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Sleep disturbances among patients with epilepsy

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Aim: The aim of this study was to analyze the prevalence of sleep disorders among patients with epilepsy and to compare the incidence of sleep disorders between the clinical and demographics factors.

Materials and methods: The study was conducted among 302 patients with epilepsy. Sleep disturbances were measured with the Polish version of the Pittsburgh Sleep Quality Questionnaire (PSQI). The questionnaire prepared and applied by the authors contained questions relating to sociodemographic characteristics, clinical status, and sleep.

Results and conclusion: Mean PSQI score in the study group was 9±2 points, with the range of 4–16 points. PSQI test results were analyzed with regard to clinical and demographic characteristics of those suffering from epilepsy: gender, age, profession, body mass index, illness duration, number of medicines taken, type of seizures, frequency of seizures, time which elapsed since last seizure, provocative factor of seizure attacks, occurrence of adverse effects of antiepileptic drugs (AEDs). Furthermore, the existence of a relationship between PSQI test result and particular sleep-related factors or particular sleep conditions was examined. However, the examination of a relationship between certain independent variables and the final PSQI test result did not prove the existence of a statistically relevant influence (in all cases $P>0.05$).

Keywords: epilepsy, sleep disturbances, sleep, PSQI

Introduction

Sleep disorders pose a serious health problem in the contemporary world.[1] In Poland, approximately 23.7% of the population suffer from sleep disorders.[2] A study conducted in a group of 1,000 Polish citizens showed that 39% of all sleep disorders are caused by insomnia.[3] Among important factors influencing sleep, there are several diseases, such as epilepsy and taking numerous chemicals. Literature have shown that epileptic population had significantly lower efficiency of sleep, had more N2 nonrapid eye movement (NREM) sleep, and had less rapid eye movement (REM) sleep with prolonged latency to REM sleep in comparison to general population.[4–7] The relationship between epilepsy and sleep dysfunction/disorders is complex. On the one hand, seizures may be exacerbated by sleep deprivation and on the other hand, some seizures occur mainly during sleep. Furthermore, while sleep disorders may negatively impact epilepsy, epilepsy may aggravate certain sleep disorders.[4] Antiepileptic drugs (AEDs) may interfere with a normal sleep pattern and excessive daytime sleepiness. The correlation between AEDs and sleep dysfunction/disorders is unclear. Some authors have shown a strong influence effect of AEDs on daytime virility and sleep,[8,9] but other researchers did not report any effect of antiepileptic medication on sleep.[10] However, sudden withdrawal of antiepileptic drugs is a risk factor for the occurrence of status epileptic seizures in previously pure sleep epilepsy.[11] Sleep is a potent activator of seizures.

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Objective

The aim of this study was to analyze the prevalence of sleep disorders in patients with epilepsy and to compare the incidence of sleep disorders with regard to clinical and demographic factors.

Materials and methods

Study design and participants

The study was conducted among patients with epilepsy in the period from October 2015 to October 2016. Participants were recruited through multiple channels, including online websites, a forum for people suffering from epilepsy, and a neurological outpatient clinic in Warsaw. The inclusion criteria were the age of ≥18 years, patient's epilepsy, and consent to participate in the study. Exclusion criteria included mental retardation, psychiatric comorbidities, and night or shift work.

Initially, 356 patients agreed to participate in the study. The final analysis covered surveys completed by 302 patients (response rate 84.8%). The remaining 54 surveys were rejected due to missing information.

Clinical assessment and sleep questionnaires

Sleep disturbances were measured with the Polish version of the Pittsburgh Sleep Quality Questionnaire (PSQI). The PSQI has internal consistency and a reliability coefficient (Cronbach's alpha) of 0.83 for its 7 components. The PSQI is a 19-item self-rated questionnaire used for evaluating subjective sleep quality during the previous month. The PSQI is a questionnaire designed to evaluate the following: overall sleep quality, sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, medication use, and daytime dysfunction.[12] Each answer was scored on a scale of 0–3 (0= no difficulty, 3= severe difficulty). Component scores were added to obtain a global score of 0–21. Higher scores indicated worse sleep quality. A global sum of ≥5 was considered poor overall sleep quality and ≥10 was severely disturbed sleep.

The questionnaire prepared and applied by the authors contained questions relating to sociodemographic characteristics, clinical status, and sleep.

