Sleep and epilepsy

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Abstract

Introduction: Sleep and epilepsy have a bidirectional relationship. Children with epilepsy have a higher prevalence of sleep problems. In turn, these sleep disturbances can exacerbate seizures, contribute to cognitive and behavioral disturbances and impact the quality of life of both children and families. In this study we explored the prevalence and nature of sleep problems in children with epilepsy and its impact on parents.

Methods: A validated sleep questionnaire was presented to the parents of children with epilepsy (aged between 6 months and 18 years).

Results: Parents of 106 children (59 males, 47 females) completed the questionnaire. Mean age was 8.4 years (SD ± 5.1). Chronic insomnia was present in 21% of the patients, and an additional 37% experienced mild settling or night waking problems. Most children experienced problems maintaining sleep, while difficulties related to sleep initiation were less frequent (54% versus 13%). The prevalence of sleep problems decreased with age. Sleep difficulties have a serious impact on the parents, with 64% of the parents experiencing a negative influence from the sleep problems of their child, with daytime fatigue, concentration problems but also feelings of incompetency, irritability, or even depressive feelings.

Conclusion: One out of 5 children with epilepsy has a chronic insomnia, mainly due to problems related to waking up during the night. Settling problems are less frequent. The impact of these sleep problems for children and their parents is huge. Screening for sleep problems should be part of the integrative care of children with epilepsy.

Introduction

Sleep is an active process with varying important functions, related to brain development, synaptic plasticity, learning and attention, emotional regulation, and behavior (1). Sleep difficulties are frequent in children and adolescents, ranging between 25 and 40% in healthy children. In children with neurodevelopmental problems and / or epilepsy, the incidence of sleep difficulties is even higher (2, 3).

Sleep disturbances do not only alter sleep processes but also negatively impact cognitive functioning, behavior, emotions and may exacerbate seizures in patients with epilepsy (4-6). In addition, disruption of the sleep has a negative impact on the quality of life of patients and their caregivers (7, 8). Caregivers of children with epilepsy often already lack restful sleep due to the fear of seizures in their child's sleep or sudden unexplained death in epilepsy (SUDEP) (9).

To adequately treat the sleep problems, it is important to differentiate between the different sleep problems. Seven major sleep disorders are described in the 3rd edition of the International Classification of Sleep Disorders (ICDS-3) including insomnias, parasomnias, sleep-related movement disorders, sleep-related breathing disorders, central disorders of hypersomnolence, circadian rhythm sleep-wake disorders and other sleep disorders. Diagnosis of insomnia requires repeated difficulties with sleep initiation or sleep maintenance that occur despite age-appropriate time and opportunity for sleep and results in daytime functional impairment for the child and/or family.

In this paper we studied the prevalence of sleep problems and more specifically insomnia and its components in children with epilepsy.

Methods

Patients with epilepsy, aged 6 months up to (and including) 18 years, followed at our outpatient pediatric epilepsy clinic at the Antwerp University Hospital could be included. The survey consisted of the Dutch translation of the '*Sleep Behavior Questionnaire by J.F. Simonds & H. Parraga (SQ-SP), modified version for use in individuals with intellectual disability (ID)*' (10, 11). This sleep questionnaire has been used in individuals with ID or genetic syndromes (12-14) and assesses several types of sleep problems with their level of severity. Completed questionnaires can be evaluated by different scores: Composite Sleep Index (CSI) and 5 different sleep factor scores (FS). The CSI reflects the level of severity of sleep problems. A CSI of ≥ 4 is an indicator of a severe sleep problem. There are 5 different factor scores; snoring, daytime sleepiness, complaints related to sleep, sleep apnea and anxiety related to sleep. The FS 'complaints related to sleep' refers to movements, excessive sweating, and episodes of confused behavior during sleep. Sleep problems were defined according to the definition of Wiggs and Stores (table 1) (15).

