Jurnal Healthsains
Printed ISSN: 2722-7782
Electronic ISSN:2722-5356
jurnal.healthsains.co.id

SLEEP DISORDERS IN CHILDREN WITH EPILEPSY AND FACTORS-ASSOCIATED

Praevilia M Salendu, Dwi Putro Widodo, Rini Sekartini
Department of Pediatrics, Faculty of Medicine, University of Indonesia, Jalan Salemba Raya No.6, Jakarta, 10430, Indonesia
Email: praevilias@gmail.com

Keywords:
child sleep disorders, child epilepsy, seizure type, typefrequency, antiepileptic drugsRemove antiepileptic drugs, intractable epiliepsy

ABSTRACT
Background: Sleep disorders often occur in epilepsy with diverse properties and complex etiologies. Epilepsy causes sleep disorders that result in decreased quality of life. The purpose of this study was to determine the prevalence of sleep disorders in children with epilepsy as well as risk factors that influence sleep disorders in children with epilepsy. Research Methods: Analytical research with a cross-sectional approach. The research site at the Kiara Children's Polyclinic at Cipto Mangunkusumo Jakarta Hospital involved 99 subjects suffering from epilepsy. Determination of the sample using consecutive sampling. Data analysis used the chi-square test and logistic regression. Results: In the study of 99 subjects, the highest age range was 7 - 12 years (46.5%), women (50.5%) and men (49.5%). Common types of seizures (64.6%). The frequency of seizures per month ≥ 5 times (15.2%), the frequency of seizures <5 times (28.3%), and never had seizures (56.5%). Polytherapy (63.6%) and the use of nonbenzodiazepine drugs (88.9%). Intractable epilepsy (22.2%), cerebral palsy (28.3%), and abnormal EEG (51.5%). The prevalence of sleep disorders is 71.7%, and the most common types of sleep disorders are disorders starting and maintaining Sleep (62%). There was a relationship between seizure type, polytherapy, OAE type, intractable epilepsy, cerebral palsy, and EEG images with sleep disorders in children with epilepsy (p <0.005). Conclusion: the prevalence of sleep disorders is 71.7%, with factors that affect sleep disorders in children with epilepsy such as generalized seizures, polytherapy, nonbenzodiazepine drugs, intractable epilepsy, cerebral palsy, and abnormal EEG images.

INTRODUCTION

Sleep is an essential need for each individual. Sleep can be interpreted as a regular resting condition with reduced body movements and decreased awareness of the surroundings, reversible and fast. Sleep needs for each age vary.[1,2] Sleep profoundly affects the health of the mental, emotional, physical, and immune systems. Changes in sleep patterns can also be a marker of abnormalities in the brain. Sleep disturbances will result in the opposite effect.[3] Sleep disorders can occur if the need for sleep hours is not fulfilled. The impact of sleep disorders on individuals includes impaired growth, cardiovascular disorders, cognitive function, and daily behavior.[2] Good sleep patterns in children are important things that must be considered. This is very related to the growth, both physical and intellectual, of the child. If it is not achieved in meeting its sleep needs, the child will experience sleep

disorders.[4] Sleep disorders are a collection of conditions in the form of disturbances in the amount, quality, or time of Sleep in individuals.[5] Sleep disorders in children are increasingly becoming a problem today. This is evidenced by the prevalence of sleep disorders in children aged 0-18 years, which is 3.7%.[2] Sleep disorders are higher in children who have diseases, such as epilepsy. This is in line with the opinion conveyed by Hysing et al. that the prevalence of sleep disorders is increasing in children with epilepsy accompanied by recurrent seizures, cerebral palsy, and other conditions related to epilepsy causing sleep disorders in children.[6] Sleep disorders often occur in people with epilepsy with diverse sleep disorders and complex etiologies. Significant sleep disturbances are often associated with epilepsy, seizures, and taking some antiepileptic drugs (OAE). Seizures can greatly affect sleep architecture, which lasts longer than the postictal period. Persistent daytime sleepiness in patients with epilepsy does not always occur due to side effects of some OAE and may be independently associated with sleep fragmentation.[7] Children with epilepsy accompanied by recurrent seizures, mental retardation, and other conditions associated with epilepsy cause sleep disturbances in children. As a result, the quality of life of a child with epilepsy may decrease.[8] Sleep disorders in children are one of the common causes of developmental regression, conduct disorders, learning disabilities, memory deficits, and poor school performance.[9]

The specific objectives of this study are:

1. Knowing the prevalence of sleep disorders in children with epilepsy.
2. Knowing the distribution of sleep disorders in children with epilepsy based on age, sex, seizure type, number of seizures, type of OAE, number of OAE, intractable epilepsy, cerebral palsy, and EEG picture.
3. Knowing the relationship between sleep disorders in epileptic children based on age, sex, seizure type, number of seizures, type of OAE, number of OAE, intractable epilepsy, cerebral palsy, and EEG picture.

