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Sleep respiratory parameters in children with idiopathic epilepsy: A cross-sectional study

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ABSTRACT

Background: The aim of this study is to explore and compare through polysomnography respiratory sleep parameters between children with idiopathic epilepsy and healthy children.
Methods: Our cross-sectional study included 40 children with idiopathic epilepsy and 27 healthy children, who underwent overnight polysomnography. Data about sleep respiratory parameters were obtained and statistically analyzed. The level of statistical significance was set at 0.05.
Results: The prevalence of Obstructive Sleep Apnea Syndrome was significantly higher in the epilepsy group (35% vs 7.4%, $p < 0.01$). Moreover, the odds ratio of an obstructive apnea index ≥ 1 in the epilepsy group was 10.6 (95% Confidence Intervals: 3.08–37.08) in comparison to the control group. The mean value of the obstructive apnea-hypopnea index was significantly higher in children with epilepsy compared to healthy children (2.46 ± 1.22 vs 1.21 ± 0.83, $p = 0.027$). The mean values of central apnea index and desaturation index were comparable between these two groups. Longest apnea duration was significantly higher in the group of poor seizure control. All other sleep respiratory variables did not differ significantly between children with poor and good seizure control and between children with generalized and focal epilepsy.
Conclusions: Children with epilepsy seem to present more prominent sleep breathing instability in comparison to healthy children, which mainly includes a predisposition to obstructive respiratory events. More studies are needed to investigate the relationship between sleep apneas and seizure control.

1. Introduction

Sleep co morbidities have been increasingly studied in patients with epilepsy and are thought to have a negative impact on life quality and disease course in this population (Dhamija et al., 2014; Grigg-Damberger and Ralls, 2014). According to sleep questionnaire studies, sleep breathing disorders (SBD) are one of the most frequently reported sleep problems among patients with epilepsy (Ong et al., 2009; Ruangkana et al., 2014).

In literature there are clinical polysomnographic studies assessing a high prevalence of SBD among children with epilepsy. However, these studies lack control groups of healthy children, focus only on obstructive apneas, are mainly based on children with epilepsy referred to sleep centers due to underlying sleep complaints and possible anatomical risk factors for SBD (e.g. increased BMI or hypertrophic tonsils/adenoids) have not always been taken into account (Becker et al., 2004; Jain et al., 2013a,b; Kaleyias et al., 2008). The above methodological issues may cause a bias in the estimation of the real prevalence of SBD in this pediatric population. Moreover, although questionnaire-based studies imply that SBD predispose to poor seizure control, there are no polysomnographic studies clearly confirming this finding (Jain et al., 2012; Kaleyias et al., 2008).

The aim of our study is to compare polysomnographic respiratory parameters between children with idiopathic epilepsy and healthy children.

Abbreviations: AASM, American Academy of Sleep Medicine; BMI, body mass index; CAI, central apnea index; DI, desaturation index; OAI, obstructive apnea index; OAHI, obstructive apnea-hypopnea index; OSAS, obstructive sleep apnea syndrome; PSG, polysomnography; REM, rapid eye movement; SBD, sleep breathing disorders; SpO_2, subcutaneous oxygen saturation of hemoglobin; TST, total sleep time.

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2. Methods

2.1. Subjects

A cross-sectional study approved by the Ethical Committee of the Aristotle University of Thessaloniki was conducted. All parents were asked to sign an informed consent form.

Children with epilepsy were recruited from the Outpatient Clinic for Pediatric Neurology of the University General Hospital of Thessaloniki, AHEPA. Diagnosis and classification of epilepsy was based on the International League Against Epilepsy guidelines (Iliescu and Craiu, 2013). The patients with at least 1 seizure within the past 6 months of polysomnography were classified as having poor seizure control. Exclusion criteria included epilepsy caused by a progressive brain disorder (tumor, neurodegenerative disorder), as well as a history of underlying diseases (e.g. asthma, inborn errors of metabolism).

The control group included healthy children without epilepsy or any other significant past medical history who were recruited from the Outpatient Clinic for General Pediatrics of the University General Hospital of Thessaloniki, AHEPA during their annual health check-up.

Table 1 summarizes basic clinical traits of our study sample.

2.2. Procedures

During the initial visit a thorough medical history was taken by the parents through personal interviews. All children underwent full multisystem clinical evaluation and were screened for hypertrophic tonsils or adenoids. Somatometric data (weight, height) were measured and Body Mass Index (BMI) z-scores were calculated according to World Health Organization guidelines. During the second visit children underwent overnight polysomnography (PSG) in the Sleep Laboratory of the 2nd Department of Pediatrics of the Aristotle University of Thessaloniki, in the University General Hospital AHEPA, Thessaloniki, Greece.

