

Sleep Problems and Daytime Sleepiness in Children with Nocturnal Enuresis

Yun-Mo Gu, M.D.¹
Jung Eun Kwon, M.D.²
Gimin Lee, M.D.²
Su Jeong Lee, M.D.²
Hyo Rim Suh, M.D.²
Soyoon Min, M.D.²
Da Eun Roh, M.D.²
Tae Kyoung Jo, M.D.²
Hee Sun Baek, M.D.²
Suk Jin Hong, M.D.³
Hyeeun Seo, M.D.¹
Min Hyun Cho, M.D.²

Department of Pediatrics¹, Busan St. Mary's Hospital, Busan, Department of Pediatrics², Kyungpook National University School of Medicine, Daegu Department of Pediatrics³, Catholic University of Daegu School of Medicine, Daegu, Korea

Corresponding author: Min Hyun Cho, M.D.
Department of Pediatrics, Kyungpook National University Medical Center, 807 Hogukno, Buk-gu, Daegu 41404 Korea
Tel: +82-53-200-2741
Fax: +82-53-200-2039
E-mail: chomh@knu.ac.kr

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Purpose: Nocturnal enuresis (NE) is one of the most common problems in childhood. NE has a multifactorial etiology and is influenced by sleep and arousal mechanisms. The aim of the present study was to prospectively evaluate sleep problems and patterns in children with NE compared with normal healthy controls.

Methods: Twenty-eight children with NE and 16 healthy controls were included in the study. To evaluate sleep habits and disturbances, parents and children filled out a questionnaire that included items about sleep patterns and sleep-related behaviors prior to treatment for NE. Demographic factors and other data were compared for the two groups based on the responses to the sleep questionnaire.

Results: Night awakening, sleepwalking, and periodic limb movements were more prevalent in children with NE, but symptoms of sleep-disordered breathing were not increased in this group. There were statistically significant differences in periodic limb movements and daytime sleepiness between the two groups.

Conclusion: Children with NE seemed to have more sleep problems such as night awakening, sleepwalking, and periodic limb movements. In addition, a higher level of daytime sleepiness and hyperactivity in patients with NE suggested a relationship between NE and sleep disorders.

Key words: Nocturnal enuresis, Children, Sleep disorder, Periodic limb movement

Introduction

Nocturnal enuresis (NE) is commonly called nighttime bedwetting and refers to discrete episodes (≥ 1 time/month) of urinary incontinence during sleep in children ≥ 5 years of age¹. NE is a common problem in children, occurring in approximately fifteen percent of five-year-old children. Children with NE can suffer from emotional stress or psychological injury, such as low self-esteem, depression, guilt, discouragement, and anxiety². In spite of perceived risk of psychosocial problems associated with NE, the treatment for NE may be prolonged and is often associated with relapses because the etiology is ambiguous and multifactorial³⁻⁵.

Among many potential causes of NE, increased nocturnal urine production, bladder instability, and decreased nocturnal bladder capacity are considered as the main pathophysiological mechanisms. On the other hand, a correlation between sleep disorder and NE could also be considered as a cause, as found by some previous studies^{6,7}. The children affected by NE could have a high

threshold of cortical arousability, so they are unable to awake when the bladder reaches its maximum capacity. Some authors noted that the prevalence of obstructive sleep apnea and periodic limb movements were increased in enuretic children. Moreover, bedwetting could disturb the children's sleep, as they would have to change out of wet clothes and in turn evoke problems of daytime sleepiness. Therefore, we should be interested in the sleep habits of children affected by NE.

The aim of this study was to evaluate the association between NE and sleep related problems including daytime sleepiness among Korean children.