Theoretical Review

Epilepsy, according to the International League Against Epilepsy (ILAE), is defined as abnormalities in the brain accompanied by seizure symptoms that occur at least two unprovoked seizures in more than 24 hours. One seizure that is not provoked and still may pose a risk of recurrent seizures after having two unprovoked seizures and a diagnosis of epileptic syndrome.[10,11] The incidence of epilepsy in children is twice as much as in adults. Today, an estimated 10.5 million children have epilepsy, with an incidence of 4–6 per 100 children, and most occur in developing countries. The existence of an excitation process in the brain that is more dominant than the process of inhibition can cause epileptic awakening. Changes in afferent excitation, disinhibition, shifts in extracellular ion concentrations, voltage-gated ion-channel opening, and strengthened neuronal synchronization are essential for initiating and propagating epileptic arousal activity. Neuronal activity is regulated by the concentration of ions within the extracellular and intracellular space and by the movement in and out of the ions that break through the neuronal membrane. Epileptogenic generation of neural tissue is generally influenced by two factors, namely excitability and synchronization.[4] Disturbances in the process of excitation and synchronization can cause epileptic seizures. Excitatory neurotransmitters are mainly glutamate, aspartate, and acetylcholine, while inhibitory neurotransmitters are gamma amino butyric acid (GABA) and glycine.[4] Epileptic seizures are classified based on clinical findings and electroencephalography (EEG)

examination. Based on the International League Against Epilepsy (ILAE) in 1981.[10,] The diagnosis of epilepsy can be determined based on directed history, physical examination, electroencephalography (EEG), and laboratory examination. A good history can select the type of seizure or epileptic awakening and its etiology. Imaging examination that is an option in cases of epilepsy is magnetic resonance imaging (MRI) of the head. Imaging is done to detect brain lesions or accompanying neurological developmental abnormalities. Imaging results also affect prognosis and management plans. The accuracy of epilepsy diagnosis can determine the appropriate type of medication, drug dose, duration of therapy given, and prognosis of epilepsy. Sleep disorders may occur in children with difficulty starting sleep, maintaining sleep, or experiencing disorders related to breathing. Changes in waking and sleeping states are complex neuronal processes, and many internal and external factors can interfere. Any factor that interferes with the ascending reticular activating system (ARAS) can increase wakefulness and reduce the likelihood of falling asleep.[1] Sleep functions restoratively, namely repairing the body's organs at each stage of Sleep. The rapid eye movement (REM) phase will affect the formation of new connections in the cortex and neuroendocrine system to the brain, while the non-rapid eye movement (NREM) phase affects anabolic processes and the synthesis of ribonucleic acid (RNA) macromolecules. The presence of sleep disorders can be a marker of pathological conditions that occur in the body so that restorative function cannot run.[12] The scale of Sleep Disorders in Children by some researchers and clinicians is widely used to detect a sleep disorder. The SDSC questionnaire consists of 26 questions with a scale method filled out by parents regarding children's sleep patterns in the last six months.[13] SDSC questionnaires have been used as measuring instruments in studies ranging in age from 3–18 years.[14] Sleep disorder therapy improves epilepsy control.[15] Epilepsy is a neurological disorder that often has neurobehavioral comorbidities related to problems, both psychiatric, cognitive, and social. Sleep disorders often occur in epilepsy patients.[16] Types of seizures, age of onset and occurrence of seizures, and antiepileptic drugs are factors that influence the disruption of sleep patterns and decreased sleep quality. Conversely, sleep disorders can also lower the seizure threshold so that seizure control disorders occur.[17] Antiepileptic drugs (OAE) reported to cause sleep disturbances, such as barbiturates, benzodiazepines, phenytoin, valproic acid, gabapentin, carbamazepine, and other antiepileptic drugs cause sleep disturbances with varying effects. The amount of antiepileptic drugs, both given monotherapy and polytherapy, causes sleep disturbances in children with epilepsy.[18,19,20] The pathophysiology of epilepsy can cause lengthening of sleep onset, sleep phase disturbance, lengthening of NREM phases 1 and 2, decreasing spindle sleep density, and decreasing REM phase.[21.22]

METHOD

This study used an analytical design with a cross-sectional approach. Data was collected by tracing the medical records of patients undergoing outpatient Treatment at the Kiara Children's Polyclinic, RSUPN Cipto Mangunkusumo, Jakarta. The study sample was all children aged 4-18 years who had epilepsy. Inclusion criteria in the form of children diagnosed with epilepsy, intractable epilepsy, epilepsy with cerebral palsy, parents understand Indonesian and are willing for their children to participate in the study. The exclusion criteria did not answer the Sleep Disturbance Scale for Children (SDSC) questionnaire questions. Patients already have primary sleep disorders such as obstructive sleep apnea (OSA), epileptic syndrome, intellectual disability, autism spectrum disorder, and ADHD. Sampling method by consecutive sampling. Research procedures by tracing data from medical records (age, sex, seizure type, frequency of seizures, type of OAE, number of OAE, intraocular epilepsy, epilepsy with cerebral palsy) as well as supporting examination data needed then conducting anamnesis to the patient's family (patient's parents) and filling out the SDSC questionnaire. The dependent variable is sleep disturbance. Independent variables: age, sex, type of seizures, frequency of seizures, type of antiepileptic drugs, amount of antiepileptic medications, intractable epilepsy, epilepsy with cerebral palsy, EEG picture. Data analysis using Chi-Square test (X2), Fisher exact test, and multivariate analysis with logistic regression test.

