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Evaluation of Sleep Disorders in Patients with Monosymptomatic Enuresis Nocturna

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ABSTRACT

Aim: It was aimed to investigate the relationship between the sleep disorders and monosymptomatic enuresis nocturna (MEN) and also to evaluate the possible etiological factors causing MEN.
Material and methods: Fifty patients having complaints of enuresis nocturna were evaluated. All of the cases were examined in detail and patients with secondary organic causes were excluded from the study. As a result of the anamnesis and examinations, 34 patients (68.0%) determined to have primary MEN underwent sleep test all night with full polysomnography method. **Results:** Twenty nine (85.3%) of the patients were diagnosed with different degrees of obstructive sleep apnea syndrome (OSAS) and included in the study. Correlation of the apnea score values with the patients' age, frequency of bedwetting, body mass index (BMI) and bladder capacity were analyzed; and there was only a statistically significant positive correlation with BMI (r=0.384, p=0.047). The patients were divided into weight groups and compared in terms of apnea score, bed wetting frequency and bladder capacity; and the median apnea score of the obese group was found to be statistically significantly higher than the normal and overweight groups (p=0.019). **Conclusion:** OSAS and obesity are present in a significant proportion of patients diagnosed with MEN, and these two diseases are effective factors in the development of MEN.
Key words: Nocturnal enuresis; Obstructive Sleep Apnea Syndrome; Child; Polysomnography

ÖZET

Amaç: Bu çalışmada uyku bozuklukları ile monosemptomatik enürezis nokturna (MEN) arasındaki ilişkinin araştırılması ve MEN'e neden olan olası etiyolojik faktörlerin değerlendirilmesi amaçlandı.Gereç ve **Yöntemler:** Enürezis noktürna şikâyeti olan 50 hasta değerlendirilmeye alındı. Tüm olguların ayrıntılı incelemesi sonucunda ikincil organik nedenleri olan hastalar çalışma dışı bırakıldı. Ayrıntılı anamnez ve detaylı muayeneler neticesinde, primer MEN olduğu saptanan 34 hastaya (%68,0) bütün gece tam polisomnografi yöntemi ile uyku testi yapılarak kayıt altına alındı. **Bulgular:** Çalışmada değerlendirilen elli hastanın yirmi dokuzuna (%85,3) farklı derecelerde obstrüktif uyku apne sendromu tanısı konuldu ve bu hastalar çalışmaya dâhil edildi. Elde edilen apne skor değerlerinin; hastaların yaşı, alt ıslatma sıklığı, vücut kitle indeksi ve mesane kapasitesi ile korelasyonu analiz edildi ve analizler sonucunda sadece apne skoru değerleri ile vücut kitle indeksi arasında istatistiksel olarak anlamlı pozitif korelasyon tespit edildi (r=0,384; p=0,047). Hastalar ek olarak ağırlık gruplarına ayrılarak apne skoru, alt ıslatma sıklığı ve mesane kapasitesi açısından karşılaştırıldı ve alt ıslatma sıklığı ile mesane kapasitesi açısından anlamlı farklılıklar tespit edilmezken; obez grubun ortanca apne skoru normal ve fazla kilolu gruplardan istatistiksel olarak anlamlı derecede yüksek bulundu (p=0,019).**Sonuç:** Obezite ve obstrüktif uyku apne sendromu, MEN tanısı konan hastaların önemli bir kısmında mevcuttur ve bu iki hastalık, MEN gelişiminde etkili faktörlerdir.

Anahtar kelimeler: Gece idrar kaçırma; Tıkayıcı uyku apne sendromu; Çocuk; Polisomnografi