Table 1: definition of sleep problems according to Wiggs L et al. (15)

Sleep problem	Definition
Severe settling problem	Occurred ≥3 nights per week, whereby it took more than 1 hour to fall asleep and parents or other caregivers were disturbed during this time
Mild settling problem	Occurred 1-2 nights a week and falling asleep took >30 minutes and parents or other caregivers were disturbed during this time
Severe night waking problem	Occurred ≥3 nights per week and the child woke up for more than a few minutes and disturbed parents or other caregivers during that time
Mild night waking problem	Occurred 1-2 nights a week and the child woke up for more than a few minutes and disturbed parents or other caregivers during that time
Severe early waking problem	Waking before 5 o'clock in the morning several times per week

The digital questionnaire (Qualtrics Survey Software) was presented on an electronic device to the parents of patients with epilepsy during their ambulatory visit at the outpatient epilepsy clinic. The questionnaire could be completed during the visit. The study was approved by the ethics committee of the Antwerp University Hospital. Participation was completely voluntary. The anonymised data was extracted out of the Qualtrics Survey Software into IBM SPSS Statistics version 27 for statistical analysis. Chi square was used for comparison of group differences for categorical variables.

Results

Responses of 106 children with epilepsy were collected (59 males and 47 females). Questionnaires were mainly completed by the mother (80.2%). The median age was 7.4 years (SD 5.1, range 1 – 18 years). All patients had epilepsy although the etiology was heterogeneous, ranging from absence epilepsy to a Lennox-Gastaut Syndrome (a severe epileptic encephalopathy). Most of the patients had a genetic or structural etiology for their epilepsy. Almost all patients took at least one antiseizure medication (97.2%), with a median of 2 (range 0 – 5). Many patients (36.8%) used a benzodiazepine for their epilepsy. An intellectual disability (mild – severe) was present in 71.4% and a motor impairment in 60.4%. Approximately 10% was not able to turn around in bed without help.

The seizure frequency was variable, with 23.6% of the patients having ≥1 convulsive seizure per week while 39% was seizure free during the last month. Nocturnal seizures were seen in 51% although the majority of the patients (68.2%) mainly had seizures during the day. Most of the patients slept alone in their room (67%). In 20% parents used a nocturnal detection device (to detect nocturnal seizures or due to fear of SUDEP).

Without providing criteria or definitions of sleep problems, approximately 29% of the parents responded positively on the question 'Do you think your child has a sleep problem?' (figure 1). Parents identified the sleep problems mainly as problems with sleeping through the night. In 70% of the patients these sleep problems were present for >1 year.

Based on the SQ-SP questionnaire (CSI score ≥4), a serious sleep problem was present in approximately 1 out of 6 patients (17.9%). A mild or severe night waking problem was seen in 54% of the patients, a mild or severe settling problem in 13% and early waking problems in 8.5% (figure 2). With age the prevalence of sleep problems diminished, especially the night waking problems, although even in the older age groups, severe sleep problems remained present (figure 3). The prevalence of sleep problems was not significantly higher in patients with frequent nocturnal seizures (≥1 per week) or patients with mainly nocturnal seizures. Patients using a benzodiazepine, more frequently had mild night waking problems (p=0.003), but severe night waking problems (p=0.266) or settling problems were not significantly different.

Figure 1 : *Parental report of sleep problems*
*Legend. *Question ('Do you think your child has a sleep problem?') was presented to one of the parents of 106 children with epilepsy, 2 parents did not complete this question. This question was presented without definition of sleep problems.*

