

Utility of Voiding Dysfunction Symptom Score in Diagnosis and Treatment of Enuresis Nocturna

Enürezis Nokturnanın Tanı ve Tedavisinde İşeme Bozuklukları Semptom Skorunun Etkinliği

Yılören Tanıdır, Çağrı Akın Şekerci, Tuncay Top, Farhad Talibzade, Ahmet Şahan, Tarık Emre Şener, Tufan Tarcan, Ferruh Şimşek, Cem Akbal

Marmara University Faculty of Medicine, Department of Urology, İstanbul, Türkiye

What's known on the subject? and What does the study add?

Urotherapy, alarm therapy and medications are options to treat monosymptomatic enuresis nocturna. However, there is no specific tool to identify which children might benefit from each individual treatment. Voiding dysfunction symptom score (VDSS) can identify monosymptomatic and non-monosymptomatic enuresis nocturna, where specific individual treatments like anticholinergics can be offered. Interestingly, current study also elucidate another role for VDSS in differentiating treatment success in monosymptomatic enuresis nocturna.

Abstract

Objective: The aim of this study was to determine the effectiveness of the voiding dysfunction symptom score (VDSS) in evaluation of children with nocturnal enuresis.

Materials and Methods: Four hundred children with nocturnal enuresis were included in the study. They were evaluated with VDSS, physical examination, urinalysis and 2-day voiding diary. All children with nocturnal enuresis symptoms were treated with desmopressin and/or urotherapy. However, children with overactive bladder symptoms were also treated with anticholinergics. Treatment success and change in VDSS were compared and assessed between different treatment methods.

Results: Two hundred forty-five children (61.25%) were male and 155 (38.75%) were female. The mean age was 7.6 ± 3.0 years (range: 5-18). The mean VDSS was 9.2 ± 6.3 . 35% of children with nocturnal enuresis had concomitant daytime symptoms. 126 children (31.5%) had a VDSS of nine or above and majority of these children were treated with anticholinergic therapy. VDSS questionnaire could not help determine treatment success in children with non-monosymptomatic nocturnal enuresis. However, children treated with urotherapy and desmopressine showed significant difference in VDSSs according to their treatment response.

Conclusion: VDSS has shown to decrease after treatment in children with mono-symptomatic nocturnal enuresis. The treatment strategies should be checked and modified if VDSS does not decrease after proper therapy as this would increase the success of treatment.

Keywords: Symptom score, voiding dysfunction, urotherapy, enuresis nocturna, desmopressin

Öz

Amaç: Enürezis nokturnası olan çocukların değerlendirilmesinde işeme bozuklukları semptom skorunun (İBSS) etkinliğinin araştırılmasıdır.

Gereç ve Yöntem: Enürezis nokturna nedeniyle başvuran 400 çocuk çalışmaya dahil edildi. Çocukların hepsi fizik inceleme, İBSS, idrar analizi ve işeme günlüğü ile değerlendirildi. İnceleme sonrası enürezis nokturnası olan çocuklar üroterapi ve/veya desmopressin ile tedavi edilirken eşlik eden aşırı aktif mesanesi olanlar ise antikolinerjikler ile tedavi edildi. Uygulanan tedavilerin başarısı ve İBSS değerleri arasındaki ilişki karşılaştırıldı.

Bulgular: Çalışmaya katılan çocukların iki yüz kırk beşi erkek (%61,25), yüz elli beşi kız (%28,75) ve ortalama yaşları $7,6 \pm 3,0$ (aralık: 5-18) olarak saptandı. Ortalama İBSS skoru $9,2 \pm 6,3$ olarak saptandı. Çocukların %35'inde enürezis nokturnaya eşlik eden gündüz semptomları vardı. İBSS değeri dokuz ve üzeri olan yüz yirmi altı çocuk (%31,5) antikolinerjik ilaçlar ile tedavi edildi. İBSS monosemptomatik olmayan enürezis nokturnası olan çocuklarda tedavi başarısının ayırt edilmesinde anlamlı bir fark göstermedi. Ancak üroterapi ve desmopressin ile tedavi edilen çocuklarda tedavi yanıtına göre İBSS değerlerinde anlamlı fark saptandı.

