

Enuresis Nocturna and the Symptoms of Upper Airway Obstruction in Primary School age Children: Is there a Relationship?

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Abstract

Objective: Enuresis Nocturna (EN) associated with symptoms of upper airway obstruction was frequently observed in various studies. In this study, EN associated with symptoms of upper airway obstruction (breathing problem while sleeping, sleep apnea syndrome, sleeping with open mouth, snoring) was examined.

Methods: This study was conducted on 2314 students between 6-14 years age, from 3 primary schools in Ankara between January-May 2011. The questionnaires, questioning EN and the symptoms of upper airway obstruction, were distributed to students to be filled in by parents.

Results: The mean age of 2314 study participants (1123 male, 1191 female) was 9.21 ± 2.08 (6-14 years). When students were evaluated as groups with EN and without EN, a statistically significant difference was detected between groups regarding upper airway obstruction symptoms (breathing problem while sleeping, sleep apnea syndrome, sleeping with open mouth and snoring) (respectively $p=0.002$, $p=0.036$, $p<0.001$, $p<0.001$). When students were examined by dividing into 3 age groups as Group I(6-8 age), Group II(9-11 age) and Group III(12-14 age), a statistically significant difference was detected between age groups with EN (+), regarding breathing problem while sleeping and sleep apnea syndrome (respectively $p=0.025$, $p=0.004$).

Conclusion: As was detected in this study, EN could accompany upper airway obstruction symptoms as was detected in this study. Thus, taking a detailed medical history and physical examination at the primary care centers is significant.

Key words Nocturnal enuresis; airway obstruction; child

Introduction

The adenoids and tonsils in the upper airway are very small at birth and then they grow during the first 4 years of the life. They tend to shrink toward the adolescence period (1). During this period, children with adenoid and tonsillar hypertrophy could show some pathological symptoms and signs. It is stated that recurrent acute and chronic inflammation cause adenoid hypertrophy in some children (2). Adenoid and tonsillar hypertrophy can cause serious diseases from snoring to Obstructive Sleep Apnea Syndrome (OUAS), based on pharyngeal obstruction and respiratory disorders while sleeping. Snoring, mouth breathing, apnea and enuresis nocturna (EN) are detected as the most frequently seen symptoms during night (1).

It is found that EN during adolescence and childhood period is related with obstructive respiratory disorders occurring during night (3). EN can be described as involuntary urination or urinary incontinence of children above 5 during the night (4). Enuresis is a clinical problem, which diminishes the quality of life for children and their families. Thus, children have emotional and learning-based problems, which affect their social life (5). It is detected that many children with enuresis have a genetic susceptibility (6). In the studies, it is stated that two possible physical disorders could cause this situation. One of them is functional bladder disorder while the other one is the maturational delay in nocturnal arginine vasopressin secretion (7).

The purpose of the study is to see the relationship of EN with the symptoms of upper airway obstruction in children at primary school-age.

Methods

Study design and subjects: This study was a cross-sectional study and performed at 3, randomly selected, primary schools in Ankara during January-May 2011. The counselor and school administrators were informed about the details of study. A total of 2500 students were approached for this study through convenient sampling and around 2314 students agreed to participate with a response rate of 92%.

Survey questionnaire: a pretested self-administered questionnaire was used for data collection. A Questionnaire was comprised of questions related to socio-demographic characteristics of participants, such as age, sex, income level, the education level of parents, symptoms of upper airway obstruction i.e.; breathing problem while sleeping, sleep apnea syndrome, sleeping with open mouth, snoring etc, and about their EN status. The participants were also asked about frequency of being diagnosed with recurrent upper respiratory tract infection (URTI) and acute otitis media (AOM). EN was described as urinary incontinence of more than once a month in children above 5 years old, without any related symptoms. EN can be divided into primary EN (80%) and secondary EN (20%). In primary EN, it is possible to have lifelong urinary incontinence, while in secondary EN;

urinary incontinence begins after at least six months of staying dry. In this study we included patients presenting with primary enuresis while patients with secondary enuresis were excluded and student group with enuresis nocturna was described as EN (+) and without enuresis nocturna was described as EN (-). Sleep apnea syndrome was evaluated as the most serious upper respiratory tract obstruction symptom. The sleep apnea syndrome was described as respiratory arrest lasting more than 5-10 seconds during sleep due to any reason. If apnea attacks happened more than 4 times a week, it was described as "during every sleep"; if it was 3-4 times a week, it was described as "frequently"; if it was twice a week, it was described as "sometimes" and if it was once a week, it was described as "rarely".