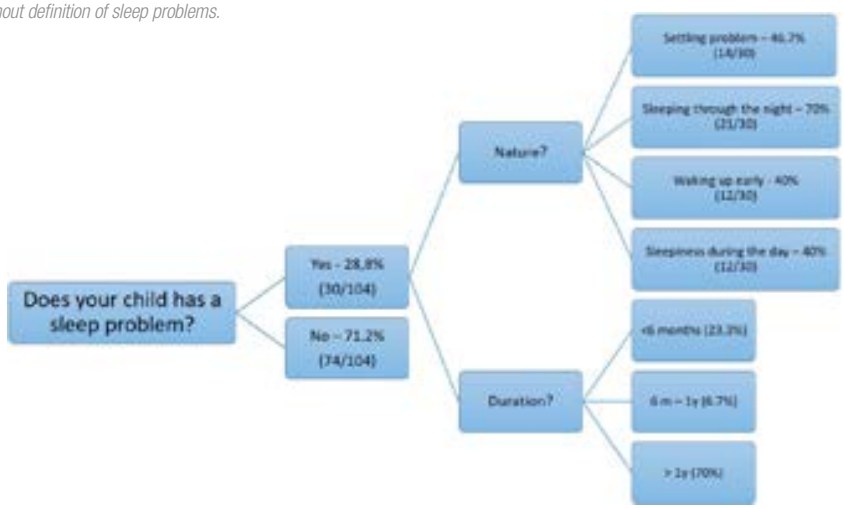


Figure 2 : *Illustration of the prevalence of sleep problems in patients with epilepsy*
*Legend. Illustration of the prevalence of sleep problems in patients with epilepsy based on the SQ-SP questionnaire and definition of Wiggs and Stores. *overall is the combination of patients with a mild or severe sleep problem. #Severe early waking problems is defined as waking up before 5am >2 times per week. Mild early waking problems is defined as waking up before 5am 1-2 times per week. °Sleep problem is the combination of night waking, settling and early waking problems. CSI, composite sleep index. A CSI of ≥4 is defined as a severe sleep problem.*

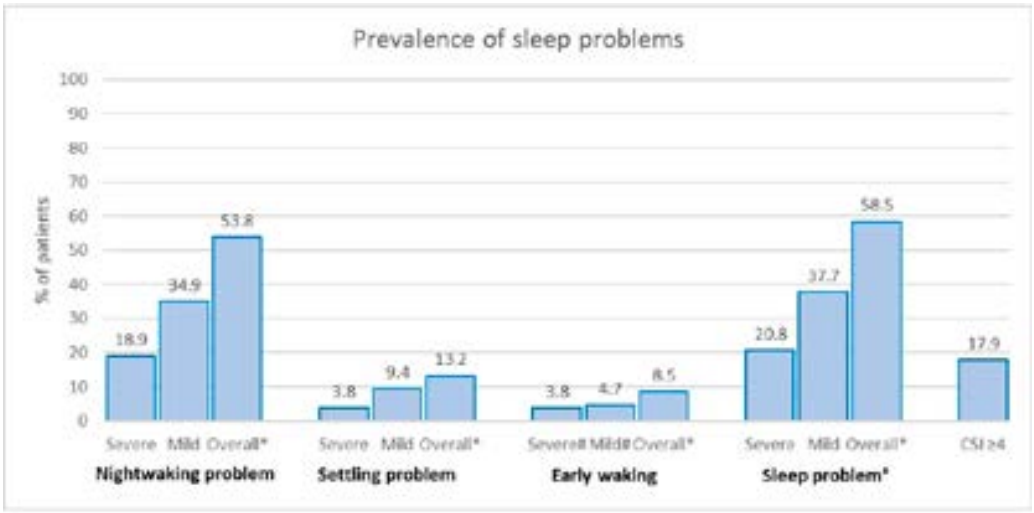
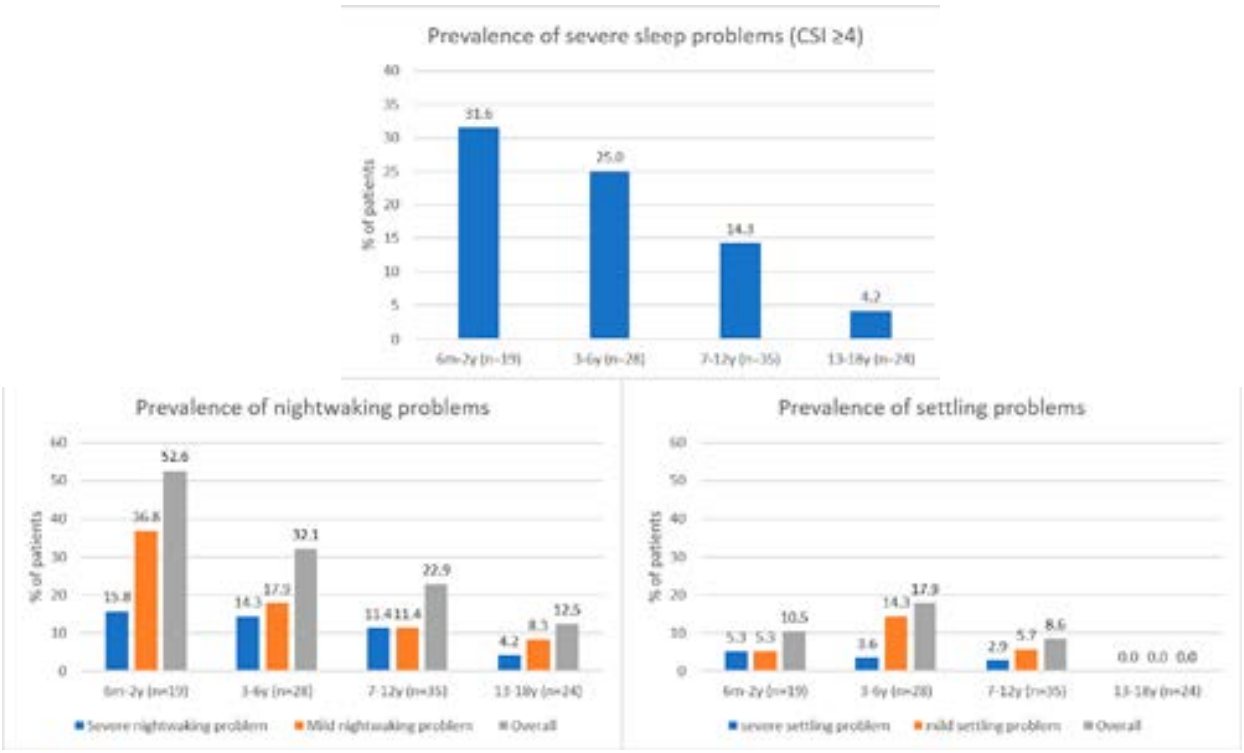