Materials and methods

The study was carried out among children who were diagnosed as suffering from NE in Kyungpook National University Hospital during a 7-month period from April 2013 to October 2013. NE was defined as repeated urination into the bed or clothes during sleep, occurring ≥ 1 time per month for at least three consecutive months in a child ≥ 5 years of age. All children previously diagnosed with NE or found to be suffering from NE due to secondary etiologies on history taking, routine blood and urine analysis were excluded from the study. Those with urinary incontinence associated with a well-known urological dysfunction or neurological disease and taking some form of medication for enuresis were also excluded. The subjects in the control group were recruited from the healthy children who were involved in the study of normal polysomnographic characteristics⁸⁾. To obtain data about their sleep pattern and problems associated with sleep, the sleep questionnaire was used in both groups.

The sleep questionnaire was designed for children and parents to collect information about baseline sleep patterns and problems. Baseline clinical characteristics of sleep patterns include sleep duration, time to sleep and sleeping place. The sleep questionnaire about sleep patterns includes 4 domains: (1) bedtime behaviors and insomnia symptoms (4 items), (2) symptoms of sleep disturbance during the night (5 items), (3) symptoms of sleep disordered breathing (3 items), (4) symptoms of excessive somnolence and behaviors of daytime (10 items) (Table 1, Appendix). A 5-

point response scale is used on each question (0=never a problem; 1=almost never a problem (0-1 day per week); 2=sometimes a problem (2-4 days per week); 3=often a problem (more than 5 days per week); 4=unknowingness). The items were selected from Sleep Disturbances Scale for Children (SDSC), Pediatric Sleep Questionnaire (PSQ), and Pediatric Daytime Sleepiness Scale (PDSS) by the authors, and these were translated into the local language. The questionnaire was completed jointly by the parents and children during their first hospital visit. In addition, their demographic data and medical history were also collected. The questionnaire of control group was filled out by their parents. This study was approved by the institutional review board of Kyungpook National University Hospital (KNU MC 13-1020). The aim of the study was described in the top of the sleep questionnaire and all parents and children gave their written informed consent.

Statistical analysis was performed using PASW statistical

Table 1. Sleep Questionnaire Items used for the Subjects

Bedtime behaviors and insomnia symptoms
The child has irregular bedtime routine.
The child goes to bed reluctantly.
How long after going to bed does your child usually fall asleep? (more than 30 min)
The child wakes up more than twice per night.
Symptoms of sleep disturbance during the night
You have observed the child talking in his/her sleep.
You have observed the child sleepwalking.
The child grinds his/her teeth during sleep.
The child has jerking of legs while asleep.
You have observed periodic limb movements of child during sleep.
Symptoms of sleep disordered breathing
The child snores.
The child gasps for breath or is unable to breath during sleep.
You have observed the child mouth-breathing.
Symptoms of excessive somnolence and behaviors of daytime
The child awakes in the morning feeling tired.
The child is difficult to wake up in the morning.
The child falls asleep or gets drowsy during class.
The child is tired and grumpy during the day.
The child does not seem to listen when spoken to directly.
The child has difficulty organizing tasks and activities.
The child is easily distracted by extraneous stimuli.
The child fidgets with hands or feet or squirms in seat.
The child in "on the go" or often acts as if "driven by motor".
The child interrupts others (conversation or games).

software version 18.0 (IBM, Somers, NY, USA). Analysis of results was performed using Kolmogorov-Smirnov test of normality. A chi square test was also used to compare the statistical difference between NE group and control group. P -value ≤ 0.05 was considered significant.

Results

1. Demographic Characteristics and Baseline Sleep Patterns of the Subjects

Forty-four subjects were included in this study, which included twenty-eight children affected by NE (NE group) and sixteen healthy children (control group). The mean age of the children in NE group was 8.4 ± 3.2 years, (range: 5-17 years) and gender ratio 13:15 (male: female). In control group, the mean age was 6.7 ± 2.0 years, (range: 5-10 years)

Table 2. Demographic Characteristics and Baseline Sleep Patterns of the Subjects

	NE Group	Control Group
No	n=28	n=16
M: F	13:15	11:5
SL (min)	16.8 ± 13.19 (range: 2-60)	16.2 ± 14.23 (range: 5-40)
SD-WD (min)	538.6 ± 69.06 (range: 360-630)	564.4 ± 41.31 (range: 480-660)
SD-WE (min)	567.1 ± 50.17 (range: 480-660)	561.9 ± 62.11 (range: 420-680)
Co-sleeping	n=18 (64.3%)	n=12 (75.0%)
Age (yr.)	8.4 ± 3.19 (range: 5-17)	6.7 ± 1.98 (range: 5-10)

Data are presented as mean \pm SD.

