

PROFILE OF SUBJECTIVE SLEEP DISTURBANCE IN PATIENT WITH ANTIEPILEPTIC DRUGS

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Article History:

Received: October 16, 2018

Accepted: February 14, 2019

Published: July 1, 2019

Cite this as:

Zahra FA, Islamiyah WR, Budiono B. Profile of subjective sleep disturbance in patient with antiepileptic drugs. *Malang Neurology Journal*; 2019;5:61-64. DOI: <http://dx.doi.org/10.21776/ub.mnj.2019.005.02.2>

ABSTRACT

Background: Epilepsy and sleep are well recognized for having bidirectional influences upon one another. The effects of antiepileptic drugs (AEDs) on sleep are of particular concern.

Objective: The objective of this study is to know the profile of AEDs effect in patient's sleep cycle.

Methods: This analytical observational study observed total sleep time, sleep onset latency, sleep efficiency, daytime sleepiness, and insomnia in epileptic patient with AEDs of Neurology Clinic Airlangga University Hospital during May-September 2016. A cross sectional study was done by questionnaire and interview directly to the epileptic patients. Data collected was being analyzed analytically.

Results: This research was conducted among 27 patients with epilepsy based on inclusion and exclusion criteria. Sleep disturbances that had been found in patients with phenytoin are prolong sleep onset latency (11.11%), decreased sleep efficiency (11.11%), and excessive daytime sleepiness (66.67%). Sleep disturbances that had been found in patients with valproate are decreased total sleep time (33.33%), prolong sleep onset latency (11.11%), decreased sleep efficiency (11.11%), excessive daytime sleepiness (66.67%), and insomnia (11.11%). Sleep disturbances that had been found in patients with carbamazepine are decreased total sleep time (44.44%), prolong sleep onset latency (33.33%), decreased sleep efficiency (22.22%), excessive daytime sleepiness (77.78%), and insomnia (11.11%).

Conclusion: In conclusion, this study shows that epileptic patients who consumed AEDs regularly may have sleep disturbance that vary based on the type of AEDs, patients with carbamazepine may have bigger sleep disturbance than with phenytoin and valproate. It is necessary to give information and education to the epileptic patients who consumed AEDs regularly so that they will become aware of the sign of sleep disturbance.

Keywords: Epilepsy, antiepileptic drugs, sleep disturbance

Introduction

Epilepsy is a chronic non-communicable disorder of the brain that characterized by recurrent seizures. While recurrent seizures are brief episodes of involuntary movement, and it may involve a part of the body (partial) or the entire body (generalized), and are sometimes accompanied by loss of consciousness and control of bowel or bladder function. Epilepsy is also defined as having 2 or more unprovoked seizures.¹ Epilepsy treatment tends to be chronic and until now antiepileptic drugs (AEDs) still remain as the main treatment for epilepsy cases.²

Epilepsy affects people of all ages and worldwide. Approximately 50 millions of people worldwide have epilepsy, and making it as one of the most common neurological disease globally. Estimated that 2.4 million people diagnosed with epilepsy every year.¹ In Indonesia itself, prevalence of epilepsy patient is around 0.5-4% or 8.2 for every 1000 people, this number is counted higher than Thailand as the same country from South East Asian. Data from Surat Keputusan Direktur RSUD Dr. Soetomo

2014 showed that in 2013 epilepsy was the fifth top disease in outpatient installment in RSUD Dr. Soetomo.

Epilepsy and sleep are well recognized for having bidirectional influences upon one another. Epilepsy can lead to the sleep-related disorders and parasomnias can also worsen the epilepsy at the same time.³ A study stated that sleep can be a potent activator of seizure.⁴ The quality of sleep is affected by the presence and frequency of seizures, type of antiepileptic therapy utilized, and coexisting primary sleep disorders.⁵

A recent research shows sleep disturbances that occurred in epileptic children may be caused by the effect of drugs used to treat epilepsy itself.³ Some AEDs have effect on particular part of sleep architecture.⁶ The effects of AEDs on sleep are of particular concern, AEDs may interfere with normal sleep pattern and excessive daytime sleepiness.⁴

Methods

This analytical observational study observed total sleep time, sleep onset latency, sleep efficiency, daytime

sleepiness, and insomnia in epileptic patient with AEDs of Neurology Clinic Airlangga University Hospital during May-September 2016. A cross sectional study was done by questionnaire and interview directly to the epileptic patients who diagnosed and treated with AEDs by the doctor.