This research has received permission from the Research Ethics Commission of the Faculty of Medicine, University of Indonesia, with number 0603 / UN2. F1/ETIK/2018, as well as approval of research permits from the Head of the RSCM Research Section with service memorandum number LB.02/2.2.1/0635/2018.

RESULTS AND DISCUSSION

In the study conducted on 99 subjects, the highest age range was obtained at the age of 7-12 years, which was 46 people (46.5%); most of the research subjects were female, as many as 50 people (50.5%), while men were 49 people (49.5%). The most common type of seizure was generalized seizures in 64 people (64.6%). The frequency of seizures ≥5 times per month, as many as 15 people (15.2); the frequency of seizures <5 times per month, as many as 28 people (28.3); and never recurrent seizures, as many as 56 people (56.5%). Polytherapy for as many as 63 people (63.6%), and monotherapy for as many as 36 people (36.4%). The use of OAE for nonbenzodiazepine groups was 88 people (88.9%), and benzodiazepine groups as many as 11 people (11.1%). Intractable epilepsy was 22 people (22.2%) and did not suffer from intractable epilepsy as many as 77 people (77.8%). Cerebral palsy was 28 people (28.3%) and non-cerebral palsy was 71 people (71.7%). Abnormal EEG features were 51 people (51.5%), and normal EEG was 48 (48.5%). Complete data on the characteristics of the subject of this study are presented in the following table 1.

Table 1. Characteristics of Research Subjects

Characteristics of respondents	n (%)
Age of Subject	
4-6 years	31 (31,3)

7–12 years	46 (46,5)
13–18 years	22 (22,2)
Gender	
Man	49 (49,5)
Woman	50 (50,5)
Types of seizures	
Common	64 (64,6)
Partial	35 (35,4)
Frequency of Seizures (per month)	
≥ 5 times	15 (15,2)
< 5 times	28 (28,3)
Never	56 (56,5)
Number of OAE	
Polytherapy	63 (63,6)
Monotherapy	36 (36,4)
Types of OAE	
Nonbenzodiazepines	88 (88,9)
Benzodiazepines	11 (11,1)
Intratractable epilepsy	
Yes	22 (22,2)
Not	77 (77,8)
Cerebral palsy	
Yes	28 (28,3)
Not	71 (71,7)
EEG Overview	
Abnormal	51 (51,5)
Usual	48 (48,5)

Of the study subjects experienced sleep disorders, as many as 71 people (71.7%), and those who did not experience sleep disorders, as many as 28 people (28.3%). Based on the SDSC questionnaire is divided into six categories of types of sleep disorders in children with epilepsy, namely disorders of starting and maintaining Sleep as many as 44 people (62%), respiratory disorders during Sleep as many as three people (4.2%), disturbances of consciousness during Sleep as many as two people (2.8%), disorders of the sleep-wake

transition as many as six people (8.5%), excessive somnolent disorders as many as 14 people (19.7%), and hyperhidrosis during Sleep as many as two people (2.8%For complete data on Sleep disorders in children with epilepsy are presented in the following table 2.

Table 2.Sleep Disorders in Children with Epilepsy

SDSC Results	n (%)
Sleep disorders	
Yes	71 (71,7)
Not	28 (28,3)
Types of Sleep Disorders	
Disorders of starting and maintaining Sleep	44(62)
Respiratory Disorders During Sleep	3 (4,2)
Impaired consciousness	2 (2,8)
Sleep-wake transition disorders	6 (8,5)
Excessive somnolent disorders	14 (19,7)
Hyperhidrosis during sleep	2 (2,8)

In this study, bivariate analysis was carried out to determine the relationship between independent and bound variables using the chi-square and Fisher's exact tests (if the expected count value is less than five by > 20%). The factors analyzed in this study include type of seizures, frequency of seizures, cerebral palsy, intractable epilepsy, EEG description of epilepsy patients, type of antiepileptic drugs used, and the number of antiepileptic medications consumed. Each of these factors was analyzed for sleep disorders in children. Bivariate analysis data on factors affecting sleep disturbances in children with epilepsy can be seen in Table 3 below.