Sonuç: Çalışmamızda monosemptomatik enürezis nokturnası olan çocukların tedavi sonrası İBSS değerinin düştüğü gösterildi. Uygun tedavi sonrası İBSS değerinde düzelme olmayan çocukların tedavisinin gözden geçirilmesi tedavi başarısını artırabilir.

Anahtar Kelimeler: Semptom skoru, işeme bozukluğu, üroterapi, enürezis nokturna, desmopressin

Correspondence: Cem Akbal MD, Marmara University Faculty of Medicine, Department of Urology, İstanbul, Türkiye

Phone: +90 532 341 07 79 **E-mail:** cakbal@gmail.com

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Introduction

Lower urinary tract symptoms constitute one of the major health issues encountered in childhood, and account for 20% of cases presenting to pediatric urology outpatient clinics (1). The rate of children who have completed toilet training by ages 2, 2.5 and 3 years are 25%, 85% and 98%, respectively (2). Voiding dysfunction occurs when a neurologically normal child exhibits abnormal bladder emptying due to mislearned toileting habits during toilet training. This occurs due to overactivity or inadequate relaxation of the pelvic floor muscles, which are striated muscles and are under voluntary control.

Enuresis nocturna is defined as nocturnal incontinence in neurologically normal children at appropriate age to remain dry (3). Fifteen percent of children with nocturnal enuresis have daytime symptoms (4); combined (day and night) wetting has been reported in 3.3% of 7-year-olds (5) and in 4% of children aged 5-12 years (6). Enuresis nocturna is the second most frequently encountered chronic problem in childhood (7). This condition reportedly occurs in 15%, 10% and 5% of pediatric patients aged 5, 7 and 10 years, respectively, and spontaneous remission generally takes place around 15 years of age (8).

Apart from the psychological effects on children and their parents, inability to gain voiding control by required ages (i.e. day care or school age) and/or the persistence of pathological voiding habits causes frequent recurrent urinary tract infections (UTIs) (3). The voiding dysfunction symptom score (VDSS) is a validated, non-invasive method for assessing children who present with nocturnal enuresis (9). The aim of this study was to evaluate this diagnostic tool in two ways: (1) as a method of detecting lower urinary tract dysfunction (LUTD) in patients with nocturnal enuresis; and (2) as a means of guiding therapy and improving treatment outcomes.

Materials and Methods

A total of 400 children aged between 5 and 18 years, who presented with the complaint of nocturnal bed-wetting between November 2012 and January 2015, were included in the study. Data from the patient medical records were evaluated retrospectively. A standard evaluation included detailed urological history regarding the status of voiding habits, daytime and nocturnal symptoms, urinary incontinence, holding maneuvers, constipation and medications taken, a 2-day voiding diary, urinalysis results, and validated VDSS questionnaire (see details below) (9). Patients with recurrent UTI, vesicoureteral reflux, neurogenic bladder and dysfunctional voiding that require biofeedback and/or α -blocker therapy were excluded from the study.

Patients with monosymptomatic nocturnal bed-wetting received urotherapy as a first-line treatment. Urotherapy involves motivation of the children and families with educational materials, self assessment with voiding diary, restriction of fluid intake, the last void before sleep, and waking for night time void. Children refractive to urotherapy either received desmopressin and/or enuretic alarm therapy. Children with concomitant daytime symptoms due to overactive bladder (OAB) also received oxybutynin as a first-line treatment.

Diagnosis and Treatment of Overactive Bladder: Patients who met the following three criteria were classified as suffering from OAB and were selected as the study group: (1) sudden, imperative urinary urgency with or without urge incontinence; (2) need for holding maneuvers; (3) a minimum of seven small-volume urinations per day. Findings supporting the diagnosis of OAB were normal or low bladder capacity and a post-void residual urine volume of <20 mL (10). Each patient completed a 2-day bladder diary with entries as per the International Children's Continence Society recommendations (10). Patients with OAB were treated with oxybutynin (0.1-0.3 mg/kg) for minimum 6 months.

Definition of Treatment Success: Treatment success is defined as absolute dryness throughout the night time within a consecutive 3-month period.