Sample collection technique was total sampling with inclusion criteria: epileptic patient, adult (>16 years old), treated with AEDs, monotherapy drug treatment (phenytoin, valproate, and carbamazepine), patients who able to communicate fluently and willing to participate in this study and exclusion criteria: polytherapy drugs treatment and patients with previous sleep problem before

using AEDs. The collected data was being analyzed analytically. Data processing techniques were inspection, computerization, review, and lastly arrangement.

Results

The number of epileptic patient in Neurology Clinic of Airlangga University Hospital from May-September 2016 was 78 patients, however only 27 (34.61%) patients that fulfilled the inclusion criteria of this research. The research result was shown as below.

Table 1. Characteristics of research sample (categories data).

Variable	N	Percent (%)
Age		
• 16-24 years old	8	29.63
• 25-44 years old	11	40.74
• 45-64 years old	7	25.93
• ≥ 65 years old	1	3.7
Sex		
• Male	10	37.04
• Female	17	62.96
Type of epilepsy		
• General	19	70.37
• Focal	8	29.63
AEDs		
• Phenytoin	9	33.33
• Valproate	9	33.33
• Carbamazepine	9	33.33

Table 2. Sleep Disturbance in Patients with AEDs.

	PHT (n(%))	VPA (n(%))	CBZ (n(%))
Decreased total sleep time	0 (0)	3 (33.33)	4 (44.44)
Prolonged sleep onset latency	1 (11.11)	1 (11.11)	3 (33.33)
Decreased sleep efficiency	1 (11.11)	1 (11.11)	2 (22.22)
Excessive daytime sleepiness	6 (66.67)	6 (66.67)	7 (77.78)
Insomnia	0 (0)	1 (11.11)	1 (11.11)

Discussion

Total Sleep Time

Based on CDC⁷, normal total sleep time that an adult spent a night is about 7-8 hours. Research showed that 11.11% of patients with phenytoin has longer total sleep time, and the rest 88.89% have normal total sleep for about 7-8 hours a night.

Meanwhile in patients with valproate, more patients have total sleep time for more than 8 hours which is 33.33%, patients with normal total sleep time is also 33.33%, and the rest 33.33% have shorter total sleep time.

Like in patients with phenytoin, only 11.11% of patients with carbamazepine has longer total sleep time, 44.44% have normal total sleep time for 7-8 hours, and the rest 44.44% have total sleep time for less 7 hours at night. Jain⁶ stated that carbamazepine increase total sleep time, the difference of the results might be caused by the few number of subjects and poor sleep hygiene. Walker et al also stated that patients with carbamazepine have shorter total sleep time.⁸ Meanwhile Giorelli et al⁹ stated that some epilepsy patients which consuming valproate might have decrease in total sleep time.

Sleep Onset Latency

Sleep onset latency is defined as total time needed to fall asleep and can be categorized within normal limit until 30 minutes.¹⁰ Based on the research conducted, 66.67% patients with phenytoin have sleep onset latency less than 15 minutes, 22.22% are 15-30 minutes, and 11.11% have sleep onset latency more than 30 minutes. Based on Jain⁶, Shvarts and Chung⁵, and Walker et al⁸ patients with phenytoin tend to have low number of sleep onset latency, like in this research 66.67% of patients with phenytoin have sleep onset latency for less than 15 minutes. While Shvarts and Chung⁵ stated that patients with valproate tend to have normal sleep onset latency that can be vary from 0-30 minutes, like in this research 88.89% of patients with valproate have sleep onset latency that vary from 0-30 minutes.