Table 3. Relationship Between Sleep Disorders in Children with Epilepsy and Influencing Factors

Variable	Sleep disorders n(%)		P	OR	IK 95%
	Yes	Not			
Age*					
13 – 18 years old	17(77,3)	5(22,7)	0,74	1,61	0,46-5,64
7 – 12 years	33(71,7)	13(28,3)		1,20	0,45-3,25
4 – 6 years	21(67,7)	10(32,3)		Ref	
Gender*					
Man	37 (75,5)	12(24,5)	0,54	1,45	0,60-3,50

Woman	34 (68)	16(32)			
Seizure Type*					
Common	56 (87,5)	8 (12,5)	<0.001	9,33	3,43-25,33
Partial	15 (42,9)	20 (57,1)			
Seizure Frequency*					
≥ 5 times	11 (73,3)	4 (26,7)	0,301	1,41	0,39-5,03
< 5 times	23 (82,1)	5 (17,9)		2,36	0,77-7,19
Never	37 (66,1)	19 (33,9)		Ref	
Number of OAE*					
Polytherapy	52 (82,5)	11 (17,5)	0,003	4,23	1,68-10,64
Monotherapy	19 (52,8)	17 (47,2)			
OAE Type**					
Nonbenzodiazepines	67 (76,1)	21 (23,9)	0,011	5,83	1,48-20,95
Benzodiazepines	4 (36,4)	7 (63,6)			
Intratractable Epilepsy*					
Yes	20 (90,9)	2 (9,1)	0,046	5,09	1,10-23,50
Not	51 (66,2)	26 (33,8)			
Cerebral palsy*					
Yes	26 (92,9)	2 (7,1)	0,007	7,51	1,64-34,24
Not	45 (63,4)	26 (36,6)			
EEG Overview*					
Abnormal	46 (90,2)	5 (9,8)	<0.001	8,46	2,86-24,94
Usual	25 (52,1)	23(47,9)			

*Performed with Chi-Square Test
** Performed with Fisher's Exact Test

In this study, a multivariate analysis was carried out with logistic regression tests to determine the factors that affect sleep disorders in children with epilepsy. Multivariate analysis carried out logistic regression testing with the Backward method obtained an Omnibus Test of Model Coefficients value of <0.001 so that it can be concluded that there is at least one independent variable that can affect the dependent variable. In the Model Summary, an R-value $^{of\ 2}$ ^{of} 0.726 was obtained, which means the influence of determinant factors can be explained by the test model of 72.6% and the value of the Classification Table in the regression model of 86.9, which means that the logistic regression test model in this study is good enough because it can guess correctly 86.9% of the conditions that occur. In this study,

the independent variables involved in the test model for sleep disorders in children were the type of seizure, cerebral palsy, intractable epilepsy, EEG picture, type of OAE, and the amount of OAE use. Meanwhile, age, sex, and frequency of seizures were not included because the bivariate analysis had no association with sleep disturbances. The results of the logistic regression test can be seen in Table 4 below.

Table. 4. Multivariate Analysis of Factors Influencing Sleep Disorders in Children with Epilepsy

Variable	Bivariate analysis		Multivariate analysis	
	P value	OR (IK95%)	P value	OR (IK95%)
Seizure Type (General)	<0.001	9,33 (3,43-25,33)	0,001	0,056 (0,01-0,32)
Cerebral palsy	0,007	7,51 (1,64-34,24)	0,021	0,04 (0,00-0,61)
Intractable epilepsy	0,046	5,09 (1,10-23,50)	0,037	0,061 (0,00-0,84)
Abnormal EEG	<0.001	8,46 (2,86-24,99)	<0.001	0,035 (0,00-0,22)
Types of OAE (Non-benzodiazepines)	0,011	5,58 (1,48-20,95)	0,035	0,009 (0,00-0,70)
Number of OAE (Polytherapy)	0,003	4,23 (1,68-10,64)	0,085	0,261 (0,05-1,20)

*****Logistic regression test with Backward LR method

In the multivariate analysis, the influential variables (p< 0.05) on sleep disorders in children with epilepsy were intractable epilepsy, seizure type, cerebral palsy, abnormal EEG images, and use of nonbenzodiazepine OAE. Meanwhile, OAE polytherapy did not affect sleep disorders in children with epilepsy (p = 0.08).

In this study (**Table 1**), the highest age range was found to be 7-12 years (46.5%), women (50.5%), and men (49.5%). This result is by previous research conducted by Sari et al.[16], who reported the highest age range in children with epilepsy at ages >6–12 years. In most population studies, the incidence of epilepsy is higher in men than in women.[23] Asadi and Hojabri24 report that men may be a risk factor for epilepsy. The most common type of seizure was generalized seizures (64.6%). Research conducted by Andrianti et al.[25] reported the most common seizure types in children with epilepsy at 55.3%. Tjandrajani26 reported a prevalence of generalized seizure types in childhood epilepsy of 78.6%. According to Banerjee and Hauser, generalized seizures are the most common type of seizure in population studies.Twenty-three seizures did not occur the most (56.5%). Thus, it can be concluded that most of the subjects had a state of controlled epileptic seizures. According to Agung and Elisabeth[27, the frequency] of recurrent (uncontrolled) seizures after obtaining OAE in epileptic patients can be influenced by the frequency of seizures before therapy >10 times, status epilepticus, the presence of neurological deficits, the presence of concomitant neurological abnormalities, and the administration of antiepileptic drugs that are not immediate. Polytherapy (63.6%) and the use of OAE in the nonbenzodiazepine group (88.9%) were more than the benzodiazepine group (11.1%). The results of this study are different from those conducted by Sari et al.[16], who reported more epilepsy patients in children receiving monotherapy (67.7%) than those with