Demographic characteristics consisted of 5 items: gender, age, educational level, height, and weight. Clinical status consisted of 10 items: duration of disease, kind of seizures, frequency of seizures, last seizure, mode of therapy, type of AEDs, side effects of AEDs associated with sleep, provocative factors of seizure attacks, sleep disorders and kind of sleep disorders. In the third part, the respondents provided answers to questions concerning factors affecting sleep (7 questions) and conditions conducive to sleeping (5 questions). Tables 1–5 show all possible answers. The respondents were advised about the purpose of the study. Participation was voluntary and anonymous. Completion of the survey meant that the patients gave their consent to participate in the study.

Ethics

The study was approved by the Ethics Committee, Medical University of Warsaw (No AKBE/159/16).

Statistical analysis of the obtained results

The single factor analysis of variance (ANOVA) and Kruskal–Wallis test were used for the purpose of statistical analysis of results variance between the study groups. The nonparametric Mann–Whitney *U*-test and Student's *t*-test were used for the comparison of differences between the 2 study groups. The level of significance ($P<0.05$) was accepted as statistically reliable. The statistical analysis of obtained results was performed using STATISTICA (10.0) software.

Results

Demographic data of the respondents

There were 302 patients: 116 males and 186 females. The mean age in years was 34.2±13.3 with the range 18–75 years. Mean body height and weight were 171.6±9.5 cm and 71.9±17.1 kg, respectively. The mean body mass index (BMI) was 24.9±5.2 kg/m^2, range 17.1–38.1 kg/m^2, with 26 patients being underweight, 50 obese, and 66 overweight.

Table 1 Sociodemographics characteristics of the respondents

Variable	N (%)
Gender	
Male	116 (38.4)
Female	186 (61.6)
Age (years)	
Mean ± SD, range	34.2±13.3, 18–75
Height (cm)	
Mean ± SD, range	171.6±9.5, 150–198
Weight (kg)	
Mean ± SD, range	71.9±17.1, 43–140
BMI (kg/m^2)	
Mean ± SD, range	24.9±5.2, 17.1–38.1
Employment status	
Unemployed	48 (16.0)
Employed	120 (39.7)
Student	68 (22.5)
Pension	46 (15.2)
Own business	20 (6.6)

Abbreviation: BMI, body mass index.

Table 2 Clinical characteristics of the respondents

Variables	N (%)
Duration of epilepsy, months (mean ± SD)	197.9±160.6
Range	2–708
Seizure frequency	
<1/year	116 (8.4)
<1/month	36 (11.9)
1–3/month	62 (20.5)
>1/week	88 (19.1)
Type of seizure	
Partial	90 (29.8)
Primarily generalized	84 (27.8)
Secondarily generalized	92 (30.5)
Secondarily generalized + partial	36 (11.9)
How long is a patient seizure-free	
>1/year	90 (29.8)
<1/month	34 (11.3)
1–3/month	42 (13.9)
>1/week	136 (45.0)
Most common provocative factors of seizure attacks	
Lack of sleep	82 (27.2)
Alcohol or other stimulant	48 (15.9)
Stress	110 (36.4)
Change the AEDs	24 (7.9)
There is no reason	22 (7.3)
Other	16 (5.3)
Mode of therapy	
Free of medication	10 (3.3)
Monotherapy	160 (53.0)
Polytherapy	132 (43.7)
Type of AEDs*	
CBZ	98 (32.5)
BZD	10 (3.3)
ETX	2 (0.7)
GBP	22 (7.3)
LSM	4 (1.3)
LTG	48 (15.9)
LEV	62 (20.6)
OXC	32 (10.6)
VPA	136 (45)
TGB	12 (4)
TPM	28 (9.3)
VGB	8 (2.6)
Side effects of AEDs associated with sleep	
Yes	120 (39.7)
No	182 (60.3)
Sleep disorders	
Yes	176 (58.3)
No	126 (41.7)
Kind of sleep disorders	
Insomnia	54 (17.9)
Hypersomnia	34 (11.3)
Sleep apnea	44 (14.6)
RLS	44 (14.6)

Note: *The data did not give a total of 100% because the respondents could choose multiple answers.

Abbreviations: AEDs, antiepileptic drugs; BZD, benzodiazepine; CBZ, carbamazepine; ETX, ethosuximide; GBP, gabapentin; LEV, levetiracetam; LSM, lacosamide; LTG, lamotrigine; OXC, oxcarbazepine; RLS, restless legs syndrome; TGB, tiagabine; TPM, topiramate; VGB, vigabatrin; VPA, sodium valproate.

