Excessive Daytime Sleepiness and Obstructive Sleep Apnea in Thai Epileptic Patients

Ponson Ruangkana MD*,
Yotin Chinvarun MD, PhD*, Chesda Udommongkol MD, PhD*,
Parnsiri Chairungsaris MD*, Samart Nidhinandana MD*,
Jithanorm Suwantamee MD*, Pasiri Sithinamsuwan MD*

** Division of Neurology, Department of Medicine, Phramongkutklao Hospital and College of Medicine, Bangkok, Thailand*

Background: *Sleepiness is a common complaint in epilepsy. Also obstructive sleep apnea (OSA) is increasingly detected and would affect the epilepsy prognosis. We aimed to determine the frequency and predictors of sleepiness and OSA in epileptic patients.*

Material and Method: *This was a cross-sectional descriptive study using Epworth Sleepiness Scale questionnaire (ESS) and Sleep Apnea scale of the Sleep Disorders Questionnaire (SA-SDQ) to identify excessive daytime sleepiness and OSA in our consecutive epileptic patients in Neurology out-patient clinic.*

Results: *Overall 113 patients (male 55%) answered a personal survey and completed ESS and SA-SDQ. Mean age was 47 years (range 15-93). Average body mass index (BMI) was 24. Excessive daytime sleepiness (ESS $\geq$10) was demonstrated in 37%, and the prevalence of OSA diagnosed by using SA-SDQ was 20% (male 18%, female 22%). OSA were identified 68% among individuals whose BMI of more than 25, which was significant higher frequency than in the normal BMI group (32%). The predictors of having OSA were older age and higher BMI. Epworth Sleepiness Scale score was also higher in the OSA group than in non-OSA group.*

Conclusion: *Excessive daytime sleepiness was identified around one third of our epileptic individuals. Twenty percent had met the questionnaire criteria of having OSA. Overweight was the most important and modifiable risk factor of OSA.*

Keywords: *Epilepsy, Sleepiness, Obstructive sleep apnea, OSA, Sleep problems, Epworth sleepiness scale, ESS, Sleep apnea scale of the sleep disorders questionnaire, SA-SDQ*

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The prevalence of obstructive sleep apnea (OSA), a readily treatable disorder, in the general population is reported to be as high as 24% in men and 9% in women[1]. Epilepsy accounts for approximately 1% in the population. Importantly, in one report, it was found that up to one-third of epilepsy patients who do not respond to medication have coexisting OSA[2]. From previous surveys, the presence of OSA has been found in 5-63% of patients with epilepsy. Frequency rates were higher in patients with refractory epilepsy[2-5] and lower in unselected populations[6-8]. The pathogenesis, clinical relevance and therapeutically consequences of the association between OSA and epilepsy remain poorly understand. Devinsky et al[9] described an improvement of seizure control in 2 out of 5 patients with epilepsy and OSA treated by continuous positive airway pressure (CPAP). A reduction in seizure frequency without concomitant changes in antiepileptic drug (AED) treatment was observed in 3 out of 15 patients[3]. So far, only one prospective study assesses the effect of CPAP treatment on seizure frequency[8]. Several case series have documented that the treatment OSA may reduce seizure frequency and lessen daytime sleepiness in adults[9-11] and children[7-12] with epilepsy. Excessive daytime sleepiness (EDS) is another common condition, occurring in 0.5-5.0% of the population[13]. Several reports have indicated a high prevalence of excessive daytime sleepiness in epileptic patients[14-16]. Diagnosis and treatment of sleep disorders has important implications in the epilepsy population because treatment not only improves EDS but may also enhance seizure control[3,9-11].

Correspondence to:
Sithinamsuwan P, Division of Neurology, Department of Medicine, Phramongkutklao Hospital and College of Medicine, Bangkok 10400, Thailand.
Phone: 0-2354-7600 ext. 93027, Fax: 0-2354-7637
E-mail: pasiripmk@gmail.com

Both obstructive sleep apnea and excessive daytime sleepiness co-morbidities have a number of questionnaires developed to screen. To assess sleep-related breathing disorders[17], a questionnaire, the Sleep Apnea scale of the Sleep Disorders Questionnaire (SA-SDQ), a 12-item measure of sleep-related breathing disorders, has been validated in large numbers of patients with OSA as well as in epilepsy[5,18]. Additionally, Epworth sleepiness scale (ESS) is developed, validated and widely used to detect excessive daytime sleepiness. The authors here aimed to search for the prevalence of OSA and excessive daytime sleepiness in our epileptic patients and find some predictive factors of these conditions in our specific population.