polytherapy (32.3%). Andrianti et al.[25] also reported a greater number of epilepsy patients in children receiving monotherapy (96.1%) than polytherapy (3.9%). Valproic acid is the most widely used monotherapy drug as an antiepileptic treatment (89.3%).[25] Valproic acid is widely used because of its higher success rate as monotherapy (64.7%).[28] In addition to its high success rate, valproic acid is also effective in all types of seizures, especially the abscess type. Valproic acid can be used in both generalized and focal-partial seizures. Other drugs, such as barbiturates and benzodiazepines, which are sedative drugs, tend to be limited in use.[26] Intractable epilepsy (22.2%), according to Zanzmera et al.[7,] reports that approximately 36% of epilepsy patients continue to have seizures (intractable epilepsy). One of the risk factors that can influence the occurrence of intractable epilepsy is lack or disruption of sleep.[7] Cerebral palsy (28.3%) less than those without cerebral palsy (71.7%). Sari et al.[16]. reported as many as 31 subjects (21%) children with epilepsy had cerebral palsy. The frequency of epilepsy in cerebral palsy varies between 15-60% depending on the type of cerebral palsy. The course of epilepsy in children with cerebral palsy tends to be intraocular epilepsy; 13% of cerebral palsy patients with epilepsy achieve remission of 2 years or more.Twenty-nine abnormal EEG images (51.5%) were more than normal EEG images (48.5%). Andrianti et al.[25] reported, among 81 patients, abnormal EEG results 59 (72.8%), and also Tjandrajani's 26, which reported 82.3% abnormal EEG results. Keep in mind that not always impaired brain function can be reflected in EEG recordings. Normal EEG images can be found in children who are suffering from brain disorders and vice versa. Abnormal EEG can be found in normal and healthy children.[30] Based on the sleep disturbance scale for children (SDSC) questionnaire in this study (**Table 2**), subjects who experienced sleep disorders were found (71.7%). Sari et al.[16] reported sleep disturbances in children with epilepsy by 67.7%, and Ong et al. mentioned sleep disorders in 92 children with epilepsy by 73.7%.[10] The pathophysiology of epilepsy can cause lengthening of sleep onset, sleep phase disturbance, lengthening of NREM phases 1 and 2, decreasing spindle sleep density, and decreasing REM phase. The presence of sleep disorders in children with epilepsy is related to GABA-release disorders. A decrease in GABA or an increase in acetylcholine and norepinephrine is responsible for the pathophysiology of sleep disorders in children with epilepsy, both in epilepsy with partial and generalized seizures.[13,32] The most common sleep disorders found in this study were disturbances in starting and maintaining Sleep (62%). Disturbances in starting and maintaining Sleep are determined by sleep duration, increased sleep latency, and disturbances in sleep stages. Several factors are thought to influence the disorder of initiating and maintaining Sleep: caffeine and nicotine consumption, environment, sleep hygiene, and co-sleeping.[33] The causes of sleep disturbances in children with epilepsy may be due to side effects of antiepileptic drugs or other sleep disorders, poor seizure control, and lack of sleep.[9] Sunmonu et al. also argue similarly that the frequency of sleep disturbances is observed to be higher in people with epilepsy. In particular, excessive daytime sleepiness, insomnia, and parasomnias are most common and can lead to cognitive impairment and poorly controlled seizures.[34] In addition to conditions related to epilepsy, sleep disorders in children and adolescents are also influenced by various factors, both medical and non-medical. Non-medical factors that affect Sleep include gender, puberty, sleep habits, socioeconomic status, family circumstances, lifestyle, and environment associated with sleep disorders. Medical factors that affect Sleep include various neuropsychiatric disorders and chronic diseases, such as asthma and atopic dermatitis.[27] Rini