Voiding Dysfunction Symptom Score: The VDSS questionnaire, which was validated by Akbal et al. (9) in 2005, generates scores between 0 and 35. The instrument consists of 13 questions that focus on daytime and nighttime symptoms, voiding and bowel habits, and quality of life

		No	Sometimes	1-2 times/day	3 or more times/day
<input type="radio"/>	1. Does your child have urinary incontinence (peeing while not on the toilet) during the day?	0	1	3	5
<input type="radio"/>	2. If Yes to Question 2	A few drops	Only underwear wet	Outer clothing layers wet	
<input type="radio"/>	3. Does your child have urinary incontinence (peeing while not on the toilet) during the night?	No	1-2 nights/week	3-5 nights/week	6-7 nights/week
<input type="radio"/>	4. If Yes to Question 4	Underwear or pajamas wet		Bed wet	
<input type="radio"/>	5. My child goes to toilet to pee ...	Less than 7 times/day		7 or more times/day	
<input type="radio"/>	6. My child has to strain to pee.	No		Yes	
<input type="radio"/>	7. My child experiences pain when s/he pees.	No		Yes	
<input type="radio"/>	8. My child pees in/term itently when on the toilet.	No		Yes	
<input type="radio"/>	9. My child has to go to revisit the toilet to pee soon after s/he pees.	No		Yes	
<input type="radio"/>	10. My child has to run to the toilet when s/he feels the need to pee.	No		Yes	
<input type="radio"/>	11. My child can hold his/her pee by crossing his/her legs, squatting, or doing the "pee dance."	No		Yes	
<input type="radio"/>	12. My child wets his/her clothes before reaching the toilet.	No		Yes	
<input type="radio"/>	13. My child does not pass stool every day.	No		Yes	
QUALITY OF LIFE					
If your child experiences any of the symptoms/issues mentioned above, does this affect his/her family life or social life?					
		Not at all	Sometimes	Seriously affects	
		0	1	5	

Figure 1. Voiding dysfunction symptom score (9)

(Figure 1). Specifically, questions 1 and 2 inquire about daytime incontinence and questions 3 and 4 about nocturnal enuresis. Four questions (5, 10, 11, and 12) gather data on filling-phase symptoms and five questions (6-9 and 13) gather data on voiding symptoms. Question 14 is about quality of life (9). According to the research by Akbal et al. (9), scores above 8.5 have 90% sensitivity and specificity for detecting voiding dysfunction, and results are unaffected by gender differences. This instrument has been widely used for clinical assessment of LUTD and has also been applied in research studies (11,12). Similar tools have also been reported to be used to assess children with lower urinary tract symptoms (13). The VDSS was administered to each child and to his/her parents at initial clinical evaluation in pre-treatment period and repeated thereafter in post-treatment period. Pre- and post-treatment VDSS were compared for determining treatment success and failure.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) Software v. 20.0 (SPSS Inc, Chicago, IL). The variables were examined for the normality of their distribution using the Kolmogorov-Smirnov and Shapiro-Wilk tests. The student's t-test and chi-squared (Fisher's exact test) test were used to assess statistical significance for continuous and categorical variables, respectively. Mean and standard deviation were used to describe continuous variables, frequency, and percentages to depict categorical data. Paired sample t-test was used to assess differences between pre- and post-treatment VDSS of children. Independent sample t-test and paired sample t-test were used to assess the difference in VDSSs between and within the treatment success and failure groups in pre- and post-treatment periods, respectively. An alpha level of 0.05 was defined as statistically significant for all the tests.

Results

Of the 400 children, 245 (61.3%) were boys and 155 (38.8%) were girls. The mean age was 7.6 ± 3.0 years (range: 5-18). The mean VDSS was 9.2 ± 6.3 (range: 2-26). 260 patients (65%) had monosymptomatic enuresis, while 140 (35%) had daytime symptoms. The mean follow-up period was 9 months (range: 3-12 months).

One hundred and twenty-six children (31.5%) were found to have a VDSS of nine and above, which suggested a problem of voiding dysfunction. Of these 126 children, 69 (54.8%) showed symptomatic improvement after appropriate treatment with oxybutynin alone (n=33), desmopressine alone (n=18), urotherapy alone (n=12) and a combination of these three (n=6) (Table 1).