Material and Method

Subjects

The consecutive epileptic subjects were screened to determine eligibility for the survey between June 2010 and August 2010 in the Neurologic clinic of Phramongkutklao Hospital. The patients who met the study criteria were invited to participate in the study. The selection criteria included age ≥15 years and previously diagnosed with epilepsy. All patients had a history of recurrent unprovoked seizures consistent with International League Against Epilepsy criteria[19]. All subjects gave informed consent to participate. Eligible patients were asked to complete two sleep questionnaires as described below.

Content of survey

Two published and previously validated self-administered questionnaires were used: the Epworth sleepiness scale (ESS) and the Sleep Apnea scale of the Sleep Disorders Questionnaire (SA-SDQ).

The ESS, our outcome measure, is an eight-item scale that measures a subject's general level of subjective daytime sleepiness[20]. The ESS has high test-retest reliability (r = 0.82) and a high level of internal consistency (Cronbach's alpha = 0.88)[21]. ESS scores increase with the severity of obstructive sleep apnea (OSA)[22]. Subjects are asked how likely they are to doze off or fall asleep in specific situations (never, slight, moderate, high; 0-3). Total scores range from 0 to 24. A binary outcome measures (ESS <10 vs. ESS ≥10) are clinically indicated as normal and excessive daytime sleepiness respectively. An ESS score greater than 10 is commonly used as a cutoff for excessive daytime sleepiness as suggested by the published literatures.

The second validated measure, the SA-SDQ[18], is a 12-item survey that provides a measure of sleep apnea. The SDQ has high test-retest reliability (r = 0.84) and a high level of internal consistency (Cronbach's alpha = 0.855). Total scores range from 0 to 60. The suggested cutoff points for apnea of 29 for males and 26 for females in epileptic population[5].

Statistical analysis and ethical issue

The present study design is a cross-sectional descriptive study. Continuous variables were determined as mean, median, and standard deviation. Discrete variables were analyzed as number and percent. Major predictive variables between sleep problems including sleep apnea and epileptic characteristics were compared using Chi-square tests and independent sample t-test. For all statistical tests, the level of significance was set at $p \leq 0.05$. The statistic package used was the SPSS version 11.5. Ethical approval was obtained from the centers' institutional review boards.

Results

A total of 113 epileptic patients, 51 females and 62 males, participated in the study. These patients had a mean age of 47 years. The average body mass index (BMI) was 24. Demographic characteristics of the sample were summarized in Table 1.

Sleep assessment

All 113 patients in this study were completed the ESS and SA-SDQ. Using Epworth sleepiness scale (ESS) scores of ≥10 for excessive daytime sleepiness andSA-SDQ scores of >29 for men and >26 for women for sleep-disordered breathing particularly obstructive sleep apnea syndrome, there are 37.2% and 19.5% of epileptic patients compatible with excessive daytime sleepiness and obstructive sleep apnea (OSA) respectively. The detail of ESS, SA-SDQ in overall and each gender were summarized in Table 2.

Table 1. Demographic characteristics

Characteristic (n = 113)	Mean ± SD	Range
Age, (years)	47±16.5	15-93
Gender, number (%)		
Male	62	55
Female	51	45
Body weight, (kg)	64±13	35-98
Body mass index, (kg/m^2)	24±4.4	16.7-37.5
Age of epilepsy onset, (years)	17±13.8	1-52

Average ESS was 7.7 and forty-two patients (37.2%) had excessive daytime sleepiness (ESS ≥10). Among these 42 individuals who had excessive daytime sleepiness scored by ESS, 26 of them (62%) complained of having sleepiness symptoms. By contrast only eighteen of 71 patients (25%) who had no excessive daytime sleepiness assessed by ESS reported a symptom of sleepiness. Therefore, the positive ESS score did show a strong correlation with the symptom of sleepiness in our epileptic subjects (p<0.01) (Table 3).

Using SA-SDQ, twenty-two epileptic patients (19.5%) met criteria of obstructive sleep apnea (OSA), whereas ninety-one patients (80.5%) were normal. Among these 22 possible OSA patients, 15 (68%) had overweight (BMI >25). While only 30 of 91 patients (33%) without OSA from SA-SDQ survey had overweight (BMI >25). Overweight assessed by body mass index was significantly correlated with the OSA from the questionnaire survey (p = 0.002) (Table 4).