S. reported that increasing age in children causes more factors to influence sleep patterns, so the more likely children are to experience sleep disorders.2 In this study (**Table 3)** there was no significant association between age and sleep disturbances (p = 0.74). In addition to related to epilepsy and non-medical factors related to sleep disorders. In this study, the increasing percentage of sleep disorders in the age range of 7-12 years did not rule out the possibility caused by the role of parents (mothers) who filled out the SDSC questionnaire. The questionnaire is based on the child's sleep pattern history in the last six months. Filling out the SDSC questionnaire conducted by the patient's parents (mother) can affect the percentage of sleep disorders in that age range, which can be higher. This is like previous research conducted by Sari et al[16], which stated that the SDSC questionnaire is a screening test tool with fairly high sensitivity and specificity, but this questionnaire is based on parental reports, so it can cause bias and affect research results.Often, sleep disorders in children are not detected by parents and are not treated properly. Complaints usually conveyed by parents include irregular sleep habits, lack of or excessive sleep time, waking up at night, and drowsiness during the day.[23,36] Therefore, sleep disorders in children and adolescents often go undiagnosed and ultimately not treated properly.[27] Men had more sleep disturbances than women (p = 0.54; OR 1.45). Male patients have a risk of sleep disorders 1.45 times greater than women. Adelina et al. reported that there was no association between sex and sleep disturbances. The same thing was also found in research conducted by Dini S.[37]. The generalized seizure type had a greater percentage of sleep disturbances than the partial type (p<0.001; OR 9.33). Sari et al.[16] Of the reports that the generalized type of seizure affects sleep disturbances, generalized seizures increase the risk of sleep disturbances 5.2 times compared to partial seizures.[16] Maulana reported that seizure frequency was not significantly associated with sleep disturbances (p = 0.171).[38] Patients receiving OAE polytherapy had a greater percentage of sleep disturbances than patients receiving OAE monotherapy. There was an association between OAE polytherapy and sleep disorders (p = 0.003; OR 4.23). This result is in line with Bazil et al.[39] Antiepileptic drugs are associated with structural changes, having varying effects on sleep stages. According to Tracy et al.[40], the Treatment of epileptic patients with antiepileptic drugs (AEDs) aims to prevent further recurrence, both overall and reduce the frequency and severity by minimizing the possibility of side effects. Treatment should begin with one type of medication. Ideally, the choice of drug type depends on the type of epilepsy and the type of seizure or seizure. Improving seizure control, avoiding polytherapy, and choosing the right OAE are important to provide the best benefit in managing sleep disorders in patients with epilepsy.[36]OAE of the nonbenzodiazepine group of 76.1% has a greater percentage of sleep disturbances than the use of OAE of the benzodiazepine group of 36.4%. There was an association between the use of nonbenzodiazepine OAE and sleep disturbances (p = 0.011; OR= 5.83). Sari et al[16] who reported the most use of the type of OAE in childhood epilepsy was valproic acid. Valproic acid works by inhibiting GABA breakdown enzymes (GABA T and succinate semialdehyde dehydrogenase), inhibiting voltage-gated sodium channels and lowering the calcium current threshold. Some studies say valproate does not cause sleep disorders. In other studies mentioned, valproate rarely disrupts sleep structure, but in the study of Legros et al., valproate can interfere with Sleep by increasing phase 1 NREM, which can cause excessive sleepiness.[21] Intractable epilepsy has a greater percentage of sleep disturbances than those without intractable epilepsy. There was an

association between intractable epilepsy and sleep disturbances (p = 0.046; OR 5.09). Intractable epilepsy is generally associated with structural abnormalities of the brain and is estimated to account for 20–40% of all epilepsy.[41,42] Refractory seizures are associated with more sleep abnormalities than less frequent seizures. In particular, excessive daytime sleepiness, insomnia, and parasomnias are most frequent and lead to cognitive impairment and poorly controlled seizures.[43] Cerebral palsy has a greater percentage of sleep disturbances than those without cerebral palsy. There was an association between cerebral palsy and sleep disturbances (p = 0.007 ; OR 7.51). According to Dutt et al. report, between 23%–46% of children with cerebral palsy experience sleep problems. Sensory, motor, and cognitive symptoms in cerebral palsy (such as immobility, pain, and seizures) act as predisposing factors for sleep problems.[44] According to Newman et al.,[45] reported between 23%–46% of children with cerebral palsy had sleep disturbances. Sleep problems experienced by children with cerebral palsy include difficulty in initiating and maintaining Sleep, waking transitions, sleep breathing disorders, sleep bruxism, excessive daytime naps, nightmares, and sleep talking. Abnormal EEG images have a greater percentage of sleep disturbances than normal EEG images. There was an association between abnormal EEG images and sleep disturbances (p<0.001;OR= 8.46). This sleep disorder correlates with how often seizures, the age of the child, the length of illness, the presence of paroxysmal activity on the EEG, and behavioral problems. Sleep architecture disorders have been noted in epileptic patients. This disorder shows a different form. It may appear as a disturbance and instability of the protective REM sleep phase by shortening the duration of the REM phase.[36]In this study (**Table 4)**, the independent variables involved in the test model for sleep disorders in children were seizure type, cerebral palsy, intractable epilepsy, EEG picture, type of OAE and amount of OAE use. Meanwhile, seizure frequency was not included because the bivariate analysis had no association with sleep disturbances. P there is a multivariate analysis obtained variables that influence (p < 0.05) on sleep disorders in children with epilepsy sequentially based on the OR value in multivariate analysis are intractable epilepsy, generalized seizures, cerebral palsy, abnormal EEG images and the use of OAE nonbenzodiazepine groups. In addition, OAE polytherapy had no effect on sleep disorders in children with epilepsy (p = 0.08). Bazil et al.,[46] mention that sleep disorders in children with epilepsy can be influenced by the type of epileptic seizures, the type of drug, and the number of antiepileptic drugs. This is by the results of the research of Bazil et al. Acquired sleep disorders in children with epilepsy are influenced by the type of epileptic seizures, the type of drug, and the amount of antiepileptic drugs. Several studies have been conducted to determine the prevalence of sleep disorders in children with epilepsy. To determine the relationship between sleep disorders in children with epilepsy, it is necessary to consider several factors, namely changes in sleep habits complained by parents, based on clinical examination and polysomnography tools, seizure relationships, epileptic form images, sleep structure disorders, and effects caused by antiepileptic drugs. Inadequate sleep hygiene and circadian rhythm disturbances play a role in increasing the severity of sleep disorders. In addition, evidence suggests that the presence of epilepsy itself can disrupt Sleep, and even more evidence suggests that seizures themselves can disrupt Sleep (even when seizures occur in a conscious state). A further complication in the management of sleep disorders in epilepsy is that anticonvulsant drugs can affect Sleep, both beneficially and detrimentally, and these effects appear independent of anticonvulsant

