Original Research

Investigating the Relationship between Nocturnal Enuresis and Sleep Disordered Breathing Using Polysomnography Data of 5-10 Year-Old Children Referred to Qazvin Children's Hospital, Iran

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Received: 02 Feb. 2023 Accepted: 28 Mar. 2023

Abstract

Background and Objective: Sleep is a critical biological necessity essential for maintaining both physical and mental health in humans. Given the prevalence of nocturnal enuresis (NE) in children, this study sought to explore its potential link to sleep-disordered breathing (SDB).

Materials and Methods: This cross-sectional study involved children aged 5 to 10 years who visited Qazvin Children's Hospital, Iran, from 2016 to 2021. Data were gathered using the Iranian Children's Sleep Habits Questionnaire (CSHQ) completed by parents, alongside polysomnography (PSG) assessments conducted at the hospital. Children were categorized into two groups of with and without enuresis. The PSG data were analyzed to evaluate respiratory parameters in accordance with the American Academy of Sleep Medicine (AASM) guidelines.

Results: Of 124 participants, 64 (51%) were boys, with an average (standard deviation) age of 82.2 (24.4) months. Approximately 39.1% of the children experienced NE. Statistically significant correlations were found between NE and several factors: body mass index (BMI) ($P = 0.025$), total sleep time ($P = 0.026$), number of hypopneas ($P < 0.001$), hypopnea index ($P = 0.012$), total apnea and hypopnea events ($P = 0.004$), and the overall apnea-hypopnea index (AHI) ($P = 0.005$). However, no significant association was established between the oxygen desaturation index, arousal index (AI), and mean oxygen saturation ($P > 0.05$).

Conclusion: The findings indicate an association between enuresis and obstructive sleep apnea (OSA), suggesting that treating OSA could ameliorate enuresis symptoms. Therefore, it is advisable to evaluate children with enuresis, particularly those who are obese, for OSA.

Keywords: Enuresis; Polysomnography; Sleep breathing disorder; Children

Citation: Jalilolghadr S, Soltantooyeh Z, Alizadeh M, Khameneh Pour K, Razzaghi A, Moeeni AA. **Investigating the Relationship between Nocturnal Enuresis and Sleep Disordered Breathing Using Polysomnography Data of 5-10 Year-Old Children Referred to Qazvin Children's Hospital, Iran.** J Sleep Sci 2023; 8(1-2): 14-19.

Introduction

Sleep is a homeostatic necessity that is essential for the health of human physical and psychological functioning, during which body and mind are allowed to rest and recover. According to studies, sleep disorders in children are increasing in recent years. According to parents, 10-75 percent of children worldwide have sleep disorders, varying from simple resistance to sleep, frequent awakenings, and parasomnias (a large part of sleep disorders that cause events such as walking and screaming, etc. in sleep) to serious and dangerous events such as respiratory disorders in sleep, especially obstructive sleep apnea (OSA) (1, 2). The prevalence of sleeping problems in children has been reported up to 30%. Sleep deprivation occurs when a person does not obtain the required duration, consistency, or type of sleep, a condition that has various detrimental effects on overall health and performance. Insufficient sleep

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has negative consequences such as stress, depression, and incompetency in academic and neurocognitive performances (such as memory) (3).

Any type of acute sleep disorder (less than a week) and subsequent quantitative or qualitative disorders in children can disrupt the function of the immune, cardiovascular, and endocrine systems. With the continuation of chronic sleep disturbances (more than one month), the child's physical development and academic, behavioral, and cognitive performance are affected (4, 5). Depression, anxiety, learning, and psychological problems are among the most prevalent symptoms in children with sleep disorders (6-8).

Parents of children with OSA often complain of breathing interruption attacks, snoring, mouth breathing, sweating, and restlessness during sleep. Polysomnography (PSG) in these children is a standard method to investigate OSA. Nocturnal enuresis (NE) means frequent urination during the night in children over 5 years of age who should have acquired urinary control naturally. A clear cause for NE has not been identified so far, but predisposing and associated factors such as 24-hour antidiuretic hormone (ADH) changes in the body, urinary infection, reduced bladder capacity, delayed growth and development, sleep breathing disorders, heredity, sex, family socioeconomic status, diabetes, seizures, etc. can be involved in its occurrence (9, 10).