The predictors of having obstructive sleep apnea in our epileptic patients were older age, higher BMI, but not the epilepsy age of onset (Table 5). Epworth sleepiness scale was also significantly correlated with OSA diagnosed by sleep apnea questionnaire.

Discussion

The present study indicated a high prevalence of perceived sleep disturbance in epilepsy patients. Sleep disturbance was significantly positively correlated with the participant's body mass index (BMI). Patients with higher BMI reported higher SA-SDQ scores, indicating sleep-breathing disorders. In addition, the authors found that OSA was associated with increasing age, and Epworth Sleepiness Scale score.

The 20% prevalence of OSA in our epilepsy

Table 2. Sleep assessment result

Questionnaires	Score mean ± SD	Male (n = 62)	Female (n = 51)	*p*-value
Epworth sleepiness scale (ESS)	7.7±4.8	8.1±5.1	7.2±4.4	0.352
ESS ≥10, number (%)	42 (37.2)	26 (41.9)	16 (31.4)	0.248
SA-SDQ	22.4±6.2	23.6±2.3	20.9±5.7	0.021
Suspected OSA, number (%)	22 (19.5)	11 (17.7)	11 (21.6)	0.609

SASDQ = the sleep apnea scale of sleep disorders questionnaire

Table 3. Correlation between ESS and sleepiness symptom

ESS	Symptom		*p*-value
	No-sleepiness number (%)	Sleepiness number (%)	
Normal (score 0-9)	53 (74.6)	18 (25.4)	<0.01*
Daytime sleepiness (score >9)	16 (38.1)	26 (61.9)	

* Statistic significant

Table 4. Correlation between SA-SDQ and BMI

SA-SDQ	BMI		*p*-value
	BMI ≤25	BMI >25	
No OSA, number (%)	61 (67.0)	30 (33.0)	0.002*
OSA diagnosis, number (%) (>26 in female), (>29 in male)	7 (31.8)	15 (68.2)	

*statistic significant

Table 5. The factor associated with obstructive sleep apnea (OSA)

Variables	OSA^{+} (n = 22) mean $\pm$ SD	Non-OSA (n = 91) mean $\pm$ SD	*p*-value
Age, (years)	56$\pm$11.9	45$\pm$16.8	0.004*
BMI, (kg/m^2)	26.8$\pm$4.6	23.3$\pm$4.1	0.001*
Age onset of epilepsy (years)	23.4	26.8	0.122
Epworth sleepiness scale	9.9$\pm$4.1	7.2$\pm$4.8	0.017*

$^{+}$ Diagnosed by SA-SDQ >26 in female group and >29 in male group, * statistic significant

subjects was lower than that reported in an adult population-based study without epilepsy, in which 24% was men and 9% was women[1]. The reasons why prevalence rate of OSA was low in our sample as compared with non-epilepsy patient populations are uncertain. Specific antiepileptic drug (AED) regimens would alleviate OSA, or AED levels would influence OSA. Young's study conducted in adult workers in Wisconsin demonstrated that male gender, obesity, and habitual snoring were factors strongly associated with OSA[1]. Men were 2.0 to 3.7 times more likely to have sleep-disordered breathing than women. An increase in one standard deviation in any measures of body habitus, including BMI, produces a three-time increased risk in sleep-disordered breathing. Our survey showed significant higher in SA-SDQ score in male than female, but OSA diagnosis from the proposed cut-off showed not difference between genders (Table 2). Our sample size might be too small to be able to meet a statistical significant difference in OSA between genders. Replication of this study in a larger sample size would be required to find a gender difference in OSA among epileptic population.

Generally, the strongest predictor of OSA is obesity and otherwise include craniofacial features, genetic factors, and environmental exposures that increase airway inflammation (e.g., smoking) or decrease neuromuscular output to the upper airway (e.g., alcohol or sedatives). From our analysis the strongest predictor of OSA in epilepsy was the overweight indicated by BMI of more than 25.

Epworth sleepiness scale questionnaire (ESS), a measure of subjective daytime sleepiness, differs among subjects with and without OSA. However there are number of patients having daytime sleepiness without obstructive sleep apnea. There are several possibilities for this high sensitivity. First, not all subjects with daytime sleepiness have OSA. Second, subjects with epilepsy may be sleepy for other reasons besides OSA, including AED effects, seizures activity, or the effects of seizures on sleep. Finally, subjects may overestimate their degree of daytime sleepiness.