Research in patients with carbamazepine showed that 55.56% are less than 15 minutes, 11.11% within 15-30 minutes, and 33.33% have sleep onset latency more than 30 minutes. Shvarts and Chung⁵ stated that like in patients with phenytoin, patients with carbamazepine also tend to have shortened sleep onset latency, like in this research 55.56% of patients with carbamazepine have sleep onset

latency for less than 15 minutes. Despite high result of shortened sleep onset latency in this research, the research by Jain⁶ showed that some patients with carbamazepine may have prolonged sleep onset latency, like in this research 33.33% of patients with carbamazepine have sleep onset latency for more than 30 minutes.

Sleep Efficiency

In normal subjects, value of normal sleep efficiency should be more than 90%.⁵ Patients with phenytoin and valproate showed same result. Result showed that 88.89% of patients with phenytoin and valproate have sleep efficiency more than 90% which means normal sleep efficiency and only 11.11% have sleep efficiency less than 90%. Previous research conducted by Jain⁶ showed that phenytoin and valproate may not interrupt sleep efficiency.

Result showed that 77.78% of patients with carbamazepine have sleep efficiency for more than 90% and 22.22% for 81-90%. Eventhough the result might shows lower number compared to phenytoin and valproate, most of patients with carbamazepine have normal sleep efficiency. Walker et al⁸ stated that whether patients with phenytoin, valproate and carbamazepine all have normal sleep efficiency.

Excessive Daytime Sleepiness

Excessive daytime sleepiness is defined as inability to stay alert during major awake period of the day which resulting in falling asleep at inappropriate time.¹¹ Patients with phenytoin and valproate shows same results of excessive daytime sleepiness which are 66.67% of the patient have excessive daytime sleepiness, while 33.33% other don't have daytime sleepiness problem. Shvarts and Chung⁵ stated that 23.1% of patients with phenytoin and 2.3-45% of patients with valproate have excessive daytime sleepiness. Bigger number showed in research compared to the previous research might be caused by the few number of subjects.

In patients with carbamazepine, 77.78% of the patients have excessive daytime sleepiness which shows bigger results compared to patients with phenytoin and valproate. In research conducted by Shvarts and Chung⁵, excessive daytime sleepiness in patients with carbamazepine also showed bigger number than in other drugs which is 22-32.3%. Same as stated on MIMS, one of major adverse drug reactions in phenytoin usage is drowsiness. Bigger number showed in research compared to the previous research might be caused by the few number of subjects.

Insomnia

Research criteria defines insomnia as sleep latency of more than 30 minutes, sleep efficiency of less than 85%, and sleep disturbance occurring more than 3 times per week.¹⁰ Result showed that there are no patients with phenytoin have insomnia problem, while 11.11% of patients with valproate and carbamazepine have insomnia. Based on Shvarts and Chung⁵, insomnia in patients with valproate is 3.4%, while 2.2% of patients with carbamazepine might have insomnia, bigger number showed in research compared to the previous research might be caused by the few number of subjects. Conway and Tallian¹² also stated that patients with valproate might have insomnia. While based on MIMS, one of adverse drug reaction of phenytoin is insomnia, the difference might be also caused by the few number of subjects that doesn't covered the major patients.

Conclusion

In conclusion, this study shows that epileptic patients who consumed AEDs regularly may have sleep disturbance that vary based on the type of AEDs, patients with carbamazepine may have bigger sleep disturbance than with phenytoin and valproate. Sleep disturbances that had been found in patients with phenytoin in Neurology Clinic of Airlangga University Hospital from May-September 2016 are increased sleep onset latency, decreased sleep efficiency, and excessive daytime sleepiness. Sleep disturbances that had been found in patients with valproate in Neurology Clinic of Airlangga University Hospital from May-September 2016 are decreased total sleep time, increased sleep onset latency, decreased sleep efficiency, excessive daytime sleepiness, and insomnia. Sleep disturbances that had been found in patients with carbamazepine in Neurology Clinic of Airlangga University Hospital from May-September 2016 are decreased total sleep time, increased sleep onset latency, decreased sleep efficiency, excessive daytime sleepiness, and insomnia. It is necessary to give information and education to the epileptic patients who consumed AEDs regularly so that they will become aware of the sign of sleep disturbance.

Acknowledgement

The author thanks to Airlangga University and Airlangga University Hospital, Surabaya, East Java, Indonesia for facilitating this research.

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