness, which was attributed by the authors to a delay in arousal.[11]

The limitation of our study was the lack of analysis of electroencephalographic changes associated with respiratory cycle, and changes belonging to sleep microstructure such as microarousal index and cyclic alternating pattern. Moreover, smoking status was not used as a variable. We also suggest that lack of objective assessment of presence of EDS in patients may have influenced the sensitivity of the study.

Based on the ESS score, possible polysomnographic determinants of EDS in patients with OSA were OSA severity (a higher AHI) and fragmented sleep characterized by increased number of arousals. Age and BMI, on the other hand, are clinical determinants of excessive daytime sleepiness in OSA patients.

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