Each child's sleep was continuously recorded to a computerized system and scored manually in 30-s epochs according to American Academy of Sleep Medicine (AASM) standardized criteria (Iber et al., 2007). PSG measurements included electroencephalograms (EEG: C3-A2, C4-A1), right and left electro-oculogram, electrocardiogram, mental-submental electromyogram, leg electromyogram, thoracic and abdominal wall motion (respiratory inductance plethysmography), pulse oximetry, end-tidal carbon dioxide monitoring, combined nasal/oral thermistor and nasal pressure. Body position was determined by a sensor and confirmed by direct observation throughout the night.

2.3. Definitions

Sleep was subdivided into 30-s epochs and sleep staging was performed according to AASM criteria. Total sleep time (TST) is the time in hours from sleep onset to the end of the spinal sleep epoch minus time awake. Percentage of TST spent in sleep stages N1 & N2 (N1 + N2%), N3 (%) and Rapid Eye Movement-REM (REM%) was also calculated (Iber et al., 2007).

Respiratory events were scored according to AASM pediatric scoring criteria, too (Iber et al., 2007). An *obstructive sleep apnea* (OSA) is scored when an ≥90% drop in the signal amplitude of airflow was detected for ≥90% of the entire event, compared with the baseline amplitude and the event lasts for at least two breaths with continued respiratory effort. An *hypopnea* is defined as a ≥50% drop in airflow signal amplitude, compared with the baseline amplitude, for ≥90% of the duration of the event. In addition, the event must last for at least two missed breaths and should be associated with an arousal, awakening or a ≥3% desaturation. A *central apnea* is associated with absence of inspiratory effort throughout the duration of the event and one of the following: (1) the event lasts for ≥20 s or (2) the event lasts for at least two missed breaths and is associated with an arousal, an awakening or a ≥3% desaturation. In *mixed apneas* the event is associated with an absent inspiratory effort in the initial phase of the effort, followed by respiratory effort before the end of the event.

The *obstructive apnea index* (*OAI*) is the number of obstructive and mixed apneas per hour of sleep, expressed as total number of obstructive and mixed apneas/total sleep time in hours. The *obstructive apnea-hypopnea index* (*OAHI*) is the number of obstructive and mixed apneas and hypopneas per hour of sleep, expressed as total number of obstructive and mixed apneas and hypopneas/total sleep time in hours. *Obstructive Sleep Apnea Syndrome* (*OSAS*) is diagnosed when OAI ≥ 1. The central apnea index (CAI) is defined as the number of central apneas per hour of sleep, expressed as total number of central apneas/total sleep time in hours.

Subcutaneous oxygen saturation of hemoglobin (SpO_2) was expressed in %. A desaturation was recorded when an ≥3% decrease in basal SpO_2 was detected. The *desaturation index* (*DI*) is the number of desaturations per hour of sleep, expressed as total number of desaturations/total sleep time in hours. *End-tidal* CO_2 was measured by nasal sensors and was expressed in mmHg. *Sleep-related hypoventilation* is scored when ≥25% of the total sleep time is spent with end-tidal CO_2 ≥50 mmHg (Chang and Chae, 2010; Iber et al., 2007).

2.4. Sample size

We have considered the prevalence of OSAS (OAI ≥ 1) in the epilepsy vs control group as the primary outcome of our study. All other outcomes were considered as secondary. According to literature, the prevalence of OSAS in general pediatric population is estimated at 3% (Chang and Chae, 2010). Taking into account previous studies about SBD in children with epilepsy, our estimation of OSAS prevalence in the epilepsy group was 30%. For 80% power of study and 0.05 level of significance (p value), a number of 34 participants in each group is required to detect a significant difference

Table 1
Basic epidemiological and clinical traits of our study sample (AED: antiepileptic drugs, BMI: Body Mass Index).

Variable	Epilepsy group (N = 40)	Control group (N = 27)	p
Mean age (years)	10.61 ± 2.41	11 ± 2	0.48
BMI z-score	0.76 ± 0.97	0.61 ± 0.84	0.53
Gender (female to male ratio)	1.10	1.88	0.3
Hypertrophic adenoids/tonsils%	7.5 (3/40)	7.69 (2/26)	0.97
Medication status (% on AED)	92.5		
% on 1 AED	80		
% on 2 AED	7.5		
% on >2 AED	5		
% without AED	7.5		