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INTRODUCTION

Enuresis is involuntary recurrent daytime or nighttime urinary incontinence after the age when children need to gain bladder control (1). Genetic, organic, psychosocial and developmental factors, cortical centers controlling the sleep-wake system, irregularities in bladder physiology and hormonal factors play important roles in its etiopathogenesis (2). The incidence is 15-20% in 5 years old, 10% in 7 years old, 5% in 10 years old, 2-3% in children between the ages of twelve and fourteen, and the spontaneous cure is between the ages of fourteen to sixteen. An average of 15% spontaneous remission is observed annually. In general, 60% of enuretic children are boys and 40% are girls (3). Enuresis nocturna (EN) is a pathology that occurs when children cannot suppress nighttime bladder contractions. The disease is called monosymptomatic enuresis nocturna (MEN) in patients with EN without bladder dysfunction and lower urinary tract pathologies. Although the mechanism of action of the increased MEN incidence observed in patients with obstructive sleep apnea (Obstructive Sleep Apnea Syndrome, OSAS) is not fully known; children with OSAS have a high negative intrathoracic pressure due to increased inspiratory efficacy during sleep. As a result of ongoing oscillation in intrathoracic pressure, cardiac distension develops and this can lead to the release of atrial natriuretic peptide (ANP) and brain-type natriuretic peptide (BNP) that trigger the enuresis (4). The possible relationship between OSAS and MEN has been reported in many previous retrospective studies (5-7). In this study, it was aimed to investigate the sleep disorders in patients with MEN; based on the results, the relationship between the sleep disorder and MEN was evaluated.

MATERIAL AND METHODS

Fifty patients who admitted to our Pediatrics Outpatient Clinic having complaints of EN were evaluated. This study was supported by grants from the Scientific Research Projects Unit of our university and the institutional review board approved the study (2012.04.03.102). Detailed information was given to the relatives of all patients and their informed consent was obtained. Patients over 5 years old, who had 2 or more bedwetting per week and who had bedwetting problems for more than 3 months were accepted as having EN and included in the study. All of the cases were evaluated for secondary organic causes that may cause enuresis. Patients were evaluated with detailed anamnesis and who had more than two recurrent urinary tract infections and anomalies related to the urinary system were excluded from the study. Also the patients were questioned about overactive bladder and diurnal enuresis (daily urination frequency, urgency symptoms like leg crossing and Vincent’s curtsey) and if present excluded from the study.

Detailed physical examinations were performed after taking the patients' and their family history. In addition to general pediatric

examinations, patients were also examined for bladder globe, suprapubic tenderness, signs of genital infection and costovertebral angle sensitivity.

Direct abdominal radiographs were taken while standing and lying down and patients were evaluated for urolithiasis and vertebral anomalies. Bladder volume measurements were made with urinary system ultrasonography (USG) when the bladders of the patients were fully loaded. Patients were taken to urinary system USG examination for the second time after urination and bladder residual urine amounts were measured; functional bladder capacities were found by taking the difference. Then, the expected functional bladder capacity measurement was made {(age + 2) x 30 = ml} with the formula described by Berger and Koff for each patient (8).

As a result of the anamnesis and examinations, all of the cases determined to have primary MEN underwent sleep test with Philips Resipronics ALICE-5 polysomnography device all night with full polysomnography method. During the sleep test; 3 channel electroencephalography (EEG), 2 channel electrooculography (EOG), 2 channel chin electromyography (EMG), oro-nasal thermal sensor values, nasal pressure sensor value, thoracic and abdominal breathing movements, electrocardiography (ECG), breathing sound, oxygen saturation and synchronized video footage was recorded. At the end of the test, 10 seconds or more respiratory arrest was defined as “apnea”; more than 20% decrease in the nasal cannula signal amplitude compared to baseline with more than 4% decrease in saturation compared to basal saturation prior to the event was defined as “hypopnea”.

Apnea index (AI) in childhood OSAS is above 1. Obstructive hypopnea means more than 50% reduction in air flow, more than 4% decrease in oxygen saturation, or decreasing of the saturation to less than 90% and/or awakening of the patient. Apnea hypopnea index (AHI) is the sum of obstructive apnea, mixed apnea, and hypopnea in 1 hour of sleep. Grouping was done by evaluating the patients with AHI between 1 and 5 as mild, those between 5 and 9 as moderate, and those over 10 as severe OSAS (9).

Statistical Analysis

Statistical analysis of the study was done with NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) package program. Normality assumption and homogeneity of variances for continuous variables were evaluated with the Shapiro-Wilk and Levene tests. One-Way ANOVA and Kruskal-Wallis tests were used to compare three groups according to distribution of continuous variable. Pearson and Spearman correlation analyses were used to analyze correlation between numerical variables. The results were evaluated at the level of significance $p<0.05$.