Two hundred and seventy four children (68.5%) were found to have a VDSS of eight and below. None of these children were treated with oxybutynin. Of these 270 children, 173 (63.1%) showed symptomatic improvement after appropriate treatment with desmopressine alone (n=76), urotherapy alone (n=82) and a combination of these two (n=15) (Table 2).

Detailed Analysis of VDSS Results: Of all questions, these three were most frequently answered as "Yes"; "My child goes to toilet to pee less than 7 times/day" (n=100), "My child wets his/her clothes before reaching the toilet" (n=118), "My child has to run to the toilet when she/he feels the need to pee" (n=174). The mean score of patients responsive to treatment (n=69) and refractive to treatment (n=57) were found to be 15.8 ± 6.44 and 17.83 ± 6.7 , respectively ($p=0.8$). Among all patients treated with desmopressine, the mean score of children responsive to treatment and refractive to treatment were found to be 3.4 ± 3.2 and 8.2 ± 2.5 , respectively ($p=0.001$). VDSS questionnaire could not help us in determining treatment success in children with non-monosymptomatic nocturnal enuresis. However, children treated with urotherapy and desmopressine showed significant difference in VDSS according to their treatment response.

Table 1. Children with voiding dysfunction symptom score 9 and above

Treatment success	Oxybutynin n, (%)	Desmopressine n, (%)	Urotherapy n, (%)	Combination n, (%)	Total n, (%)
Yes	33 (26.2)	18 (14.3)	12 (9.5)	6 (4.8)	69 (54.8)
No	14 (11.1)	11 (8.7)	30 (23.8)	2 (1.6)	57 (45.2)
Total	47 (37.3)	29 (23.0)	42 (33.3)	8 (6.3)	126 (100.0)

Table 2. Children with voiding dysfunction symptom score eight under

Treatment success	Desmopressine n, (%)	Urotherapy n, (%)	Combination n, (%)	Total n, (%)
Yes	76 (27.7)	82 (29.9)	15 (5.5)	173 (63.1)
No	17 (6.2)	71 (25.9)	13 (4.7)	101 (36.9)
Total	93 (33.9)	153 (55.8)	28 (10.2)	274 (100.0)

Results for treatment success relative to VDSS are summarized in Tables 3, 4.

Discussion

Enuresis nocturna is predominant pathology in male patients (14,15). Present study involved a male predominant cohort (61% male vs. 39% female). 36% of patients had urgency, 28% had urge incontinence and 23% had frequency symptoms. Similarly, in the literature, there are studies showing that 17.8% of children with nocturnal euresis have urgency, incontinence and frequency (16). There are many studies on the behavioral therapy for nocturnal enuresis with different results. Sixty percent of children with nocturnal enuresis had complete remission with behavioral therapy in a follow-up of 3 years, also it has been suggested that behavioral therapy might be as successful as desmopressin and alarm therapy but patient compliance is mandatory (17). In another study of 23 patients where 83% of children had severe enuresis symptoms, 70% had reduction in symptoms and 22% had complete resolution with behavioral therapy (18). In their study including 74 patients, Mark and Frank (19) reported that 16 patients had complete resolution, 43 had improvement in symptoms and 15 had no change in symptoms with a 4-week behavioral therapy. In our study, 42 patients with a VDSS above 9 were treated with behavioral therapy only and 12 (28%) had improvement in symptoms. In 153 patients with a VDSS below 9 and treated with behavioral therapy, 82 (53%) had improvement in symptoms. Response to each treatment was defined as >50% reduction in symptoms based on VDSS results.

