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BENIGN PARTIAL EPILEPSY OF CHILDHOOD WITH CENTROTEMPORAL SPIKES AND SLEEP DISORDERS

EPILEPSIA PARCIAL BENIGNA DA INFÂNCIA COM ESPÍCULA CENTROTEMPORAL E TRANSTORNOS DO SONO

EPILEPSIA PARCIAL BENIGNA DE LA INFANCIA CON ESPÍCULA CENTROTEMPORAL Y TRASTORNOS DEL SUEÑO

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ABSTRACT

Objective: Benign partial epilepsy of childhood with centrotemporal spikes (BECTS) is an idiopathic epilepsy that occurs in healthy children with normal neurodevelopment, characterized by seizures and inter-ictal discharges that predominate during nighttime sleep. This research analyzes the prevalence of sleep disorders in patients with BECTS followed in the Department of Pediatric Neurology at the Pequeno Príncipe Children's Hospital from January 2004 to January 2014. Methods: This study is observational and cross-sectional. The medical records of all children with BECTS followed in the aforementioned institution and period were analyzed, and 46 of these patients met the prerequisites to enter the study. During the investigation all children underwent neuroimaging exams (magnetic resonance or computed tomography) and digital electroencephalogram. In clinical evaluations, all patients and their parents were asked about the presence of sleep disorders. Results: To be classified as having BECTS, patients should have normal neural images and all the electroencephalographies (EEG) should have normal background activity with unilateral or bilateral spikes in centrotemporal or centrotemporal and parietal regions. All were being treated with antiepileptic drugs. The age of onset of seizures ranged from 62 to 145 months (mean 94.37 ± 21.2 months). Data showed that 33 (71.74%) out of 46 patients had experienced some kind of sleep disorder: insomnia (18 patients/39.13%), nocturnal enuresis (6 patients/13.04%), somnambulism (2 patients/4.35%), night terrors (1 patient/2.17%), nocturnal enuresis and night terrors (2 patients/4.35%), night terrors and somnambulism (2 patients/4.35%), insomnia and nocturnal enuresis (1 patient/2.17%) and insomnia, night terrors and somnambulism (1 patient/2.17%). Conclusions: Most children diagnosed with BECTS in our pediatric neurology service presented with comorbid sleep disorder. The results are consistent with the data collected in the literature, which show that sleep disorders are more common in children with this type of epilepsy than in those neurologically healthy.

Keywords: Sleep disorders; Epilepsies, partial; Neurology.

RESUMO

Objetivo: A epilepsia parcial benigna da infância com espículas centrotemporais (EPCT) é uma epilepsia idiopática que ocorre em crianças saudáveis com neurodesenvolvimento normal, que se caracteriza por convulsões e descargas interictais que predominam durante o sono noturno. Esta pesquisa analisa a prevalência de transtornos do sono em pacientes com EPCT acompanhados no Departamento de Neurologia Pediátrica do Hospital Infantil Pequeno Príncipe de janeiro de 2004 a janeiro de 2014. Métodos: Este estudo é observacional e transversal. O prontuário clínico de todas as crianças com EPCT acompanhadas na instituição e no período acima mencionados foi analisado e 46 desses pacientes satisfizeram os pré-requisitos para entrar no estudo. Durante a investigação, todas as crianças foram submetidas a exames de neuroimagem (ressonância magnética ou tomografia computadorizada) e a eletroencefalograma digital. Durante as avaliações clínicas, todos os pacientes e seus pais foram perguntados sobre a presença de transtornos do sono. Resultados: Para serem classificados como portadores de EPCT, os pacientes deviam ter imagens neurais normais e todas as eletroencefalografias (EEG) deviam apresentar atividade de fundo normal, com espículas unilaterais ou bilaterais nas regiões centrotemporal ou centrotemporal e parietal. Todos estavam sendo tratados com medicação

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antiepiléptica. A idade de início das convulsões variou dos 62 aos 145 meses (média 94,37 ± 21,2 meses). Os dados mostraram que 33 (71,74%) dos 46 pacientes tinham algum tipo de transtorno do sono: insônia (18 pacientes/39,13%), enurese noturna (6 pacientes/13,04%), sonambulismo (2 pacientes/4,35%), terrores noturnos (1 paciente/2,17%), enurese noturna e terrores noturnos (2 pacientes/4,35%), terrores noturnos e sonambulismo (2 pacientes/4,35%), insônia e enurese noturna (1 paciente/2,17%) e insônia, terrores noturnos e sonambulismo (1 paciente/2,17%). Conclusões: A maioria das crianças com diagnóstico de EPCT em nosso serviço de neurologia pediátrica apresentou-se com transtornos do sono comórbidos. Os resultados são compatíveis com os dados coletados na literatura, que mostram que os transtornos do sono são mais comuns em crianças com esse tipo de epilepsia do que nas neurologicamente saudáveis.