action.[39] In children with epilepsy of varying etiologies, based on polysomnography examination, the main abnormalities of the sleep structure picture are the reduction of total sleep time, sleep efficiency, the REM phase and the increase in other sleep phases and disturbances when waking up after sleep.[2]

CONCLUSION

The prevalence of sleep disorders in children with epilepsy was 71.7%, and the most common type of sleep disorder was the disorder of starting and maintaining Sleep (62.6%). The distribution of characteristics of subjects was found to be mostly 7–12 years of age, female sex, generalized seizure type, frequency of seizures that never had a seizure in a month, polytherapy, nonbenzodiazepine class, epilepsy that is not intractable, without cerebral palsy, and abnormal EEG images. In a multivariate analysis of risk factors that affect sleep disorders in children with epilepsy sequentially, namely intractable epilepsy, generalized seizures, cerebral palsy, abnormal EEG images, and use of OAE nonbenzodiazepine groups.

BIBLIOGRAPHY

Tanjung MFC, Sekartini R. Sleep problems in children. Sari Pediatrics. 2004;6:138-42.

Thiedke CC. Sleep disorders and sleep problems in childhood. Am Fam Physician. 2001;63:227-84.

Gilkin C. Brain Can Compensate for Short-term Sleep Deprivation. Nature. 2000;403:655-7.

Lumbantobing SM. Etiology and faalsakitanepilepsy. Textbook of neurology. Second edition. FKUI 2007;197-203.

Owens J. Classification and epidemiology of childhood sleep disorders. Prim Care Clin Off Pr 2008;2:533-46.

Hysing M, Sy PD, Sivertsen B, Stormark KM, Elgen I, Lundervold AJ. Sleep in children with chronic illness, and the relation to emotional and behavioral problems population-based study. J PediatrPsychol 2009;34:665-70.

Zanzmera P, Shukla G, Gupta A, Singh H, Goyal V, Srivastava A, Behari M. Markedly disturbed Sleep in medically refractory compared to controlled epilepsy- A clinical and polysomnography study. Seizure. 2012;21:487-490.

Liu Z, Avula S, Tolaymat A. Sleep disorders in childhood epileptic disorders. SM J Sleep Disord. 2017; 3(2):1013.

Yazdi Z, Sadeghniiat-Haghighi K, Naimian S, Zohal MA, Ghaniri M. Prevalence of sleep disorders and their effects on sleep quality in epileptic patients. Basic ClinNeurosci 2013;4:36-41.

Engel Jr. Classification of the International League Against Epilepsy: time for reappraisal. Epilepsya 1998;39:1014-1017.

National Institute for Health and Care Excellence. Epilepsyes : diagnosis and management. 2012; 8:1–20.

Walker MP. The role of Sleep in cognition and emotion. Annals of the New York Academy of Sciences. 2009; 1156(1):168-97.

Natalita C, Sekartini R, Pusponegoro H. Sleep disorders scale for children (SDSC) as a screening instrument for sleep disorders in first-level secondary school children. Sari Paediatrics 2011; 12:365-72

Bruni O, Ottaviano S, Guidetti V, Romoli M, Innocenzi M, Cortesi F. The Sleep Disturbance Scale for Children (SDSC). Construction and validation of an instrument to evaluate sleep disturbances in childhood and adolescence. J Sleep Res.1996;5:251-61.

Elkhayat et al. Melatonin and sleep-related problems in children with intractable epilepsy. Pediatr Neurol. 2010; 42(4):249-54.

Sari R, Triono S, Sutomo R. Sleep disorders in children with epilepsy. Sari Paediatrics 2017; 19(1):7-13.

Byars AW, Byars KC, Johnson CS, Ton J, Fastenau PS, Perkins S, et al. Epilepsy & behavior, the relationship between sleep problems and neuropsychological functioning in children with first recognized seizures. Epilepsy Behav2008; 13:607–13.

Al-Biltagi M. Childhood epilepsy and Sleep. World J Clin Pediatr 2014; 3:45–53.

Becker DA, Fennell EB, Carney PR. Daytime behavior and sleep disturbance in childhood epilepsy. Epilepsy Behav2004; 5:708–15.

Legros B, Bazil CW. Effects of antiepileptic drugs on sleep architecture: a pilot study. Sleep Med 2003; 4:51–5.