Although the relationship between NE and apnea-hypopnea syndrome is unclear in children, several studies have pointed out the possible relationship between these two phenomena (11, 12). However, it is still unclear why some children with apnea-hypopnea syndrome have NE. A theory has been proposed that upper airway obstruction leads to increased intrathoracic pressure fluctuations with subsequent myocardial stretching and the release of natriuretic peptides, which leads to the inhibition of ADH action. Another theory is neuroendocrine dysfunction caused by cardiac reflexes. Lungs and kidneys may play an important role in NE in children with OSA, but these hypotheses need to be investigated by more studies. Other causes such as oxidative stress and inflammatory responses also need more research (13).

In this study, we investigated the association between NE and sleep-disordered breathing (SDB) using the results of PSG in 5-10-year-old children referred to Qazvin Children's Hospital, Iran, during 2016-2022.

Materials and Methods

In this cross-sectional study that was conducted in 2023, the target population included 5-10-year-old children who visited the sleep clinic of Qazvin Children's Hospital between 2016-2022 and they were collected by convenience sampling method.

The criteria for entering this study were: 1. attending a sleep clinic, 2. being between 5-10 years old, 3. not having a history of psychiatric diseases, 4. not having mental retardation, 5- not responding to standard enuresis treatments, and 5. no history of recent urinary tract infection (UTI).

Exclusion criteria included: 1- age over 10 years, 2- having some severe cognitive disorders that prevent understanding and responding to the questions, 3- failure to complete the questionnaire, 4- failure to complete PSG test, 5- diagnosed UTI, 6- history of diabetes, and 7- history of seizure, or use of drugs for the treatment of seizure disorders.

Children's parents responded to the Children's Sleep Habits Questionnaire (CSHQ) which has been standardized for Iran (14). This questionnaire includes demographic characteristics and eight main parts that were completed by parents to evaluate children's sleep patterns in the last week before the interview. The eight main parts are: sleep resistance, sleep delay, sleep duration, sleep anxiety, night anxiety, parasomnia, respiratory diseases, and daytime sleepiness. There are three options for questions: usually (5-7 nights per week), sometimes (2-4 nights per week), and rarely (0-1 nights per week) (15). To investigate nocturnal incontinence, we used the part related to child's sleep behavior, and children who had enuresis 2 nights a week and lasted for more than 3 months, regarding the inclusion and exclusion criteria, were placed in NE group (16).

In this study, the PSG test was used to have the respiratory analyses (the number of obstructive, central, and mixed hypopneas, and the basal oxygen saturation). PSG included electroencephalography (EEG) recording, electrooculography (EOG), chin electromyography (EMG), organ EMG, nasal-oral airflow, respiratory plethysmography (chest and abdomen), arterial blood oxygen saturation, body position, snoring, and video recording of the patient. To perform the PSG test, the test room was equipped with a suitable bed, a standard space with a suitable temperature, and an echogen environment so that the patient felt a comfortable sleeping environment similar to his/her sleeping room at home. The preparation

time before performing PSG was 4 hours. The electrodes were connected by an experienced nurse according to the latest recommendations of the American Academy of Sleep Medicine (AASM). Patients went to bed according to their usual sleeping habits. The test started with turning off the room light and ended after turning on the light. The test lasted about 300 minutes, on the average, for each subject. Recording and collecting of the data were done by the researcher manually according to the standards of AASM (17).

Obstructive sleep apnea-hypopnea syndrome (OSAHS) was diagnosed in children with apnea-hypopnea index (AHI) > 1. The AHI refers to the mean number of apnea and hypopnea per hour of sleep and is divided into three categories: mild AHI: 1-4, moderate: 5-10, and severe: above 10.

Sleep apnea was divided into three categories: obstructive apnea, central apnea, and mixed apnea. Apnea was defined as a 90% decrease in nasopharyngeal airflow compared to baseline. Obstructive apnea was defined to be associated with the respiratory effort of the chest and abdominal muscles. As our definition criteria, this effort is interrupted in central apnea, and in mixed apnea; the first part is central apnea and the second part is obstructive apnea (18).