Descritores: *Transtornos do sono; Epilepsias parciais; Neurologia.*

RESUMEN

Objetivo: La epilepsia parcial benigna de la infancia con espículas centrotemporales (EPCT) es una epilepsia idiopática que ocurre en niños saludables con neurodesarrollo normal, que se caracteriza por convulsiones y descargas interictales que predominan durante el sueño nocturno. Esta investigación analiza la prevalencia de trastornos del sueño en pacientes con BECTS acompañados en el Departamento de Neurología Pediátrica del Hospital Pequeno Príncipe desde enero de 2004 a enero de 2014. Métodos: Este estudio es observacional y transversal. El prontuario clínico de todos los niños con EPCT acompañados en la institución y en el período arriba mencionado fue analizado y 46 de esos pacientes cumplieron con los prerrequisitos para entrar en el estudio. Durante la investigación, todos los niños fueron sometidos a exámenes de neuroimagen (resonancia magnética o tomografía computada) y a electroencefalograma digital. Durante las evaluaciones clínicas, todos los pacientes y sus padres fueron preguntados sobre la presencia de trastornos del sueño. Resultados: Para ser clasificados como portadores de EPCT, los pacientes debían tener imágenes neurales normales y todas las electroencefalografías (EEG) debían presentar actividade de fondo normal, con espículas unilaterales o bilaterales en las regiones centrotemporal o centrotemporal y parietal. Todos estaban siendo tratados con medicación antiepiléptica. La edad de inicio de las convulsiones varió de los 62 a los 145 meses (promedio de 94,37 ± 21,2 meses). Los datos mostraron que 33 (71,74%) de los 46 pacientes tenían algún tipo de trastorno del sueño: insomnia (18 pacientes/39,13%), enuresis nocturna (6 pacientes/13,04%), sonambulismo (2 pacientes/4,35%), terrores nocturnos (1 paciente/2,17%), enuresis nocturna y terrores nocturnos (2 pacientes/4,35%), terrores nocturnos y sonambulismo (2 pacientes/4,35%), insomnia y enuresis nocturna (1 paciente/2,17%) e insomnia, terrores nocturnos y sonambulismo (1 paciente/2,17%). Conclusiones: La mayoría de los niños con diagnóstico de EPCT en nuestro servicio de neurología pediátrica se presentó con trastornos del sueño comórbidos. Los resultados son compatibles con los datos colectados en la literatura, que muestran que los trastornos del sueño son más comunes en niños con ese tipo de epilepsia que en los neurológicamente saludables.

Descriptores*: Trastornos del sueño; Epilepsias parciales; Neurología .*

INTRODUCTION

Benign partial epilepsy of childhood with centrotemporal spikes (BECTS), also known as benign rolandic epilepsy or benign rolandic epilepsy of childhood, is placed among the idiopathic localization-related epilepsy. It is one of the most common epilepsy in children. BECTS is an idiopathic epilepsy that occurs in healthy children with normal neurodevelopment. The seizures are usually partial, with motor manifestation, and are more frequent during nighttime sleep. They often begin on face (patients usually have a feeling of tingling on one side of their mouth, tongue, lips, gum and cheek) and then progress to the arm and leg on the same side of the body. During the seizure the speech can be impaired. The evolution to generalized seizures (generalized tonic-clonic seizure) is relatively common, especially in younger children.

Some epilepsies are closely associated with sleep, such as awakening grand mal, juvenile myoclonic epilepsy, childhood epilepsy with occipital paroxysm, autosomal dominant frontal lobe epilepsy, Landau-Kleffner syndrome and BECTS. Specifically in BECTS, discharges are intensely activated by sleep.

Although ineffective sleep is common in epilepsy patients, how epilepsy or the epileptic discharges affect sleep is not yet completely know. One of the most accepted theories is that nocturnal seizures can disrupt the neurophysiology of sleep, producing sleep fragmentation, suppression of REM sleep and increased spontaneous arousals. Cortesi et al.[1] showed that children with idiopathic epilepsy had more sleep disturbances than neurologically healthy children, and these sleep disturbances were associate with seizure frequency, paroxysmal activity on EEG, duration of epilepsy and behavioral problems.

Even though seizures increase the incidence of sleep disorders in children, the administration of antiepileptic drugs (AED) can also significantly alter the physiology of sleep.

