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Temporal lobe epilepsy is a predisposing factor for sleep apnea: A questionnaire study in video-EEG monitoring unit☆

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ABSTRACT

Objective: The interaction between epilepsy and sleep is known. It has been shown that patients with epilepsy have more sleep problems than the general population. However, there is no recent study that compares the frequency of sleep disorders in groups with medically refractory temporal lobe epilepsy (TLE) and extratemporal lobe epilepsy (ETLE). The main purpose of this study was to investigate the occurrence of sleep disorders in two subtypes of epilepsy by using sleep questionnaire forms.
Methods: One hundred and eighty-nine patients, out of 215 who were monitored for refractory epilepsy and were followed by the video-EEG monitoring unit, were divided into a group with TLE and a group with ETLE. The medical outcome study-sleep scale (MOS-SS), Epworth sleepiness scale (ESS), and sleep apnea scale of the sleep disorders questionnaire (SD-SDQ) were completed after admission to the video-EEG monitoring unit. The total scores in the group with TLE and group with ETLE were compared.
Results: Of the patients, TLE was diagnosed in 101 (53.4%) (45 females), and ETLE was diagnosed in 88 (46.6%) (44 females). Comparison of MOS-SS and Epworth sleepiness scale scores in the two subgroups did not reveal significant differences. In the group with TLE, SD-SDQ scores were significantly higher compared to that in the group with ETLE.
Conclusion: Patients with temporal lobe epilepsy have higher risk of obstructive sleep apnea (OSA) according to their reported symptoms. Detection of OSA in patients with epilepsy by using questionnaire forms may decrease the risk of ictal or postictal respiratory-related 'Sudden Unexpected Death in Epilepsy'.

1. Introduction

Sleep disorders are common and frequently occur in patients with epilepsy. Disturbed sleep may cause sleep deprivation and worsen seizure control [1]. Thus, treatment of coexisting sleep disorders may improve seizure control [2]. More recent adult and childhood studies have researched the prevalence of sleep disorders in patients with epilepsy [3]. However, there are few reports in populations with in the group with drug-resistant epilepsy [4,5]. These studies show that sleep disturbances are more common in patients with refractory epilepsy than in healthy individuals. The aim of this study was to determine the frequency of sleep disturbances in patients with drug-resistant temporal lobe epilepsy (TLE) and extratemporal lobe epilepsy (ETLE) by using the standardized sleep questionnaire forms.

2. Methods

2.1. Patients and procedure

We reviewed all subjects undergoing Video EEG monitoring (VEMU) with scalp electrodes for evaluation of epilepsy surgery between 2010 and 2013. All of these patients were hospitalized for routine clinical purposes and had no history of sleep disorders. The diagnosis of drug-resistant epilepsy was discussed in a multidisciplinary case conference. Their clinical, electrographic features, magnetic resonance imaging (MRI) findings, positron emission tomography, and if necessary, ictal or interictal single photon emission computerized tomography were evaluated. Patients' seizure types and epilepsy syndromes were determined according to the International League Against Epilepsy (ILAE) classifications [6]. Each patient was monitored in a video-EEG monitoring unit using a 32-channel EEG system (Telefactor). The T1 and T2 scalp electrodes were placed according to the standard 10–20 system. Electrooculogram (EOG), submental electromyogram (EMG), and electrocardiogram (ECG) were included in the recording parameters. Patients diagnosed with temporal lobe epilepsy and ETLE were included. The other partial epilepsy syndromes, unclassified patients, and generalized epilepsy syndromes were excluded.

☆ The study was done in the neurophysiology laboratory in Hacettepe University Hospital.

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2.2. Questionnaires

All the patients in the video-EEG monitoring unit completed a questionnaire form, including the medical outcome study-sleep scale (MOS-SS), Epworth sleepiness scale (ESS), and sleep apnea scale of the sleep disorders questionnaire (SD-SDQ). The total scores were compared in the group with ETLE and group with TLE.

The answers to all questionnaires were digitized for further processing. If there were missing answers, the patient was contacted by the video-EEG monitoring unit nurse. Those missing answers in questionnaires were excluded from the study.

The MOS-SS contains 12 validated items with six subscales measuring snoring, awakening short of breath or with headache, sleep somnolence, and sleep disturbance to estimate the sleep quality in the previous four weeks. Higher scores for this questionnaire indicate worse sleep outcomes.