Ethical Approval: The parents of students were informed about the study purpose and their written consent was taken. Ethics approval was taken from the ethical committee of Gulhane Military Medical Academy (GMMA) (No:1491-941-09/1539) and also necessary permission was obtained from Ankara Provincial Directorate of National Education.

Statistical analysis: SPSS 15.0 for Windows (Chicago-USA) package program was used for evaluating the data obtained from the study. Descriptive statistical methods were used to state categorical variables in numbers and percentages, and continuous variables in mean \pm standard deviation. Chi-square test was used to compare discrete variables. While examining the upper airway obstruction symptoms related with EN in children in the sample group, logistic regression analyses was performed by encoding EN (+) as 1 and EN(-) as 0. Calculation of odds ratios (OR) for EN (+) group and 95% confidence intervals (CI) were made using univariate logistic regression model. The level of $p < 0.05$ was considered significant.

Results

A total of 2500 primary school-age children parents were approached out of which 2314 completely filled the questionnaire with a response rate of 92.56%. The average age of study group was 9.21 ± 2.08 with a male predominance; i.e. 5%.

For analysis purpose students were divided into three groups; as Group I of 6-8 years old students ($n=958$), Group II of 9-11 years old students ($n=1014$) and Group III of 12-14 years old students ($n=342$). The overall prevalence of EN for all students was found to be 9.9% ($n=230$) in general. When assessing prevalence in terms of age groups, the rate of EN was 14.1% ($n=135$) for the students of Group I, 8.1% ($n=82$) for the students of Group II and 3.8% ($n=13$) for Group III ($p < 0.001$).

The frequency of upper respiratory tract obstruction symptoms (breathing problem while sleeping, sleep apnea syndrome, sleeping with open mouth, snoring) in EN (+) and EN (-) groups are shown in Table 1. Sleep apnea was recognized as the most serious upper airway

obstruction symptom. In EN (+) group, 31 students had sleep apnea syndrome, the distribution of them regarding the age groups was as follows: 12 students were in Group I and 19 students were in Group II. The frequency of apnea attacks was evaluated in EN (+) group; it was detected that 24 students had it "very rare", 2 students had it "sometimes" and 5 students had it "during every night".

Table 1: Comparison of upper respiratory tract obstruction symptoms of students in EN (+) and EN (-) groups

	EN (+)	EN (-)	Univariate regression models	
	% (n)	% (n)	p	OR (95% CI)
<i>Breathing problem while sleeping (+)</i>	22,2% (51)	14.3% (299)	0.002	1.70 (1.21-2.37)
<i>Sleep apnea syndrome (+)</i>	13.5% (31)	9,2% (191)	0.036	1.54 (1.02-2.31)
<i>Sleeping with open mouth (+)</i>	42.2% (97)	27.6% (576)	< 0.001	1.90 (1.44-2.52)
<i>Snoring (+)</i>	23.5% (54)	13.9% (289)	<0.001	1.90 (1.37-2.64)

When the students with EN were evaluated regarding age groups (Group I, II, III), a statistically significant difference was determined between groups, regarding breathing problem while sleeping and apnea attack (respectively, $p=0.025$, $p=0.004$). When the groups were evaluated regarding sleeping with open mouth and snoring, there was not a statistically significant difference ($p>0.05$) (Table 2).

Table 2: The comparison of upper airway obstruction symptoms regarding age groups

	Group I	Group II	Group III	p
	% (n)	% (n)	% (n)	
<i>Breathing problem while sleep (+)</i>	17.8 (24)	31.7 (26)	7.7 (1)	0.025
<i>Sleep apnea syndrome (+)</i>	8.9 (12)	23.2 (19)	0 (0)	0.004
<i>Sleeping with open mouth (+)</i>	38.5 (52)	46.3 (38)	53.8 (7)	0.359
<i>Snoring (+)</i>	24.4 (33)	22 (18)	23.1 (3)	0.915

We performed a logistic regression analysis to determine the most effective discriminating variable(s). Hence, we could see the most effective variable(s) at the last step of the model. The model coefficients were tested by omnibus test and they were statistically significant ($p<0.05$). In addition, according to Hosmer and Lemeshow Goodness-of-Fit test the model is statistically significant (Chi-Square=0.148; df =2; $p>0.05$). When the relational statistics Cox & Snell R Square and Nagelkerke R Square values are seen, it could be interpreted that these statistics were moderately low. It is known that there are many other variables affecting EN in real life; however we applied the model just for four of them, so we evaluated these relational values as acceptable. Finally the model with variables and the statistics from them can be seen in Table 3.