Table 3 PSQI scores of the study group

PSQI	Mean
Sleep quality (C1)	1.80±1.00
Sleep latency (C2)	1.00±1.00
Sleep duration (C3)	0.95±0.88
Sleep efficiency (C4)	1.09±1.19
Sleep disturbance (C5)	1.85±0.35
Medication use (C6)	0.68±0.95
Daytime dysfunction (C7)	1.22±0.76
Total score	9.00±2.00

Abbreviation: PSQI, Pittsburgh Sleep Quality Questionnaire.

The majority of the study population were employed (39.7%). Table 1 shows the sociodemographic profile of the study participants.

Clinical data of the respondents

Mean duration of epilepsy in months was 197.9±160.6. The majority of patients had secondarily generalized seizures (30.5%), followed by complex partial seizures (29.8%). Thirty-one patients (20.5%) had 1–3 seizures per month, 19.1% >1 seizures per week, and 11.9% <1 seizures per month. Forty-five (29.8%) of all patients had been seizure-free for more than 1 year and the majority of patients had their last seizure more than 1 week before.

Stress (36.4%) was the most common provocative factor associated with seizure attacks, followed by sleep deprivation (27.2%). Twelve patients (7.3%) had no apparent triggers.

Medication analysis revealed that 53% of the participants were on monotherapy, whereas 43.7% were on polytherapy and 3.3% were medication-free. The majority of patients were taking valproate (45%). Carbamazepine (32.5%) was the second most common drug. Side effects of AEDs associated with sleep were reported in 39.7% patients.

In their responses to clinical questions, 41.7% of the participants did not indicate any sleep-related problems, 17.9% had insomnia, an equal number of respondents had restless leg syndrome and sleep apnea (14.6% each), and only 11.3% had hypersomnia. Table 2 shows the clinical profile of the study participants.

Table 4 Factors affecting sleep among the study group

No	Questions	Yes, n (%)	No, n (%)
1	Problems at work	184 (60.9)	118 (19.1)
2	Financial problems	96 (31.8)	206 (68.2)
3	Family/emotional or relationship problems	90 (29.8)	212 (70.2)
4	The loss of a loved person	122 (40.4)	180 (59.6)
5	Sadness and low self-esteem	210 (69.5)	92 (30.5)
6	Epilepsy/seizure	210 (69.5)	92 (30.5)
7	Social gatherings	86 (18.5)	216 (71.5)

Table 5 Conditions conducive to sleeping in the study group

No	Questions	Yes, n (%)	No, n (%)
1	Do you have your own bedroom?	162 (63.6)	140 (46.4)
2	Is your bedroom located in a quiet place?	174 (57.6)	128 (42.4)
3	Is there an appropriate temperature in your bedroom?	254 (84.1)	48 (15.9)
4	Do you have a comfortable bed and bedding?	160 (53.0)	142 (47.0)
5	Do you fall asleep in front of the television, computer, or reading a book?	134 (44.4)	168 (55.6)

Sleep disorders in PSQI

Mean PSQI score in the study group was 9±2 points, with the range of 4–16 points. The worst rating concerned the domain of sleep disturbances with a mean of 1.85. Six of the 302 patients had undisturbed sleep, whereas 296 of them had disturbed sleep, including 92 suffering from severely disturbed sleep. Detailed scores obtained are presented in Table 3.

In the study group, epilepsy/seizure, sadness, and low self-esteem were factors affecting sleep (Table 4) for an equal number of respondents (69.5% each). The majority of the respondents had their own bedroom (63.6%), comfortable bed (53.0%), and situated in a quiet place (57.6%), where the temperature was adjusted to sound sleep (84.1%) (Table 5).

Statistical analysis

PSQI test results were analyzed with regard to clinical and demographic characteristics of those suffering from epilepsy: gender, age, profession, BMI, illness duration, number of medicines taken, type of seizures, frequency of seizures, time which elapsed since last seizure, provocative factor of seizure attacks, and occurrence of adverse effects of AEDs. Furthermore, the existence of a relationship between PSQI test result and particular sleep-related factors or particular sleep conditions was examined. However, the examination of a relationship between certain independent variables and the final PSQI test result did not prove the existence of a statistically relevant influence (in all cases $P>0.05$).