Figure 3 : *Prevalence of sleep problems according to the age.*
Legend. Illustration of sleep problems according to the age in children with epilepsy based on the SQ-SP questionnaire. CSI, composite sleep index. A CSI of ≥4 is defined as a severe sleep problem.



The factor scores (figure 4) indicate a relative higher prevalence of snoring and especially daytime sleepiness. Apnea, complaints related to the sleep and anxiety related to sleep were generally lower.

Parents tried sleep regulating medication in 20.8% (mainly melatonin or antihistamines with a sedative effect) although the efficacy was low or only temporary.

The sleep problems seriously impact the family, with 63.7% of the parents indicating a negative influence of the sleep problems on their daily life, leading among others to fatigue, concentration problems and feelings of incompetency (figure 5).

Discussion

Sleep problems are frequently reported in patients with epilepsy, especially in childhood. In our cohort of patients, chronic insomnia was present in one out of 5 patients. Most patients experienced problems with maintaining sleep, while initiation of sleep (expressed as settling disorder) was less frequent disturbed. Overall, the prevalence of sleep problems decreased with age.

Several factors contribute to the higher prevalence of sleep problems in patients with epilepsy, including the epilepsy itself, but also higher prevalence of comorbidities and environmental factors (figure 6). Due to the fear of nocturnal seizures, co-sleeping was frequent. Even between the age of 5 – 15 years, 35% of the patients did not sleep alone in their room. Co-sleeping can have a negative influence on the sleep quality of children with greater fragmentation of night sleep and might cause or sustain sleep problems. Köse et al described a 13fold increased risk to develop sleep problems in case of co-sleeping with a parent (16). In addition, parents sleeping together with their children may be more aware of sleep problems of their children and might therefore report more sleep problems. Improved and more reliable seizure detection systems will help to give parents / caregivers the confidence to leave their children with epilepsy sleep alone.

Daytime sleepiness is an important problem with a major impact on the daily functioning of the patient. Based on this study we are not able to detect whether the daytime sleepiness is related to the disturbed sleep, medication or epilepsy. Many patients receive multiple antiseizure medications (mean number of 2.2) including benzodiazepines. Antiseizure medications itself have an impact on the sleep, especially polypharmacy (17, 18).

Identification of the type of sleep problem and potential contributing factors (comorbidities and environmental factors) is important to offer the most appropriate advice and treatment.

Good sleep practices and behavioral interventions remain the first recommended treatment but are often more difficult due to the epilepsy (fear of nocturnal seizures or SUDEP) and comorbidities (behavioral problems and intellectual disability). Based on the consequences of sleep problems on the patient and family, pharmacologic treatment can be considered but should be combined with behavioral interventions. Most pharmacological treatments are used off label since they are not recognized for the treatment of insomnia in pediatric patients. For settling disorders mainly melatonin, antihistamines (with sedative effect) and benzodiazepines (mainly clonazepam) are used. For night waking problems (long-acting) melatonin can be tried although it is less successful compared to the treatment of settling problems. In addition, benzodiazepines, sedative antihistamines, atypical antipsychotics or sedative antidepressants (like trazodone) can be tried (19, 20). The presence of comorbidities can help in the choice of the most optimal treatment per patient.