As seen in Table 3, "Sleeping with open mouth" variable is statistically significant for all steps. When we examine the third step, "Sleeping with open mouth" (Wald=9.711; $p<0.05$) and "Snoring" (Wald=2.940; $p<0.10$) can be accepted as the most efficient variables for EN (+) and EN (-) discrimination.

When EN (+) and EN (-) groups were evaluated regarding the frequency of upper respiratory tract infection, 12.2% of the students in EN (+) group had URTI 5-6 times a year and this rate was 6.7% in EN (-) group ($p=0.003$) (Table 4).

When EN (+) and EN (-) groups were evaluated regarding recurrent acute otitis media (AOM), 33.5% of the students in EN (+) group had AOM problem 1-2 times a year and this rate was 25.9% in EN (-) group ($p=0.041$) (Table 5).

Table 3: Logistics regression model coefficients

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1(a)	Breathing problem while sleep (1)	-,186	,271	,471	1	,493	,830
	Sleep apnea syndrome (1)	-,028	,306	,008	1	,927	,972
	Sleeping with open mouth (1)	-,470	,170	7,668	1	,006	,625
	Snoring (1)	-,286	,204	1,964	1	,161	,752
	Constant	-1,486	,223	44,575	1	,000	,226
Step 2(a)	Breathing problem while sleep (1)	-,203	,192	1,126	1	,289	,816
	Sleeping with open mouth (1)	-,471	,170	7,703	1	,006	,624
	Snoring (1)	-,282	,201	1,977	1	,160	,754
	Constant	-1,498	,175	73,733	1	,000	,223
Step 3(a)	Sleeping with open mouth (1)	-,513	,165	9,711	1	,002	,599
	Snoring (1)	-,334	,195	2,940	1	,086	,716
	Constant	-1,596	,150	112,954	1	,000	,203

Table 4: Comparison of URTI frequencies in EN (+) and EN (-) student groups

URTI frequency	EN (+) % (n)	EN (-) % (n)	p
None	6.5 (15)	12.5 (260)	0.003
1-2 times per year	50 (115)	51.3 (1069)	
3-4 times per year	28.7 (66)	26.2 (545)	
5-6 times per year	12.2 (28)	6.7 (139)	
> 6 times per year	%2.6 (6)	%3.4 (71)	

Table 5. Comparison of AOM frequencies in EN (+) and EN (-) student groups

AOM frequency	EN (+) % (n)	EN (-) % (n)	p
None	60.9 (140)	69.2 (1443)	0.041
1-2 times per year	33.5 (77)	%25.9 (540)	
3-4 times per year	3.9 (9)	%4.0 (84)	
5-6 times per year	1.7 (4)	%0.7 (14)	
> 6 times per year	0 (0)	%0.1 (3)	

For the rate of students, who had surgical operation due to upper airway obstruction symptoms (tonsillectomy, adenoidectomy, adenotonsillectomy) was 7.6% (n=175), the mean age of students was 5.71 ± 1.83 (2-11 years old), when they had the operation. 57.1% (n=100) of the students, who had the operation, were male and 42.9% (n=75) were female. The distribution of operations was as follows: 10.9% (n=19) was tonsillectomy, 33.1% (n=58) adenoidectomy, 56% (n=98) adenotonsillectomy. Even if the difference was not statistically significant, 8.6% of the students, who had a surgical operation related to upper airway obstruction, had EN while this rate was 10.1% for students, who did not have a surgical operation.

Discussion

During childhood, there are many factors, particularly adenoid and tonsillar hypertrophy, which restrict air flow through the upper airway. Adenoid and tonsillar hypertrophy is taken normally during this period, when children have nasal and throat infections frequently (1, 8). Enlarged adenoids can block air flow through the nasal cavity. This situation can result in snoring, mouth breathing, and nasal speech (7). EN is another clinic case, thought to develop during this period as a result of upper airway obstructions. In this study, it was detected that symptoms of upper airway obstruction such as breathing problem while sleeping, apnea attacks, sleeping with open mouth and snoring were seen more frequently in children with EN. When the children with Enuresis were evaluated regarding the age groups, it was detected that there was a difference between groups regarding breathing problem while sleeping and apnea attacks and it was determined that this difference depended on the increasing number of these two symptoms in Group II (9-11 years old) students.