The data were prepared and collected based on the checklist prepared from the questionnaire and PSG data, and SPSS software (version 26, IBM Corporation, Armonk, NY, USA) was used to analyze the data. Mean and standard deviation (SD) indicators were used to describe quantitative data and frequency and percentage were used to describe qualitative data. Parametric/non-parametric inferential tests were used to compare parents' reports of children's sleep disorders with PSG findings. In all tests, a significance level of 0.05 was considered.

All stages of the research were carried out following ethics standards and after obtaining consent from the subjects to enter the research. According to the previous studies and to increase the generalizability of the results, subjects were divided into two main groups based on the parents' answers to the question about the presence of enuresis in their children. The two groups were those who did not have NE ("none" or "rarely") and those who had NE ("sometimes" or "usually"). Hence, to compare in this research, the t-test for independent groups was used**.**

This study was approved with code IR.QUMS.REC.1402.114 in the Ethics Committee of Qazvin University of Medical Sciences.

Results

In this study, the information of 124 children was examined, including 64 boys (51%). The results showed that the mean age of children was 82.2 months with an SD of 24.4 months. The minimum age was 60 months and the maximum was 120 months. The mean weight of children was 26.2 kg and the SD was 11.7. The minimum weight was 9 kg and the maximum was 70 kg. The mean body mass index (BMI) was 18.9, the SD was 5.96, the minimum was 7.6, and the maximum was 39.2. The findings of children's PSG are listed in table 1.

Data analysis showed that 60.9% of children rarely and 39.1% of them had moderate to severe NE. Data analysis showed a statistically significant relationship between enuresis and BMI, mixed-apnea, number of respiratory apneas, total number of respiratory apnea and hypopneas, index of total respiratory apnea and hypopneas, and percentage of stage N2 sleep.

Table 1. Analysis of polysomnography (PSG) findings

Variables	Unit	Mean ± SD	Minimum	Maximum
Total sleep time	Hour	6.29 ± 1.58	2.25	9.13
Sleep quality	-	78.73 ± 12.44	44.20	99.90
Arousal index	Number per hour	25.97 ± 8.82	7.00	74.00
Average oxygen	%	94.61 ± 3.97	70.00	98.00
Oxygen loss index	Number per hour	14.11 ± 7.39	0	17.90
Obstructive apnea	Number	49.63 ± 7.55	0	87.00
Central apnea	Number	12.82 ± 3.45	0	20.00
Mixed apnea	Number	3.23 ± 1.93	0	10.00
Respiratory apnea	Number	53.70 ± 32.66	0	95.00
Respiratory hypopnea	Number	73.12 ± 9.83	0	156.00
Total respiratory apnea hypopnea	Number	125.72 ± 17.63	4.00	231.00
Total respiratory apnea hypopnea index	Number per hour	23.89 ± 7.64	0.80	124.20

SD: Standard deviation

Table 2. Analysis of polysomnography (PSG) findings

Variables	Group with enuresis (mean ± SD)	Group without enuresis (mean ± SD)	P-value
BMI (kg/m^2)	19.20 ± 5.93	18.60 ± 5.96	0.008
Total sleep time (hour)	6.51 ± 1.76	6.83 ± 1.19	0.067
Sleep quality	79.75 ± 12.65	76.21 ± 7.34	0.059
Arouzal index	26.91 ± 12.39	24.33 ± 17.39	0.360
Average oxygen (%)	96.86 ± 6.76	94.19 ± 5.34	0.085
Oxygen loss index	12.21 ± 8.68	14.41 ± 7.43	0.446
Obstructive apnea	58.33 ± 13.89	41.86 ± 6.03	0.108
Central apnea	14.34 ± 6.02	7.16 ± 1.34	0.058
Mixed_apnea	10.51 ± 3.54	2.54 ± 1.52	0.016
Respiratory hypopnea	72.03 ± 10.69	63.61 ± 8.85	0.001
Respiratory apnea	77.84 ± 14.30	55.56 ± 7.02	0.003
Respiratory apnea + hypopnea	149.86 ± 23.85	118.17 ± 14.86	0.003
Respiratory apnea + hypopnea index	27.64 ± 9.09	22.68 ± 4.24	0.003

BMI: Body mass index; SD: Standard deviation

Moreover, with increasing BMI, the possibility of nocturnal urination increased. The relationship between other parameters of PSG and NE is presented in table 2.