Recognizing and treating sleep disorders in epilepsy patients has important implications not only for improving quality of life, but also for seizure control. Several case series have reported an improvement in seizure control when OSA was treated[3,9-11], implying that OSA may facilitate seizures. A variety of seizure-provoking mechanisms have been proposed. Cerebral hypoxemia, decreased cardiac output, and cardiac arrhythmias are commonly found in OSA. Other proposed mechanisms include sleep deprivation and fragmentation of sleep with frequent stage shifts, arousals, and entries into sleep after arousal. If sleep deprivation is the assumed mechanism, one might expect that seizures during both sleep and wakefulness would be facilitated in patients with epilepsy with OSA. In contrast, if sleep fragmentation and frequent stage shifts resulting from apneas are responsible for provoking seizures, then seizures during sleep may be facilitated preferentially in patients with epilepsy with OSA. The authors cannot comment on the effects of OSA treatment on seizure control and daytime sleepiness in our sample because only a few subjects were treated. Although case series have suggested that treating OSA is beneficial for seizure control and for improvement of daytime sleepiness, randomized clinical trials will be necessary to definitively answer this question and to identify those patients in whom seizures will respond to treatment. The present study has some limitation as the authors didn't perform subgroup analysis to identify whether generalized seizures cause more excessive daytime sleepiness than focal epilepsy or not.

In conclusion, the present study found more than 30% of epileptic patients have excessive daytime sleepiness. Twenty percent had met the questionnaire criteria of having OSA. Overweight was the most important and modifiable risk factors of OSA in our epilepsy. The sleep-related conditions would affect

epilepsy control or quality of life in some ways. Further investigation and prompt management would be required.

Potential conflicts of interest

None.

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ภาวะง่วงในเวลากลางวัน (excessive daytime sleepiness) และการหยุดหายใจแบบ obstructive sleep apnea และในผู้ป่วยไทยที่เป็นโรคลมชัก

พลสันต์ เรืองคณะ, โยธิน ชินวลัญช์, เจษฎา อุดมมงคล, ปานศิริ ไชยรังสฤษดิ์, สามารถ นิธินันทน์, จิตถนอม สุวรรณเตมีย์, พาสิริ สิทธินามสุวรรณ

ภูมิหลัง: ผู้ป่วยลมชักมักมีอาการง่วงเวลากลางวันและเนื่องจากภาวะภาวะการหยุดหายใจแบบ obstructive sleep apnea (OSA) พบเป็นปัญหาบ่อยขึ้น ซึ่งจะมีผลต่อโรคลมชัก ผู้นิพนธ์จึงต้องการหาความชุกและตัวพยากรณ์ภาวะดังกล่าวในผู้ป่วยโรคลมชัก

วัสดุและวิธีการ: ศึกษาแบบตัดขวางในผู้ป่วยที่มารักษาที่คลินิกโรคลมชักโดยใช้แบบสอบถาม Epworth sleepiness scale questionnaire (ESS) และ Sleep apnea scale of the sleep disorders questionnaire (SA-SDQ) เพื่อประเมินความง่วงในเวลากลางวัน (Excessive daytime sleepiness) และความชุกของภาวะการหยุดหายใจแบบ Obstructive Sleep Apnea ตามลำดับ

ผลการศึกษา: ศึกษาผู้ป่วยโรคลมชัก 113 ราย เป็นเพศชายร้อยละ 55 ปี อายุเฉลี่ย 47 ปี ดัชนีมวลการเฉลี่ย 24 พบร้อยละ 37 ของผู้ป่วยลมชักมีค่า ESS มากกว่าหรือเท่ากับ 10 ซึ่งแสดงถึงอาการง่วงตอนกลางวันและร้อยละ 20 (เพศชายร้อยละ 18 และเพศหญิงร้อยละ 22) ร้อยละ 68 ของผู้ป่วยลมชักที่มีดัชนีมวลกายมากกว่า 25 มีภาวะ OSA ซึ่งสูงกว่าผู้ที่มีดัชนีมวลกายปกติซึ่งพบ OSA เพียงร้อยละ 32 และคะแนนความง่วงเวลากลางวันสูงในผู้ป่วยที่มีภาวะ OSA

สรุป: ผู้ป่วยโรคลมชักมีภาวะง่วงในเวลากลางวันได้ถึงร้อยละ 37 และการหยุดหายใจแบบร้อยละ 20 โดยปัจจัยเสี่ยงคือน้ำหนักตัวมากซึ่งเป็นปัจจัยน่าจะปรับเปลี่ยนได้