Discussion

The main aim of this study was to analyze the prevalence of sleep disorders in patients with epilepsy and to compare the incidence of sleep disorders with regard to clinical and demographic factors.

The prevalence of excessive daytime sleepiness in patients suffering from epilepsy is as high as 16.9%–28%,[12,13] whereas that of insomnia is 24.6%–34%.[14,15] Our study proves that in those suffering from epilepsy, insomnia is more frequent (17.9%) than hypersomnia (11.3%). In India, 24.6% of patients with epilepsy had sleep disorders.[16]

Another sleep disorder is restless legs syndrome (RLS) syndrome which occurs frequently in patients taking anti-epileptic drugs[17] and those suffering from obstructive sleep apnea. RLS syndrome prevalence in patients with epilepsy amounts to 10.2%–28.2%.[14] In our study, 14.6% of patients revealed that they suffer from the RLS and 14.6% suffer from an obstructive sleep apnea. Coincidence of epilepsy and sleep apnea syndrome may cause excessive daytime sleepiness or induce epileptic seizures.[18]

Our initial hypothesis was that the sociodemographic and clinical variables impact sleep quality. The impact of sociodemographic (age, gender, and employment status) and clinical variables (duration of epilepsy, seizure type and frequency, and type and kind of treatment) on sleep disorders was analyzed. This study did not demonstrate any correlation between sleep quality and demographic or clinical factors, or selected factors affecting sleep and conditions conducive to sleeping (in all cases, $P>0.005$). Hypothesis is rejected.

Similarly, in the studies by Moser et al,[14] Alvarez Guerrico et al,[19] and Carrion et al,[20] significant differences in PSQI according to age, gender, and type of epilepsy were not found. Sleep disorders are one of the most common factors leading to health problems. The results obtained in the current study revealed that poor sleep quality was common in patients with epilepsy, the mean score of PSQI was 9±2.

Table 6 summarizes the results among patients diagnosed with epilepsy on PSQI scale within the studies conducted in different countries. It can be observed that the only country where the result obtained by the patients (4.88 points) demonstrated good quality of sleep of those suffering from epilepsy was Austria.[14] A study conducted in Slovakia resulted in an 18.52 point score, which demonstrates a very bad quality of sleep.[25]

The data presented in Table 6 differ substantially depending on the country and the area of the world. This results from observation period, population and age of epileptic patient, seizure, and therapy. Nonetheless, it should be stressed that the groups which were compared differed in size and that the population chosen for this study by the author was the biggest (N=302).

It turned out that the biggest problem for the patients surveyed was sleep quality, which is in concordance with the results of other studies by Turaga et al[16] and Chen et al[27] (1.8 vs 0.75 vs 1.2, respectively in PSQI scale). Results of subscales of sleep disturbance are the biggest problem in our own study and in the study by Chen et al[27] (1.85 vs 1.2).

Table 6 PSQI scores of the study group and the other studies

Author, year	Study design	Place	Population	Results in PSQI (total)
Moser et al,[14] 2015	A combined retrospective and prospective study	Austria	32 patients	4.88±2.92
Wigg et al,[21] 2014	Cross-sectional	Brasil	13 patients with suicide ideation	9.5±4.8
Wigg et al,[21] 2014	Cross-sectional	Brasil	86 patients without suicide ideation	6.2±4.1
Wood et al,[22] 2008	Cross-sectional	Canada	52 mothers of children with intractable epilepsy	7.6±3.9
Turaga et al,[16] 2016	Observational study	India	199 patients	3.78±3.19
Yazdi et al,[23] 2013	Cross-sectional	Iran	152 patients	6.2
Manni et al,[24] 2013	ND	Italy	57 patients	5.2±3.6
Our work	Prospective cohort	Poland	302 patients	9.00±2.00
Klobučníková et al,[25] 2014	ND	Slovakia	17 patients with nocturnal epilepsy	18.52±7.51
Klobučníková et al,[25] 2014	ND	Slovakia	83 patients with epileptic seizures not related to sleep	6.21±3.62
Krishnan et al,[26] 2012	Cross-sectional	South India	50 with JME, on VPA only	5.16±2.98
Alvarez Guerrico et al,[19] 2013	ND	Spain	92 patients with drug resistant epilepsy	6.79±3.81
Chen et al,[27] 2011	Cross-sectional	Taiwan	117 patients	6.5±3.8

Abbreviations: JME, juvenile myoclonic epilepsy; ND, no data; PSQI, Pittsburgh Sleep Quality Questionnaire; VPA, valproic acid.