The sleep apnea scale of the sleep disorders questionnaire (SD-SDQ) also contains 12 questions and higher scores indicate apnea frequency. The SD-SDQ comprises 12 items including loud snoring, witnessed apnea, waking gasping for breath, sweating, high blood pressure, nasal congestion, problem worse when sleeping on back, problem worse after alcohol intake, weight, years of smoking, age, and body mass index [6,7].

The Epworth sleepiness scale (ESS) is a scale intended to measure daytime sleepiness. Scores of 11 and over may indicate the possibility of daytime sleepiness.

2.3. Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS 17.0). Demographic data and data acquired from the questionnaires were compared between the two groups using the independent sample t-test for normally distributed data. Also, the Mann–Whitney U and chi-square tests were used for comparison of MOS-SS, Epworth sleepiness scale, and SD-SDQ scores in the two groups. Chi-square or Fisher's exact tests were used for categorical variables. In all tests, a p-value of 0.05 was considered significant.

3. Results

3.1. Subjects

Over 3 years, 215 patients with refractory epilepsy underwent video-EEG monitoring. Twelve patients had nonepileptic paroxysmal events, 5 were diagnosed with generalized epilepsy, and 9 patients who had unclear epileptic focus were excluded. The remaining 189 patients who were diagnosed as having TLE or ETLE in a multidisciplinary epilepsy surgery case conference were included in the study. There were 101 patients diagnosed with TLE and 88 diagnosed with ETLE.

In the group with TLE, 56 patients were males, and the average age of all 101 patients was 32.6 ± 9.4 years (range: 18–72). In the group with ETLE, 44 patients were males, and the average age of 88 patients was 28.64 ± 7.33 years (range: 19–57). There was no significant difference in age between the two groups ($p = 0.43$).

The patients were divided into three groups according to antiepileptic medications. Monotherapy was used for 12 (11.8%) patients with TLE and 6 (6.8%) patients with ETLE. Two antiepileptic drugs were used for 36 (35.6%) patients with TLE and 29 (32.9%) patients with ETLE. Three and more antiepileptic drugs were used for 53 (52.5%) patients with TLE and 53 (60.2%) patients with ETLE. There was no significant difference between the group with TLE and group with ETLE as shown in Table 1.

Benzodiazepine and barbiturates were used for twenty patients. Twelve were in the group with TLE and 8 were in the group with ETLE.

Table 1
Demographic characteristics of patients.

	TLE	ETLE	p
Age (years)	32.6 ± 9.4	28.6 ± 7.33	0.43
Gender			
Male	56 (55.4%)	44 (50%)	0.24
Female	45 (44.5%)	44 (50%)	0.54
BMI (kg/m^2)	28.4 ± 4.3	29.8 ± 6.6	0.41
Number of AEDs used			
One AED	12 (11.8%)	6 (6.8%)	0.33
Two AEDs	36 (35.6%)	29 (32.9%)	0.44
Three and more AEDs	53 (52.5%)	53 (60.2%)	0.51
Benzodiazepine and barbiturates	12 (11.9%)	8 (9.1%)	0.45

3.2. Analysis of sleep questionnaires

The MOS-SS scores (as well as subscales) of the two groups with epilepsy were compared statistically. There were no significant differences between the two groups with epilepsy as documented in Table 2.

There was no statistically significant difference between the groups in terms of mean ESS score or ESS score > 9 ($p = 0.8$).

For the SD-SDQ questionnaire total score, highly significant differences were found in the group with TLE and the group with ETLE ($p = 0.04$).