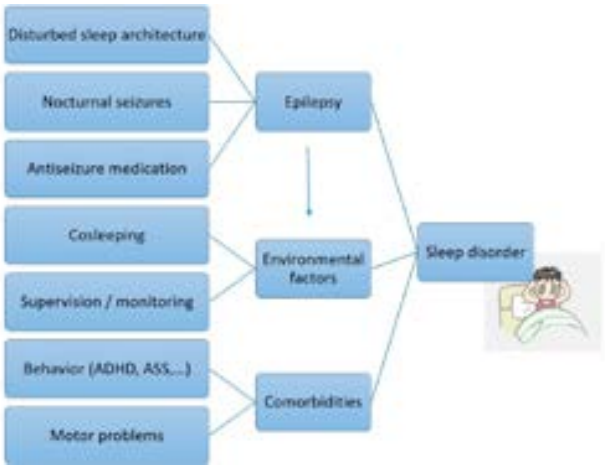
The goal of this study was to get an impression of the prevalence and type of sleep problems in our pediatric epilepsy patients. However, this study has some limitations. First the population is heterogeneous, including patients with more benign epilepsy syndromes and patients with treatment resistant developmental epileptic encephalopathies. By presenting the questionnaire to all the parents visiting the epilepsy clinic we wanted to cover the whole spectrum of epilepsy patients, instead of focussing on a specific epilepsy or genetic syndrome. Based on this study we were able to calculate the prevalence of several types of sleep problems in a broad group of patients with epilepsy. Unfortunately, due to the absence of a control group, we were not able to compare our results with the prevalence in age-matched healthy controls. Secondly, the exact response rate and reason to decline participation

Figure 4 : *Factor scores in children with epilepsy.*
Legend Illustration of factor scores based on the results from the SQ-SP questionnaire according to the age. Indication of relative scores (% of maximum). FS, factor score. The "FS_complaints" represents the refers to movements, excessive sweating and episodes of confused behavior during sleep.

Figure 5 : *Impact of sleep problems on parents*
Legend. Impact of sleep problems on parents. Percentage of parents that experience a negative emotion or effect due to the sleep difficulties of their child.

	Parents
Negative influence of sleep problems	63.7%
Daytime fatigue	34.9%
Disturbed sleep	28.3%
Concentration problems	24.5%
Feelings of incompetency	22.6%
Feelings of irritability	19.8%
Memory problems	16%
Depressive feelings	8.5%
Conflict between parents concerning approach of sleep problems	7.5%
Agressive feelings	1.9%

Figure 6 : *Etiology of sleep problems in children with epilepsy*
Legend. Schematic presentation of factors that might explain sleep problems in children with epilepsy.



were not documented. Although most parents completed the questionnaire, there might be a selection bias as parents with children with sleep problems might be more interested to participate. Since we anticipated the inclusion of patients with an intellectual disability, the SQ-SP questionnaire was used. This questionnaire has been validated in patients with intellectual disability but has no reference values for the several factor scores. In addition, the sleep problems relay on a subjective parental reporting and are not based on objective sleep studies like a polysomnography.

Assessment of sleep should be part of the care of children with epilepsy since they are more vulnerable to develop sleep problems. Simply asking whether the child has sleep problems is not enough as severe sleep problems might be missed this way. It is important to specifically question the settling (how fast children fall asleep), awakenings during sleep, waking up early and impact on parents.

Additional research is necessary to further study and understand the prevalence and etiology of sleep problems in children with epilepsy. In addition, it is important to study the effect (and limits) of behavioral and pharmacological treatment in this complex patient population. Due to the epilepsy and related fear for seizures and SUDEP, pedagogic advice is more difficult.

Conclusion

Children with epilepsy are at risk to develop sleep problems, mainly difficulties to sleep through the night. These sleep problems have an important negative effect on the daily functioning of both children and caregivers. Identification of the type of sleep disorder is important to give the most optimal support to parents.

Conflict of interest

The author has no conflict of interest to declare.

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