When considering epilepsy-related factors that may affect sleep, some studies mention frequency and type of seizures or the use of antiepileptic drugs.[28–32] For example, temporal lobe epilepsy is associated with a high rate of sleep disturbances,[31] whereas nocturnal frontal lobe epilepsy is associated with the problems of sleep fragmentation and increased daytime sleepiness.[33] Another study showed that patients with partial seizures have a higher incidence of sleep complaints than those with generalized seizures.[18] The results from the research by Chen et al[27] showed that a significantly higher prevalence of poor sleep quality was found in the partial seizure.

A correlation between seizure frequency and sleep was reported both in adults[18] and in children population.[34] However, other studies did not prove a relationship between sleep and frequency of seizure in adults with refractory partial epilepsy[35] and with nocturnal frontal lobe epilepsy.[36]

Considering the impact of AEDs on sleep, as shown in the literature, the old generation antiepileptic drugs are more detrimental to sleep than the new generation drugs.[37–39] The number and kind of antiepileptic drugs can affect sleep. Daytime sleepiness in patients with epilepsy significantly improves after reducing the number of antiepileptic drugs.[40,41]

While gabapentin improves sleep quality,[37] carbamazepine increases the NREM sleep and simultaneously reduces stage 1 and 2 of sleep.[42] Data concerning the influence of phenytoin on sleep seem to be controversial. In the initial period of use, phenytoin reduces sleep latency and slightly increases the NREM sleep. However, when used for a long time, it only reduced sleep latency and had no influence on REM sleep.[37,43] Ethosuximide has been shown to deteriorate the quality of sleep,[44] whereas valproates might cause sleep disorders by increasing stage 1 of sleep.[37] Phenobarbital and benzodiazepines have been shown to alter normal sleep architecture.[45] It is probable that topiramate, lamotrigine, and levetiracetam have no effect on sleepiness.[46]

However, other studies have not confirmed the relationship between quality of sleep and epilepsy[47,48] or antiepileptic medication and sleep.[10] Many factors that are not related to the illness influence the length and quality of sleep. The so-called environmental factors are sleep-affecting factors which are independent of patients to some extent. They include noise level, light, surrounding temperature, humidity and ventilation rate, and type of bed.

Another important issue is sleep hygiene. In this case, certain behaviors and practices are dependent of a patient. They include time of going to sleep, consumption of food and drinks before sleep, watching TV, working on the computer, using the phone, reading, or physical activity before sleep. Sleeping in a room where everyday activities are not performed or sharing bed with another person is of key importance. The authors' own study showed that the majority of patients with epilepsy have their own bedroom (63.6%) located in a quiet place (57.6%) where there is appropriate temperature (84.1%), have a comfortable bed and bed sheets (53%), and that they do not go to sleep when TV or a computer is on, or while reading a book (55.6%). The impact of other factors mentioned above on sleep was not assessed in the study.

Another important factor which might cause sleep disorders is night or shift work. In our study, this factor constituted

an exclusion criterion for the participation in the study. Foldvary-Schaefer[29] study showed that poor sleep hygiene can exacerbate seizures and excessive daytime sleepiness in patients with epilepsy.

Conclusion

Results of the study showed that more than a half of the patients with epilepsy were diagnosed with sleep-related diseases before taking the PSQI test. Insomnia was a disease which was prevalent in the majority of patients. Although the general result of PSQI test demonstrated bad sleep quality in the majority of patients, no relationship between certain clinical or sociodemographic variables and the final PSQI test result was proved. The study has some limitations, though. First, study participants were not comparable in terms of gender and AEDs used, which might have an influence on the final PSQI test result, as shown in the scientific literature. Second, study participants included patients who were on benzodiazepines, which might distort the study results due to the drugs' hypnotic effect. Further studies needed to be conducted to clarify the issue.

Limitation

One of the limitations of this study is that there was no control group (standard population) with which to compare the prevalence of sleep disorders among patients with epilepsy. However, to the best of our knowledge, this is the first published study about sleep disorders among polish patients with epilepsy. Hence, it should constitute a foundation for further detailed research.

Disclosure

The authors report no conflicts of interest in this work.

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