RESULTS

After the evaluation of 50 patients with anamnesis and examination findings, 16 patients (32.0%) who were found to have secondary EN were excluded from the study. The remaining 34 MEN patients were subjected to sleep tests and 29 (85.3%) of them were

diagnosed with different degrees of OSAS and included in the study. Sixteen (55.2%) of the children were boys and 13 (44.8%) were girls. The mean age of boys was 9.56±2.83 (range, 6-17), of girls was 9.85±3.24 (range, 6-17), and the mean age of whole group was 9.69±2.97 (range, 6-17). The age, gender, apnea score, bed wetting frequency and body mass index (BMI) values of the patients are shown in Table 1.

Table 1. Demographic and clinical characteristics of the patients

	Male (n=16)	Female (n=13)	Total (n=29)
Age (years), mean±SD	9.56±2.83	9.85±3.24	9.69±2.97
BMI (kg/m^2), mean±SD	17.99±2.40	21.78±5.27	19.69±4.37
Apnea score, median (min-max)	3.1 (1.5-8.6)	3.2 (1.5-21.5)	3.2 (1.5-21.5)
BWF (day/week), median (min-max)	5.5 (3-7)	6 (3-7)	6 (3-7)

BWF: Bed wetting frequency, BMI: Body mass index, SD: Standard deviation

Table 2. Correlation of apnea score with age, BWF, BMI, and bladder capacity rate

		Apnea Score
Age	**r**	0.264
	p	0.167
BWF (day/week)	**r**	-0.094
	p	0.627
BMI	**r**	**0.384**
	p	**0.047**
Bladder capacity rate	**r**	-0.101
	p	0.602

BWF: Bed wetting frequency, BMI: Body mass index

Median apnea score of boys was 3.1 (range, 1.5-8.6), of girls was 3.2 (range, 1.5-21.5), and the median apnea score of the whole group was 3.2 (range, 1.5-21.5). When the apnea score results were examined, OSAS degree was found to be mild (<5) in 20 patients, moderate (5-10) in 6 patients, and severe (>10) in 3 patients.

When the correlation of apnea score values with patients' age, frequency of bed wetting, BMI and bladder capacity were evaluated, a statistically significant positive correlation was observed only with BMI (r=0.384, p=0.047, Table 2).

Table 3. Correlation of bladder capacity rate with apnea score, age, BWF and BMI

		Bladder Capacity Rate
Apnea Score	**r**	-0.101
	p	0.602
Age	**r**	0.274
	p	0.150
BWF (day/week)	**r**	**-0.423**
	p	**0.022**
BMI	**r**	0.065
	p	0.739

BWF: Bed wetting frequency, BMI: Body mass index.

As a result of the correlation analysis of bladder capacity with apnea score, age, bed wetting frequency and BMI, a statistically significant negative correlation was observed only between bladder capacity values and bed wetting frequency (r=-0.423, p=0.022, Table 3).

When patients were grouped according to BMI values; 15 patients were found to be normal weight (between the 5th and 85th percentile), 5 patients were overweight (between the 85th and

95th percentile) and 9 patients were obese (over the 95th percentile). When the patients who were divided into weight groups were compared in terms of apnea score, bed wetting frequency and bladder capacity, the median apnea score of the obese group was found to be statistically significantly higher than the normal and overweight groups (p=0.019, Table 4).

Table 4: Comparison of weight groups with "Apnea score", "Bed wetting frequency" and "Bladder capacity rate"

	Normal Weight n=15	**Over weight n=5**	**Obese n=9**	**p**
Apnea Score	3.2 (2.6) [1.5-8.6]	2.8 (1.5) [1.5-3.2]	7.3 (10.9) [1.8-21.5]	**0.019**
BWF (day/week)	6 (1) [4-7]	6 (3) [3-7]	6 (3) [3-7]	0.757
Bladder Capacity Rate	68.47±30.27	69.60±28.67	65.73±32.46	0.968

DISCUSSION

As a result of this study, it was found that sleep disorder and obesity detected by polysomnography applied to patients diagnosed with MEN are a facilitating and determining factor in the etiology of enuresis.