As well as seizures may affect quality of sleep, it is also known that sleep deprivation and sleep disorders both increase the incidence of seizures in epileptic patients, making the interrelationship between epilepsy and sleep extremely complex.

Children with insomnia may have more daytime fatigue, anxiety, mood oscillations and lower ability to complete tasks. Studies show that school performance can be also impaired. Being aware that all mentioned above could cause negative impact on these patients quality of life enhance the importance of studying the relationship between sleep and seizures.

This research aims to analyze the prevalence of sleep disorders in patients with BECTS referred for the Department of Pediatric Neurology at the Pequeno Príncipe Hospital from January/2004 to January/2014. All aspects of this project were approved by the Ethics Committee on Research Involving Human Subjects at our institution (number 801.103/2014).

METHODS

This study is observational and cross-sectional. All medical records of a cohort of patients with BECTS referred for the Department of Pediatric Neurology at the Pequeno Príncipe Children's Hospital from January/2004 to January/2014 were

analyzed, an data concerned the prevalence of sleep disorders were collected.

To be part of this research the patient should have: (a) normal development skills, (b) at least one normal neuroimaging exam (magnetic resonance imaging – MRI, or computed tomography - CT) and (c) one electroencephalogram recorded for at least 30 minutes, with electrodes positioned according to the International 10-20 System, in digital EEG monitoring equipments with 21 channels (Nihon Koden®, Neurotec® and Neurovirtual Brain Wave II®), analyzed by the same physician, with results suggesting BECTS.

Forty-six patients fit all the requirements to be part of this study and were selected, 24 (52.17%) of them female and 22 (47.83%) of them male. All patients and parents had been asked about the presence of sleep disorders during medical evaluations, and this was the data collected from the medical records.

RESULTS

The age of seizures onset on the group ranged from 62 to 145 months old (mean 94.37 ± 21.2). The patient's age at the time of inclusion in the study ranged from 74 to 165 months old (mean 118.8±27.08). All patients were submitted to a neuroimaging exam, 27 of them had an MRI performed and 19 patients had a CT Scan. All these neuroimaging exams were analyzed and classified by a radiologist as normal.

All patients were also submitted to an electroencephalogram. The results were analyzed by the same physician and all of them had normal background activity with sharp waves on the centrotemporal or centrotemporal and parietal regions, uni or bilateral. These results are compatible with BECTS.

Data showed that 33 out of 46 patients (71.74%) had experienced any sleep disorder after being diagnosed with BECTS: 18 patients (39.13%) mentioned to have experienced insomnia, 6 patients (13.04%) had nocturnal enuresis, 2 patients (4.35%) had somnambulism, 1 patient (2.17%) suffered from night terror, 2 patients (4.35%) had both nocturnal enuresis and night terrors, 2 patients (4.35%) had both night terrors and somnambulism, 1 patient (2.17%) had both insomnia and nocturnal enuresis and 1 patient (2.17%) mentioned to have insomnia, night terrors and somnambulism.

All 46 patients were being treated with antiepileptic drugs: 18 of them were on oxcarbazepine (39.13%), 17 carbamazepine (36.95%), four on sodium valproate (8.70%), tree on carbamazepine and clonazepam (6.52%), two on sodium valproate and clobazam (4.35%), oneon carbamazepine and clobazam (2.17%), and one on oxcarbazepine and clonazepam (2.17%). The patient's age at the first seizure and the results of the EEG performed are shown in Table 1.

Table 1. Electroencephalographic tests and age at first seizure.

Patient	First Seizure	Electroencephalogram
1	84	Normal background. SW C-P right and left
2	75	Normal background. SW C-P-T right and left
3	70	Normal background. SW C-P-T right
4	71	Normal background. SW C-P right
5	90	Normal background. SW C-P right and left
6	79	Normal background. SW C-P-T left
7	85	Normal background. SW C-P-T left
8	80	Normal background. SW C-P left
9	68	Normal background. SW C-P right
10	74	Normal background. SW C-P right
11	81	Normal background. SW C-P right
12	102	Normal background. SW C-P-T left
13	96	Normal background. SW C-P right
14	68	Normal background. SW C-P-T right and left
15	107	Normal background. SW C-P-T right and left
16	102	Normal background. SW C-P-T right and left
17	81	Normal background. SW C-P right
18	84	Normal background. SW C-P right and left
19	93	Normal background. SW C-P right
20	102	Normal background. SW C-P right and left
21	80	Normal background. SW C-P right and left
22	76	Normal background. SW C-P right
23	67	Normal background. SW C-P left
24	109	Normal background. SW C-P right and left
25	117	Normal background. SW C-P-T right and left
26	79	Normal background. SW C-P-T right and left
27	101	Normal background. SW C-P-T right
28	94	Normal background. SW C-P right
29	99	Normal background. SW C-P right and left
30	93	Normal background. SW C-P-T right
31	110	Normal background. SW C-P-T right and left
32	123	Normal background. SW C-P left
33	141	Normal background. SW C-P-T left
34	78	Normal background. SW C-P left
35	89	Normal background. SW C-P right
36	62	Normal background. SW C-P-T right and left
37	112	Normal background. SW C-P right and left
38	143	Normal background. SW C-P right
39	132	Normal background. SW C-P-T right and left
40	102	Normal background. SW C-P right
41	87	Normal background. SW C-P left
42	89	Normal background. SW C-P right
43	92	Normal background. SW C-P left
44	93	Normal background. SW C-P-T left
45	136	Normal background. SW C-P right and left
46	145	Normal background. SW C-P-T right and left