Abbreviations: NE, nocturnal enuresis; No, number; M, male; F, female; SL, sleep latency; SD, sleep duration; WD, weekday; WE, weekend.

Table 3. Symptoms of Bedtime Behavior and Sleep Disordered Breathing in Subjects

	NE Group (n, %)	Control Group (n, %)	P value
Bedtime behavior and insomnia symptoms of the subjects			
Irregular bed time routine	7, 25	2, 12.5	0.45
Going to bed reluctantly	3, 10.7	2, 12.5	0.608
Prolonged sleep latency	6, 21.4	4, 25	0.692
Night awakening	6, 21.4	1, 6.2	0.533
Symptoms of sleep disordered breathing in subjects			
Snoring	4, 14.3	3, 18.8	0.504
Sleep apnea	0, 0	1, 6.2	0.364
Mouth breathing	14, 50	8, 50	1

Abbreviation: NE, nocturnal enuresis.

and gender ratio 11:5 (male: female) (Table 2). Table 2 shows the mean sleep latency, sleep duration and co-sleeping and similar results of two groups. In addition, there were no definite difference of sleep duration between weekday and weekend.

2. Bedtime behaviors and insomnia symptoms

Compared to control group, children in NE group showed higher prevalence of irregular bedtime (7 children, 25% vs. 2 children, 12.5%) and night awakening (6 children, 21.4% vs. 1 child, 6.2%), while they had a similar prevalence in the symptoms of reluctance to go to sleep and sleep latency (10.7% vs. 12.5%, 21.4% vs. 25%, respectively) (Table 3). However, this was not statistically significant.

3. Symptoms of sleep disturbance during sleep

The prevalence of periodic limb movement was significantly higher in NE group than in control group (10 children, 35.7% vs. 1 child, 6.2%, $P=0.036$). Other symptoms like sleep talking (21.4% vs. 12.5%), sleepwalking (7.1% vs. 0%), teeth grinding (7.1% vs. 6.2%), and kicking legs (7.1% vs. 0%), also showed higher prevalence in NE group than controls but did not differ significantly (Fig. 1).

4. Symptoms of sleep disordered breathing

Half of the children (50%) in both NE group and control group had the symptom of mouth breathing and they had a similar prevalence of snoring (14.3% vs. 18.8%). No NE individual had sleep apnea (Table 3).

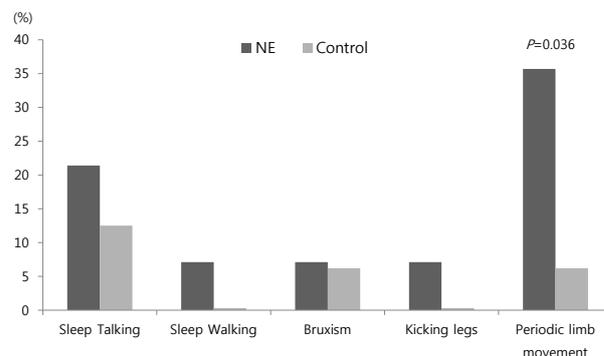


Fig. 1. During sleep, sleep talking, sleep walking, bruxism, and periodic limb movement were more prevalent in children with nocturnal enuresis. There was statistically significant difference in periodic limb movements ($P=0.036$) between the two groups. NE, nocturnal enuresis.