4. Discussion

The comorbidity between sleep disorders and epilepsy can lead to worse prognosis or treatment problems, but their pathophysiological backgrounds each have effects on the other. Despite their intimate relationship, the coexistence of epilepsy and sleep disorders is poorly investigated in the literature. Few studies examine the prevalence of sleep disturbances in patients with epilepsy by using both the ESS and MOS-SS [4,5]. In Xu et al.'s original article, 34% of 201 patients with partial onset epilepsy were diagnosed with sleep disturbance, and 10% of the patients received sleep medications. Similar to this study, de Weerd reported 38.5% as the prevalence of sleep disturbances in patients with partial epilepsy. These two studies claim that sleep disturbances are more common in patients with epilepsy than in the healthy population by using the MOS-SS. Also, sleep quality changes were discussed in pure sleep-related epilepsy [8]. Our questionnaire-based study also showed that there is no significant difference between the group with TLE and group with ETLE according to the MOS-SS and Epworth sleep scale. Contrary to our findings, patients affected by TLE often report excessive daytime sleepiness [9]. The validity of the SA-SDQ as a screening instrument for OSA in clinical research involving adults with epilepsy has been verified [10]. Obstructive sleep apnea may be observed as a comorbidity in the clinical series of adult patients with epilepsy, and treatment can improve seizure control [11,12]. Furthermore, undiagnosed obstructive sleep apnea was found to be common in patients with medically refractory epilepsy in a study

Table 2
Summary of patient questionnaires.

	Number of items	TLE	ETLE	p-Value
MOS-SS				
Sleep quantity (hours)	1	8.5 ± 1.2	8.7 ± 1.7	0.2
Sleep disturbance	4	15.4 ± 15.1	15.5 ± 15.6	0.5
Somnolence	3	27.4 ± 20.3	24.8 ± 19.6	0.6
Sleep adequacy	2	57.6 ± 21.3	65.4 ± 22.8	0.3
Snoring	1	21.2 ± 25.7	20 ± 24.8	0.6
Headache–shortness of breath	1	24.3 ± 13.9	26.2 ± 14.2	0.5
Epworth	8	11	8	0.8
SD-SDQ	12	15.9 ± 4	14.9 ± 3.3	**0.04***

* $p < 0.05$ reveals statistically significance.

using PSG [13]. However, subtypes of patients with medically refractory epilepsy such as TLE have not been studied. We found that patients with refractory TLE had high SD-SDQ scores in our study. Although we could not examine these patients with polysomnography, we suggest that TLE is linked to sleep-related breathing problems. The mechanisms of seizures which exacerbate sleep apnea are not completely understood. Seizures may spread to cerebral structures and brainstem respiratory centers. Apnea may be an ictal manifestation; on the other hand, it may occur as a postictal phenomenon [14,15]. Interictal epileptiform discharges can also lead to apnea with similar action of ictal discharges on respiratory centers [15]. The increased effect of these discharges can be expected to be more severe in patients with refractory epilepsy.

It has been reported that temporal lobe seizures may exacerbate apnea in a few cases [16,17]. Ictal apnea was documented with contralateral spread of medically refractory temporal seizures in recent studies [17,18]. With functional connectivity, temporal lobe seizures arising from the insular cortex may cause sleep-related breathlessness [19].

Seizure-induced respiratory problems may be one cause in the etiology of SUDEP [20]. Obstructive sleep apnea may be observed as comorbidity in the clinical series of adult patients with epilepsy [6]. Undiagnosed OSA was found to be common in patients with medically refractory epilepsy in a PSG study [13]. A case of TLE and autopsy-confirmed SUDEP was described in the literature as associated with episodes of central ictal apnea during video-EEG monitoring [18]. This case may suggest that TLE is a potential risk factor for apnea and SUDEP. However, patients with subtypes of medically refractory epilepsy have not been studied before. Previous reports have documented the coexistence of OSA and epilepsy and the therapeutic effects of treatment on seizure frequency and daytime sleepiness [21,22]. It has been reported that antiepileptic drugs (AEDs) affect sleep [23,24]. Daytime sleepiness-like symptoms, increased sleep efficiency, and sleep fragmentation may be reported during antiepileptic therapy [25,26]. Although we could not control for all the effects of AEDs on apnea in this study population, we can say that there was no difference between patients with TLE and ETLE in terms of numbers and types of AEDs (including benzodiazepines and barbiturates) used. Therefore, we suggest that the type and number of AEDs did not affect the increased risk of apnea in patients with TLE, compared to patients with ETLE.

In contrast to the prior drug-resistant epilepsy study, we found significant correlations between OSA and TLE. To the best of our knowledge, this is the first study that shows the relationship between TLE and OSA by using questionnaire forms. Questionnaires are inexpensive screening tools, easy to apply to patients to determine additional diseases. In the future, video-EEG multimodality monitoring may be required after detecting sleep-related problems on questionnaires completed by patients with epilepsy.

Disclosure

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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