SW - sharp wave; C - central; P - parietal; T - temporal.

DISCUSSION

The neurophysiological bases of sleep were unknown until the XX middle century. From that moment ahead, several researches showed that sleep results of the complex interaction between innumerous endogenous and exogenous factors. The most known endogenous factors are levels of excitatory and inhibitory neurotransmitters (such as acetylcholine, norepinephrine, histamine, dopamine and hypocretin), the levels of hormones and the integrity of several cortical and subcortical structures (such as the ascending reticular activating system, the hypothalamus and the pineal gland).[2] The most known exogenous factors are ambient temperature, overeating at night, light intensity and noise level.

If all these endogenous and exogenous factors interact harmoniously, the neurologically healthy children should have a predominant nocturnal sleep and maintain wakefulness during the day.[2] Any condition that causes functional or structural changes in brain structures or in the biochemical system of sleep will probably result in changes on the normal pattern of sleep, called sleep disorders.

The electrographic record of sleep, made with the polysomnography, is used to classify and divide sleep in two main stages: NREM (non-rapid eyes movement) and REM (rapid eyes movement). The NREM stage can be subdivided into light (stages I and II) and deep (stage III and IV). Although the physiologic basis of this phenomenon is poorly understood, seizures and interictal epileptic discharges are more frequent during NREM sleep (mainly in stages I and II). Seizures are rare during REM sleep, when the incidence of interictal epileptic discharge also decreases significantly. This can probably be explained by the activation of the thalamocortial rhythms during NREM sleep.[3]

Antiepileptic drugs

The use of Antiepileptic drugs (AED) is an important aspect to be considered when analyzing sleep disorders and epilepsy. Many AED are known to cause significantly sleep interference in children with epilepsy, but relationship between AED and sleep disorder is not fully known. Each drug has it's personal sleep effect: tiagabine, levetiracetam and pregabalin increase sleep stage III; topiramate decreases sleep latency; lamotrigine increases both sleep stage II and REM and decreases sleep stage III; gabapentin increases both sleep stage III and REM; ethosuximide increases sleep stage I and decreases sleep stage III; valproate increases sleep stage I and decreases sleep stage II; phenytoin increases both sleep stages I and II and decreases sleep stage III; phenobarbital increases sleep stage II and decreases REM. Carbamazepine and oxcarbamazepine almost do not affect both NREM and REM sleep. Some AED like ethosuximide, primidone, felbamate, fosphenytoin, lamotrigine, topiramate and zonisamidedo still do not have clinical effects on sleep completely known.[4]

Besides the effects on proper sleep, all AED can cause sedation depending on the dose used, which can interfere in daytime wakefulness and productivity. They can also cause impairment of cognitive performance, being phenobarbital the one that affects the most, followed by phenytoin, benzodiazepines, carbamazepine and valproate.

In our study all patients were treated with at lest one AED. As BECTS is an idiopathic focal epilepsy, 40 (86,96%) of our patients were treated with carbamazepine or oxcarbazepine (with or without association of benzodiazepines). Only 6 (13,04%) of our patients were treated with sodium valproate (with or without association with benzodiazepines). As the study was observational and cross-sectional it was not possible to evaluate if the AED used on each patient had any relation with the presence of sleep disorders.

Insomnia

According to the Brazilian Society of Sleep, insomnia is defined as a difficulty to initiate or maintain sleep, provoking an impairment in daytime activities performance.[5] It is a disease of high prevalence in the general population. Epidemiological studies have shown a prevalence of 35.4% in Brazil,[6] 17.7% in France.[7] 20% in Switzerland,[8] and 31% in Germany, but none of these studies specified the prevalence on specifics pediatrics populations.[9] Data about the prevalence of insomnia in children vary a lot according to different researches and different countries making the analysis of these data complicated.