There have been many studies demonstrating the correlation between upper respiratory tract obstruction and EN. In the study of Cinar et al., it was found that the etiologic relation between EN and upper airway obstruction was stronger than estimated (9). Alexopoulos et al. examined the relation between primary EN during childhood and snoring. This study included 1821 students (5-14 years old) and it was determined that 135 students (7.4%) had habitual snoring (HS). As a result of this study, it was determined that children with HS were diagnosed with primary EN more frequently than children without HS (3). In the study of Ersu et al, it was stated that HS was a serious problem for children and could be related with diurnal symptoms. The study included 2147 primary school students (5-13 years old) and it was detected that of students with HS (7%) had apnea, restless leg syndrome, parasomnia and nocturnal enuresis more frequently than children without HS (10). Aydin et al. examined EN and upper airway obstruction symptoms, developed by adenoid hypertrophy and 1090 primary school students (5-14 years old) were included in the study. When the students were evaluated separately under 3 groups as 5-7 years old, 8-10 years old, 11-14 years old students, contrary to the former studies, there was no significant difference between

groups regarding the relation of EN frequency with adenoid hypertrophy symptoms (7). In this study, when sleeping with open mouth and snoring were evaluated as the most simple symptoms of upper respiratory tract obstruction, it was determined that students with EN (+) had these problems more frequently than students with EN (-). This statistically significant difference between groups supported the findings of former studies. It was considered that the difference could result from disorders in neuro-hormonal mechanisms, which controlled urinary incontinence.

It was a frequently observed clinical finding that sleep apnea syndrome was accompanied with EN. In the study of Basha et al., 326 children (2-18 years old), who had tonsillectomy or adenotonsillectomy, were included and EN prevalence rate was detected as 32.8% (n=107). After a period of 44 months, it was detected during retrospective evaluation that in 61.4% of the cases patients recovered from EN completely, 22.8% EN was in remission period and in 15.8% cases EN still existed (11). In the study of Brooks and Topol, 160 children, having breathing problem while sleeping, were polysomnographically evaluated and also Respiratory Disturbance Index (RDI) was performed. It was detected that 66 (41%) of the children were enuretic. As a result of the study, it was determined that children with $RDI > 1$ had higher risk of enuresis than children with $RDI \leq 1$. This result also revealed that respiratory difficulties while sleeping increased the risk of enuresis (12). Weissbach et al. evaluated 161 children (4-18 years old) polysomnographically and examined EN in the post-adenotonsillectomy period. In an evaluation performed after nine months from the operation, it was detected that EN symptoms dramatically decreased after adenotonsillectomy operation in children with obstructive sleep apnea (13). Firoozi et al. obtained similar results (14). Weider et al determined that patients recovered from enuresis after having adenotonsillectomy, which treated chronic adenotonsillar hypertrophy and airway obstruction (15). In this study, it was determined that the rate of students, having breathing problem while sleeping or apnea attacks, was higher in EN (+) than in EN (-) group. The results of this study supported former studies. This statistically significant difference between EN (+) and EN (-) groups could be related to a weak control of the regulation of Antidiuretic Hormone (ADH) release, especially related with REM (Rapid Eye Movement) sleep, and an increased release of atrial natriuretic peptide (ANP).

In this study, the frequency of recurrent URTI and AOM was also examined in addition to upper airway obstruction symptoms. A statistically significant difference was detected between EN (+) and EN (-) student groups, regarding the frequency of recurrent URTI and AOM. Although there has been no study that directly has examined the relation of URTI and AOM with EN, it is clear that eustachian tube dysfunction, especially which which resulted from adenoid hypertrophy, forms the basis for URTI and AOM (7). Therapeutic effectiveness

of adenotonsillectomy in enuretic children, who applied due to obstructive sleep apnea symptoms, was shown in a limited number of studies (14, 16). As it was determined in this study, the relation of pathologies, which caused upper airway obstruction like adenoid hypertrophy, with EN supported indirectly the relation between EN and AOM. It was considered that increase in frequency of URI and AOM in the EN (+) group resulted from the infection, which occurred due to air passages obstruction.

Study limitations: Upper respiratory tract obstruction symptoms could be observed in children without adenoid hypertrophy. For example, these symptoms could be observed in children with allergic rhinitis, septal deviation or concha hypertrophy. However these pathologies are more rarely observed than adenoid hypertrophy in this age group. Not being able to make a differential diagnosis in children with these symptoms was one of the most important limitations of this study. Moreover, enuretic children could not be examined prospectively because of the cross-sectional study design. Another limitation of this study was that it could not be determined whether the children, who had surgical operation because of upper airway obstruction, recovered from EN or not. Because of study design, adenoids and tonsils size could not be measured by physical examination.