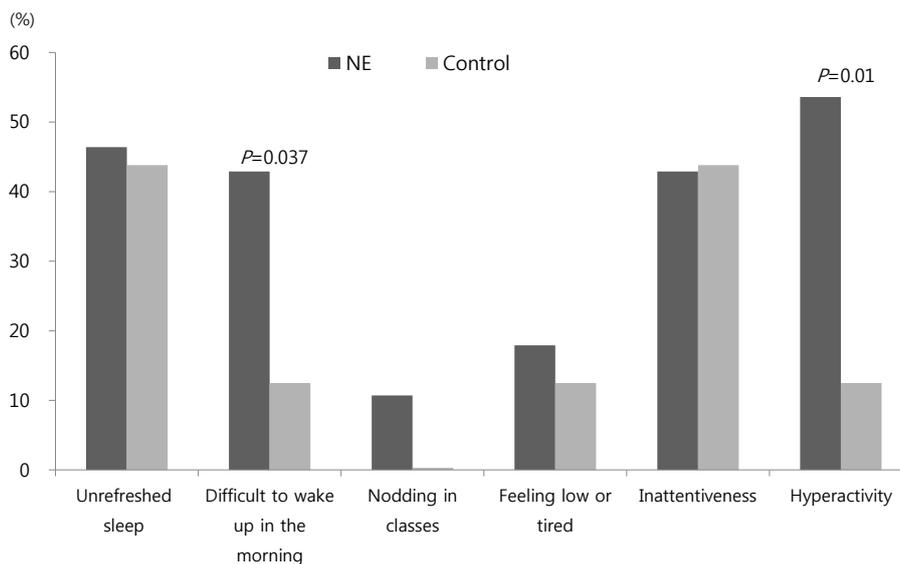


Fig. 2. Children with nocturnal enuresis have a higher level of daytime sleepiness and hyperactivity. NE, nocturnal enuresis.

5. Symptoms of daytime sleepiness

Children with NE had a higher prevalence of all symptoms concerned with daytime behaviors except inattentiveness, as compared to controls. Especially, the prevalence of some daytime behaviors like difficulty in waking up in the morning (42.9% vs. 12.5%, $P=0.03$) and hyperactivity (53.6% vs. 12.5%, $P=0.01$) was significantly higher in NE group than in control group (Fig. 2).

Discussion

This study showed the interesting finding that NE group had a higher prevalence for most sleep-related problems and bad bedtime habits as compared to the control group. Especially, the prevalence of periodic limb movements, difficulty to wake up in the morning, and hyperactivity, was significantly different between both groups. However, both groups had no difference in the prevalence of symptoms suggestive of sleep apnea.

NE could alter sleep architecture or be the consequence of an abnormal sleep structure. Previous reports show that NE could be associated with sleep-disordered breathing, especially obstructive sleep apnea⁹. Sleep-disordered breathing is a common problem during childhood and is a term that describes a spectrum of upper airway obstruction

during sleep from primary snoring to obstructive sleep apnea. One of the potential mechanisms accounting for the increased prevalence of enuresis in sleep apnea may be related to the release of both atrial and brain natriuretic peptides from cardiac myocytes after cardiac wall distension, as induced by the increased negative intrathoracic pressure following inspiratory efforts¹⁰. On the basis of these findings, it is suggested that NE could be used as a predictor of sleep-disordered breathing¹¹ and obstructive sleep apnea may be a new therapeutic target for NE.

In publishing literature, several researchers reported that therapy-resistant children with NE displayed higher periodic limb movements in sleep and sleep fragmentation than the controls¹²⁻¹⁴. They found that the periodic limb movement index and total arousal index were increased in children with NE, without a significant association with the other enuretic parameters, and suggested a hypothesis that it could refer to an autonomic imbalance as an independent pacemaker, with a possible key role for dopaminergic neurotransmission^{13,14}. However, other studies using polysomnography revealed that the sleep architecture did not significantly differ between NE children and normal controls and between wet and dry nights in a NE individual and nocturnal enuresis occurred with almost the same frequency in all sleep stages^{15,16}. It seems that further studies are needed to determine the potential factors influencing not

only awakening threshold but also sleep architecture.