Enuresis is a well-known and widely observed health problem for many years. Several factors play important roles in its etiopathogenesis including developmental problems, psychosocial and environmental factors, sleep and wake system disorders, endocrinological, neurological and urinary system pathologies (10).

In the literature, after a good evaluation, it is seen that 85% of enuretic children are MEN (11). When 50 patients with EN were evaluated for the first time in our study, secondary enuresis was found in 32.0% of the cases and MEN in 68.0%.

There are different reports in the literature about the relationship between enuresis and sleep problems. Studies on the relationship between nocturnal enuresis and OSAS also have different results; positive and negative relationships have been reported in the literature. In a cohort study on 6147 children who were subjected to a questionnaire, sleep test with a polysomnography device was applied to 597 patients and the patients were divided into OSAS + and OSAS- groups. There was no difference between these two groups in the prevalence of EN (12). Barone et al. (13) was detected OSAS in 80% of cases with MEN in a case-control study in 2009. In a recent meta-analysis, it was concluded that when the factors causing sleep disturbance were eliminated in MEN patients with sleep disorders, serious improvements in MEN symptoms were detected (14). Some of the studies reporting the high rates of sleep disturbance in patients with nocturnal enuresis were conducted in the form of a questionnaire, and it is obvious that the results of these studies cannot provide good information about the true physiological sleep (15). Tjusi et al. (16) argue that the data obtained with the sleep tests performed with polysomnography device in the hospital environment cannot provide sufficient information about the actual physiological sleep like the studies with the questionnaire forms. In the same study, sleep quality of children with

MEN was measured with contactless biomotion sensors in their own home environments and a high rate of sleep disturbance was detected compared to the control group. In our study, 34 patients who were found to have MEN had a full polysomnography test all night and OSAS was detected in 29 patients (85.3%).

Some studies show that girls are less affected by renal complications secondary to hypoxia and ischemic perfusion injury than boys; but in a cohort study by Su et al. (12), more EN association was found in girls with severe OSAS, and it was reported that this may be due to some hormonal or other reasons and further research is needed. In our study, no significant difference was found between the apnea score and therefore OSAS levels of boys and girls.

In a study by Lam et al. (17), 705 polysomnography reports were examined and the relationship between obesity, AHI and tonsil size was evaluated, a serious relation was found between BMI, tonsil size increase and AHI degree. When the patients in our study were compared in terms of BMI values and AHI scores; It was found that those with high BMI also had high AHI scores and this was statistically significant.

In a study examining 281 children, obese children were reported to have 6 times more enuresis than normal-weight children, and according to this study, it was shown that the risk of enuresis doubled with each increase in BMI-Z score (18). In a study by Erdem et al. (19) in 2006; 62-86% of patients suffering from voiding dysfunction (loss of daytime sphincter control and EN) have been shown to be obese. In our study, it was determined that 15 (51.7%) of 29 patients with MEN and OSAS (+) were normal weight, 5 (17.2%) were overweight and 9 (31.0%) were obese. In total, 14 of the 29 patients (48.3%) were overweight and obese, and this result is consistent with the literature. In a study by Okur et al. (20) in 2012, it has been shown that the reduced functional bladder capacity will cause enuresis and this reduces the response to Desmopressin used in treatment. Similarly, in a recent prospective study, reduced bladder capacity was found in the majority of children with MEN (21). Also in our study, bladder capacity was found to be insufficient in 21 (72.4%) of 29 patients with MEN and OSAS (+) and this was found to be statistically significant.

Compared with other studies, the strengths of this study are; it is prospective and includes a homogeneous patient group. As the limitations of the study, it can be shown that the number of patients is low and the control group could not be included in the study.

CONCLUSION

As a result, it has been shown that OSAS and obesity are present in a significant portion of patients diagnosed with MEN, and these two diseases are effective factors in the development of MEN. This study will shed light on more comprehensive studies including the control group to be carried out in the future.

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