Conclusions

EN is a serious disease that has a potential to cause important problems in social life. The importance of a detailed medical history and physical examination at primary care centers is evident, because the initial contact with patients begins in these centers. As it was detected in this study, even if EN seems to be a urological pathology, it is observed that it accompanies upper airway obstruction symptoms frequently (breathing problem during sleeping, sleep apnea syndrome, open mouth sleeping, snoring).

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References

1. Kara C.O., Ergin H., Kocak G., Kilic I., M. Yurdakul M. Prevalence of tonsillar hypertrophy and associated oropharyngeal symptoms in primary school children in Denizli, Turkey, *Int. J. Pediatr. Otorhinolaryngol.* 66 (2) (2002) 175-179.
2. Potsic W.P. Assessment and treatment of adenotonsillar hypertrophy in children, *Am. J. Otolaryngol.* 13 (5) (1992) 259-264.
3. Alexopoulos E.I., Kostadima E., Pagonari I., Zintzaras E., Gourgoulanis K., Kaditis A.G. Association between primary nocturnal enuresis and habitual snoring in children, *Urology* 68 (2) (2006) 406-409.
4. Van Gool JD, Nieuwenhuis E, Ten Doeschate IO, Messer TP, De Jong TP. Subtypes in monosymptomatic nocturnal enuresis. II, *Scand. J. Urol. Nephrol. Suppl.* 202 (1999) 8-11.
5. Gur E, Turhan P, Can G, Akkus S, Sever L, Guzeloz S, et al. Enuresis: prevalence, risk factors and urinary pathology among school children in Istanbul, Turkey. *Pediatr Int* 2004;46:58-63.
6. Bailey J.N., Ornitz E.M., Gehricke J.G., Gabikian P., Russell A.T., Smalley S.L. Transmission of primary nocturnal enuresis and attention deficit hyperactivity disorder, *Acta Paediatr.* 88 (12) (1999) 1364-1368.
7. Aydin S., Sanli A., Celebi O., Tasdemir O, Paksoy M., Eken M., Hardal U., Aydurhan E. Prevalence of adenoid hypertrophy and nocturnal enuresis in primary school children in Istanbul, Turkey. *International Journal of Pediatric Otorhinolaryngology* 2008;72:665-668.
8. Kornblut A.D. Non-neoplastic disease of the tonsils and adenoids, in: Paparella M.M., Shumrick D.A., Gluckman J.L., W.L. Meyerhoff W.L. (Eds.). *Otolaryngology*, third ed., W.B. Saunders Co., Philadelphia, 1991, pp. 2129-2147.
9. Cinar U., Vural C., Cakir B., Topuz E., Karaman M.I., Turgut S. Nocturnal enuresis and upper airway obstruction, *Int. J. Pediatr. Otorhinolaryngol.* 59 (2) (2001) 115-118.
10. Ersu R., Arman A.R., Save D., Karadag B., Karakoc F., Berkem M., Dagli E. Prevalence of snoring and symptoms of sleep-disordered breathing in primary school children in Istanbul, *Chest* 126 (1) (2004) 19-24.
11. Basha S., Bialowas C., Ende K., Szeremeta W. Effectiveness of adenotonsillectomy in the resolution of nocturnal enuresis secondary to obstructive sleep apnea. *Laryngoscope* 115(6) (2005) 1101-1103.
12. Brooks L.J., Topol H.I. Enuresis in children with sleep apnea. *J. Pediatr.* 142 (5) (2003) 515-518.
13. Weissbach A., Leiberman A., Tarasiuk A., Goldbart A., Tal A. Adenotonsillectomy improves enuresis in children with obstructive sleep apnea syndrome, *Int. J. Pediatr. Otorhinolaryngol.* 70 (8) (2006) 1351-1356.
14. Firoozi F., Batniji R., Aslan A.R., Longhurst P.A., Kogan B.A. Resolution of diurnal incontinence and nocturnal enuresis after adenotonsillectomy in children. *J. Urol.* 175 (5) (2006) 1885-1888.
15. Weider D.J., Sateia M.J., West R.P. Nocturnal enuresis in children with upper airway obstruction, *Otolaryngol. Head Neck Surg.* 105 (3) (1991) 427-432.