According to a nationwide epidemiological study of NE in Korean adolescents and adults, the incidence of NE was especially high in the adolescent and adult population with chronic insomnia and it could be a result of NE¹⁷⁾. Existing evidence suggests that sleep disturbances at night are associated with both emotional and behavioral difficulties in daytime and evoke cognitive impairment and learning disabilities¹⁸⁻²⁰⁾.

This study showed that children with NE have a higher prevalence of daytime sleepiness. The daytime sleepiness could be induced by NE disturbing the sleep or result from a combination of abnormal sleep structure and nocturnal enuresis²¹⁾. The majority of children with NE tend to have poor sleep quality and quantity because they awake to urinate at night by themselves or are awoken by their parents⁴⁾. While adults with sleep disturbance complain of sleepiness, children with sleep disturbances could show attention deficit or hyperactivity during the day. In our study, children with NE had a higher prevalence of hyperactivity, such as fidgetiness or difficulty to stay seated, than controls. Although it is hard to conclude this phenomenon is due to sleep disturbance resulting from NE, the clinicians have to consider this possibility and, in severe cases, consider further evaluation including psychological assessment.

Children with NE could be assailed by emotional instability or discouragement and tend to have a sad mood or low self-esteem. Bedwetting may harm the child's relationships with family or friends and could negatively affect social development. Moreover, psychosocial problems could be intensified if daytime sleepiness or declining activity is combined with NE due to sleep disturbance^{9,22)}. In general, physicians and parents of NE children tend to focus on the symptom of NE and insufficiently consider sleep disturbances or problems associated with it²³⁾.

NE is a multifactorial condition with different contributing factors; so careful evaluation and management are required to determine specific urological issues such as nocturnal polyuria or overactive bladder, psychosocial, and sleep-related problems. Therefore, it is important to be fully aware of NE-related sleep disturbance or daytime problems as well as NE itself.

NE has a high rate of spontaneous resolution. However, active intervention for NE is recommended to patients at

emotional or psychosocial risk, especially adolescents. If sleep-related problems or therapy resistance are indicated, a multidisciplinary setting should be considered for diagnosis and treatment. For example, the patients with periodic limb movement disorder need further evaluations for restless legs syndrome and medical treatment, such as dopamine agonist or iron supplementation. And surgical treatment is helpful for the children with moderate to severe obstructive sleep apnea syndrome.

One limitation of this study is the relatively small sample size. The other limitation, which should be considered, is that this is a questionnaire-based study, wherein the questionnaire is a subjective tool, without polysomnography or physical activity monitoring system. In addition, we used the questionnaire where the items were selected and organized from international sleep associated questionnaires by the authors and then translated into the local language. An internationally authorized sleep questionnaire for Korean children needs to be developed.

Conclusively, the present study is the first study on the prevalence of NE combined with sleep-related problems in Korean children. Further studies are needed to clarify whether sleep related problems are improved following treatment of NE.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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<Appendix>