Insomnia disorders are most often classified as either primary or secondary to psychiatric or other medical conditions. The main causes of insomnia in childhood and adolescence are overeating at night, cow's milk protein allergy, chronic diseases, fear, anxiety, other emotional disturbances and misguided family's orientation. Children with insomnia may experience more daytime fatigue, anxiety, mood oscillations and have lower ability to complete tasks.[10] Studies show that school performance may also be impaired.

Our data show that 43.48% of the children with BECTS treated at our hospital also had insomnia. This is compatible with data found in literature that shows that the prevalence of insomnia in patients with BECTS is considerably higher than in healthy individuals.

Nocturnal enuresis

Nocturnal enuresis (NE) is the most common disorder of childhood sleep and may occur during either NREM or REM sleep. There are different definitions for NE, however the main concept of this condition may be understood as urinary incontinence during sleep after the usual age of urinary continence acquisition. The diagnostic criteria are: (a) chronological age higher than 5 years old; (b) mental age higher than 4 years old; (c) absence of any organic disease that may be associated with incontinence; (d) two or more monthly events of urinary incontinence for children aged between 5 and 6 years old, or one or more monthly events for children over 6 years old.[10]

Norgaard et al.[11] suggest to classify nocturnal enuresis as (a) primary - children who have never had urinary continence; (b) secondary - enuresis begins after a period of at least six months of urinary incontinence; (c) familial - at least one parent has a history of nocturnal enuresis; (d) polyuric - excessive production of urine overnight. The prevalence varies considerably, but stands around 10% on 7 years old children.[12]

The etiology of nocturnal enuresis is still unknown and is most likely multifactorial. Probably this disease is related to genetic, psychological, social and anatomo-physiological (bladder size, reactivity abnormal or/and lack of vasopressin release during sleep) factors. Another contributor factor may be an immaturity of the thalamus, which could impair awakening during the night, causing the NE. However the causes of NE still remain unknown.[13,14]

Our data show that 19.56% of the children with BECTS treated at our hospital were also diagnosed with NE. This prevalence is higher than that found in non-epileptic children[12] goes along with data found on literature.

Night terrors

Night terrors (NT) is the most dramatic sleep-arousal disorder. It is a NREM sleep-arousal parasomnia that occurs from childhood to adolescence. Its prevalence varies between 1% to 5% on this age group population. The events typically begin with intense agitation followed by crying, screaming and eye opening. The patients become tachycardic, diaphoretic and mydriatic. They are inconsolable and their behavior may become violent and result in injury to themselves and others. The children usually do not remember the episode on the day after. To differentiate night terror from seizures is relatively simple: unlike seizures, after a night terror episode the consciousness recovery is always fast and complete.[10]

Our data show that 13.04% of the children with BECTS treated at our hospital were also diagnosed with NT. This prevalence is significantly higher than that reported in other studies made in healthy general population[10] e goes along with data found on literature.

Somnambulism

Somnambulism is a NREM sleep-arousal parasomnia characterized by simple or complex motor phenomena during sleep. It begins during slow wave sleep. The patient can get out of bed, walk short distances, manipulate objects, urinate, eat and talk. Less often, they may experience psychomotor agitation, tachycardia, diaphoresis and aggressive reactions (rarely). As the motor functions are active while the child is still unconscious, they do not remember anything on the next morning.[10] Somnambulism is more common in childhood (the highest incidence is between 11 to 12 years old) than in adults. Different studies show it's prevalence in healthy children between 1 and 17%.[15,16]

Our data show that 10.87% of the children with BECTS treated at our hospital were also diagnosed with somnambulism.

This prevalence is similar to the prevalence found on literature on children without epilepsy.

CONCLUSION

The data from this study show that most children diagnosed with BECTS attended in our pediatric neurology service had comorbid some sleep disorder. This is consistent to data found at literature about sleep disorders and epilepsy. Insomnia, NE and NT were more frequent in our BECTS patients than in the healthy general population. Only the prevalence of somnambulism was similar among patients with BECTS and healthy individuals.

Although it is evident that children with specific types of epilepsy have worse quality of sleep, how epilepsy or epileptic discharges alter the macro and microstructure of sleep is still poorly understood. When mistreated, sleep disorders have a negative impact on these patients quality of life, causing children to have more daytime fatigue, anxiety, mood oscillations and lower ability to complete tasks. School performance can also be impaired. Despite being more frequent in children with epilepsy than in healthy ones, the spontaneous emergence of sleep complaint is not frequent during routine evaluation of these children.[10] leaving to the physician the responsibility of the diagnose.

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