Discussion

Enuresis with OSA is a common problem in children. Studies have pointed to the relationship between bedwetting, snoring, and airway obstruction. In a study conducted in Saudi Arabia, there was a significant relationship between the frequency of nocturnal urination and snoring (19).

Enuresis in our study was associated with increased BMI, which has been confirmed in other studies. In a study conducted in China, the increase in BMI in children was associated with a 1.36-fold increase in NE, and factors such as snoring, attention-deficit/hyperactivity disorder (ADHD), and depressed mood were also associated with an increase in NE, but in a study conducted in Italy, there was no significant correlation between nocturia and weight gain or BMI (20, 21).

In our work, there was a significant relationship between NE and AHI. In Zhu et al.'s study, 68.5% of school-age children who presented with NE and OSA syndrome had AHI with a mean of 6.1 (22). In a study conducted by Alexopoulos et al., it was concluded that in children with moderate to severe OSA, the probability of NE was also higher (19), and in Alshehri et al.'s study, there was a significant relationship between NE and AHI, arousal index (AI), and bladder capacity (23).

It seems that relative hypoxia caused by airway obstruction in children, especially during sleep, can affect the function of the autonomic system and the amount of ADH secretion, which both increase urination and make it more difficult to control (24). In a study, the level of ADH in children with NE and OSA before treatment was higher in those who were treated after surgery, but the hormone level did not change in children who did not improve with surgery. These lead to the conclusion that upper airway obstruction alone cannot explain the relationship between NE and OSA syndrome (13).

In Snow et al.'s study, which compared the effect of surgical and medical treatment of OSA, it was concluded that 7 months later, NE improved 2 times more in patients who underwent adenotonsillectomy (25), but in a study conducted in Italy, no significant difference was observed in the treatment of NE after surgery (26) and no correlation between adenoid hypertrophy and NE was found in Aydin et al.'s study in Turkey (27).

Considering the finding that NE occurs mostly in N2 and N3 stages of sleep (28), in this study there was no significant relationship between NE and sleep structure except for the increase in stage N2 percentage. In the study conducted by Ono et al., there were no differences in the stages of sleep at night with and without enuresis in the results of PSG (29). Additionally, in Pedersen et al.'s study, there was no difference in the sleep structure in the two groups (30). However, in Wang's study, in children with NE, stages N1 and N2 were more common than children without NE (28).

In our study, the AI was not significantly correlated with NE compared to the second group, and in a study conducted by Sun et al., the AI was related to NE, which may be due to obesity and adrenal hypertrophy. Frequent apnea causes fre-

quent arousals and increases its threshold level and reduces sensitivity to bladder filling and contraction of the detrusor muscle, which stimulates the urge to urinate (31).

In Iran, according to a study conducted by Ghasemi et al., the frequency of NE was 5.4% in preschool children, which was also significantly related to snoring (32).

This research was done only in one center; therefore, it is recommended that it be done in other centers as well. It is also recommended that the age range of children should increase in future studies.

Conclusion

Due to the high cost, PSG is not routinely performed in Iran for symptomatic children, and in the present study, PSG was performed in patients with NE who had severe symptoms of apnea and were referred to the sleep clinic.

For further investigation, this study should preferably be done at the community level. Because children are more likely to have OSA and NE, in cases of NE that is resistant to treatment, especially in obese children, they must be checked for sleep apnea by healthcare providers, and for this to happen, it is necessary to educate families and those who are related to children, such as teachers.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

The authors are grateful to the Research Deputy of Qazvin University of Medical Sciences and all the staff of the center for their valuable help and guidance. Moreover, the authors would like to thank the participants of this study for their kind contribution.

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