Crespel A, Baldy-Moulinier M, Coubes P. The relationship between Sleep and epilepsy in frontal and temporal lobe epilepsies: practical and physiopathologic consideration. Epilepsya 1998;39:150-7.

Gutter T, Brouwer OF, de Weerd AW. Subjective sleep disturbance in children with partial epilepsy and their effects on quality of life. Behav Epilepsy 2013;28:481-8.

Poonam N B,W Allen H. In: Jerome EngelJR, Timothy A. Pedley, editors. Epilepsy: a comprehensive textbook. Second edition. Philadelphia: Lippincott Williams & Wilkins 2007.pp.45-56.

Asadi-Pooya AA &Hojabri K. Risk factors for childhood epilepsy: a case-control study. Behav's epilepsy. 2005;6:203-6.

Andrianti PT, Gunawan PI, and Hoesin F. Profile of Children's Epilepsy and Success of Treatment at RSUDDr. SoetomoYear 2013. Sari Pediatrics, 2016; 18(1):34-39

Tjandrajani A. Characteristics of epilepsy cases in our Children's and Mother's Hope Hospital in 2008-2010. Sari Paediatrics 2012;14:143-6.

Haryono A, Rindiarti A, Arianti A, Pawitri A, Ushuluddin A, Wawolumaja CW, and Sekartini R. Prevalence of sleep disorders in adolescents aged 12-15 years in Junior High School. Sari Pediatrics2009; 11:149-153

Triono A, Herini E. Prognostic factorsfailure of epilepsytherapy in children with monotherapy. Sari Paediatrics2014;16:248-53.

Panayiotopoulos CP. The epilepsyes: seizure, syndrome and management. UK: Blandon Medical Publishing; 2005. p. 29-44.

Smith SJM. EEG in diagnosis, classification, and management of patients with epilepsy. J Neurol Neurosurg Psychiatry. 2005; 76:II2-II7.

Ong LC, the WW, Wong SW, Al Siddiq F, Khu YS. Sleep habits and disturbance in Malaysian children with epilepsy. J Paediatr Child Health.2010;46:80-4.

Romeo DM, Bruni O, Brogna C, Ferri R, Galluccio C, De Clemente V. Application of the sleep disturbance scale for children (SDSC) in preschool age. Eur J Paediatr Neurol.2013;17:374-82.

Cortese S, Ivanenko A, Ramtekkar U, Angriman, M. Sleep disorders in children and adolescents. In: IACAPAP e-textbook of child and adolescent mental health. International association for child and adolescent psychiatry and allied professions. Geneva: IACAPAP; 2014.p.1–34.

Sunmonu T, Komolafe M, Ogunrin O, Ezeala B, Abubakar S, Iwuozo E. Sleep disturbances in patients with epilepsy in Nigeria. Ann Afr Med. 2015; 14(2):103-8.

Sekartini R and Adi NP. Sleep disorders in children under three years old in five cities in Indonesia. Sari Paediatrics 2006; 7:188-193

Cortesi F, Giannotti F, OttavianoS. Sleep problems and daytime behavior in childhood idiopathic epilepsy. Epilepsya1999; 40: 1557-1565

Zahara DS. The relationship between sleep disorders and growth in children aged 3-6 years in Semarang City. Journal of Young Medicine.2013.

Maulana, I. Sleep Disorders in Children with Epilepsy at Dr. Moewardi Hospital: Prevalence and Risk Factors.Thesis. University of Eleven March .2017

Bazil CW, Walczak TS. Effects of sleep and sleep stage on epileptic and nonpileptic seizures. Epilepsya. 1997;38:56-62.

Tracy G, Elinor B-M, Blaise B et al. ILAE treatmentguidelines: evidence-based analysis of antiepilepticdrug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndrome. Epilepsya 2006;47:1094-120.

Kwan P, Brodie MJ. Refractory epilepsy: A progressive, intractable but preventable condition? Seizure. 2002; 11(2):77–84.

Freitag CM, May TW, Pfafflin M. Konig S, Taring D. Incidence of epilepsyes and epileptic syndrome in children and adolescent: a population-based prospective study in Germany. Epilepsya. 2001;42:979-88.

Carrion M, Nunes M, Martinez J, PortuguezM,Costa J. Evaluation of sleep quality in patients with refractory seizures who undergo epilepsy surgery. Epilepsy &; Behavior. 2010;17:120-123.

Christensen D, van Naarden Braun K, Doernberg N.S, Maenner M.J, Arneson C.L, Durkin M.S, Benedict R.E, Kirby R.S, Wingate M.S, Fitzgerald R,et al. Prevalence of cerebral palsy, co-occurring autism spectrum disorders, and motor functioning—Autism and Developmental Disabilities Monitoring Network, USA, 2008. Dev. Med. Child Neurol. 2014, 56, 59–65.

Newman, C.J.; O'Regan, M.; Hensey, O. Sleep disorders in children with cerebral palsy. Dev. Med. Child Neurol. 2006, 48, 564–568.

Bazil CW. Behavior epilepsy and sleep disturbance. Behav's epilepsy. 2003;4:39-45.