수면 습관 설문지

1. 기본 조사					
1) 잠이 드는데 어떤 문제가 있다	<input type="checkbox"/> 예	<input type="checkbox"/> 아니오	<input type="checkbox"/> 모름		
2) 낮 동안 졸려하거나 아침에 일어나기 어렵다	<input type="checkbox"/> 예	<input type="checkbox"/> 아니오	<input type="checkbox"/> 모름		
3) 밤에 깨거나 비정상적인 행동을 보인다	<input type="checkbox"/> 예	<input type="checkbox"/> 아니오	<input type="checkbox"/> 모름		
4) 규칙적으로 충분히 잠을 잔다	<input type="checkbox"/> 예	<input type="checkbox"/> 아니오	<input type="checkbox"/> 모름		
5) 밤에 코골이나 다른 수면 장애가 있다	<input type="checkbox"/> 예	<input type="checkbox"/> 아니오	<input type="checkbox"/> 모름		
2. 수면 스케줄					
1. 잠자리에 누워서 잠들기 까지 걸리는 시간 : 분					
평일	1) 잠자리에 드는 시각 : 시 분				
	2) 아침에 일어나는 시각 : 시 분				
	3) 총 수면 시간 (밤잠, 낮잠 포함) : 시간 분				
주말	1) 잠자리에 드는 시각 : 시 분				
	2) 아침에 일어나는 시각 : 시 분				
	3) 총 수면 시간 (밤잠, 낮잠 포함) : 시간 분				
3. 수면 장소					
주로 잠드는 곳	밤 시간 동안 주로 자는 곳		아침에 주로 일어나는 곳		
<input type="checkbox"/> 자기 방, 자기 침대 (혼자)	<input type="checkbox"/> 자기 방, 자기 침대 (혼자)		<input type="checkbox"/> 자기 방, 자기 침대 (혼자)		
<input type="checkbox"/> 부모방에 있는 부모 침대	<input type="checkbox"/> 부모방에 있는 부모 침대		<input type="checkbox"/> 부모방에 있는 부모 침대		
<input type="checkbox"/> 형제방에 자기 침대	<input type="checkbox"/> 형제방에 자기 침대		<input type="checkbox"/> 형제방에 자기 침대		
<input type="checkbox"/> 형제방에 같이 쓰는 침대	<input type="checkbox"/> 형제방에 같이 쓰는 침대		<input type="checkbox"/> 형제방에 같이 쓰는 침대		
<input type="checkbox"/> 기타	<input type="checkbox"/> 기타		<input type="checkbox"/> 기타		
	없음	거의 없음 (0-1일/주)	가끔 (2-4일/주)	자주 (5일이상/주)	모름
4. 입면 습관 및 불면증상					
1) 잠자는 시간이 일정하지 않다	0	1	2	3	4
2) 자신의 방 또는 침대에서 안 자려고 한다	0	1	2	3	4
3) 잠이 드는데 30분 이상 걸린다	0	1	2	3	4
4) 잠이 들고 난 뒤 두 번 이상 깬다	0	1	2	3	4
5. 수면 중 행동					
1) 잠꼬대를 한다	0	1	2	3	4
2) 자면서 걸어 다닌다	0	1	2	3	4
3) 자면서 이를 간다	0	1	2	3	4
4) 다리를 찬다	0	1	2	3	4
5) 다리를 주기적으로 움찔거린다	0	1	2	3	4
6. 수면 중 호흡장애					
1) 코를 시끄럽게 곤다	0	1	2	3	4
2) 숨을 멈추는 적이 있거나 헐떡거린다	0	1	2	3	4
3) 입을 벌리고 자거나 입으로 숨을 쉰다	0	1	2	3	4
7. 낮 동안 졸음정도 및 행동 양상					
1) 아침에 상쾌하게 일어나지 못한다 (피곤해한다)	0	1	2	3	4
2) 아침에 아이를 깨우기가 힘들다	0	1	2	3	4
3) 수업 시간 중 졸거나 잔다	0	1	2	3	4
4) 낮 시간 동안 피곤하여 신경이 예민해진다	0	1	2	3	4
5) 직접 얘기를 해도 말을 안 듣는 것처럼 보인다	0	1	2	3	4
6) 과제와 활동을 적절히 수행하는데 어려움이 있다	0	1	2	3	4
7) 외부의 자극에 쉽게 산만해진다	0	1	2	3	4
8) 자리에 앉아서 손이나 발을 가만히 못 둔다	0	1	2	3	4
9) 늘 걸터다니고 종종 바퀴가 달린 듯 돌아다닌다	0	1	2	3	4
10) 대화를 방해하거나 갑자기 끼여든다	0	1	2	3	4