This difference between these 2 groups was due to the polysymptomatic nature of these children and was due to additional voiding symptoms. Desmopressin, chemically modified form of vasopressin, is one of the pharmacological treatment options for enuresis nocturna. Desmopressin is a more potent antidiuretic than vasopressin with no vasopressor effect. Its efficacy in enuresis nocturna is due to decrease in nocturnal urine output (20). In published studies, the success rate of desmopressin changes between 60% and 70% (21). The major problem with desmopressin use is the high recurrence rates after cessation of treatment (22). In a published study with 114 monosymptomatic children with nocturnal enuresis with a mean age 9.8 years, 21 (18%) patients had complete resolution and 29 (25%) had partial resolution of nocturnal symptoms (23). Lottmann et al. (24) reported that with a 1-week treatment with desmopressin, 77.8% of 744 children aged 5 years and older had positive results and 50% relapsed after cessation of treatment. In the current study, among 93 patients with a VDSS below 9, 76 (82%) had positive response to treatment. In patients with a VDSS above 9, 18 (62%) of 29 patients treated with desmopressin, 33 (70%) of 47 treated with oxybutynin had improvement in symptoms. These results can show us that treatment success with desmopressin is low in patients with voiding dysfunction diagnosed by VDSS questionnaire and that oxybutynin should be considered in such cases.

Study Limitations

Our study has some limitations. This is a retrospective study and there is not any data on long-term results.

Table 3. Treatment modalities according to voiding dysfunction symptom score 9

Treatment modality	Voiding dysfunction	Treatment success		p Significance
		Yes n, (%)	No n, (%)	
Desmopressine	≥9	18 (19.1)	11 (39.2)	0.0417
	<9	76 (80.9)	17 (60.7)	
Urotherapy	≥9	12 (12.7)	30 (29.7)	0.005
	<9	82 (87.2)	71 (70.2)	

Fisher's exact test

Table 4. Treatment success according to voiding dysfunction symptom score

Treatment	n	VDSS score (before treatment)	Standard deviation	VDSS score (after treatment)	Standard deviation	p
Desmopressine	122	9.23	3.09	2.96	3.72	0.001
Oxybutynin	47	14.27	5.78	5.54	3.23	0.003
Combination	36	14.41	4.18	3.58	3.08	0.223
Urotherapy	195	5.46	5.31	3.88	3.18	0.005
Total	400	8.87	3.87	3.41	3.89	0.001

Student t-test, VDSS: Voiding dysfunction symptom score

Conclusion

Concomitant voiding problems can be detected in children presenting with nocturnal enuresis by using VDSS questionnaire. Treatment strategies should be decided accordingly. The VDSS questionnaire is a useful non-invasive method in detecting voiding dysfunction and following the response to treatment. This study addresses the importance of diagnosis of the concomitant lower urinary tract symptoms in patients with nocturnal enuresis. However, further studies more thoroughly investigating the clinical use of VDSS are warranted.

Ethics

Ethics Committee Approval: Retrospective study, Informed Consent: Retrospective study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Çağrı Akın Şekerci, Cem Akbal, Ferruh Şimşek, Concept: Yılören Tanidir, Çağrı Akın Şekerci, Cem Akbal, Design: Yılören Tanidir, Çağrı Akın Şekerci, Cem Akbal, Data Collection or Processing: Çağrı Akın Şekerci, Tuncay Top, Farhad Talibzade, Ahmet Şahan, Tarık Emre Şener, Analysis or Interpretation: Yılören Tanidir, Ahmet Şahan, Literature Search: Yılören Tanidir, Çağrı Akın Şekerci, Tuncay Top, Farhad Talibzade, Ahmet Şahan, Tarık Emre Şener, Supervision: Cem Akbal, Tufan Tarcan, Ferruh Şimşek, Writing: Yılören Tanidir, Çağrı Akın Şekerci, Cem Akbal.

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References

1. Butler RJ, Heron J. The prevalence of infrequent bedwetting and nocturnal enuresis in childhood. A large British cohort. *Scand J Urol Nephrol* 2008;42:257-264.
2. Rushton HG. Wetting and functional voiding disorders. *Urol Clin North Am* 1995;22:75-93.
3. Harari MD, Moulden A. Nocturnal enuresis: what is happening? *J Paediatr Child Health* 2000;36:78-81.
4. Wojcik LJ, Kaplan GW. The wet child. *Urol Clin North Am* 1998;25:735-744.
5. Butler RJ, Golding J, Northstone K; ALSPAC Study Team. Nocturnal enuresis at 7.5 years old: prevalence and analysis of clinical signs. *BJU Int* 2005;96:404-410.
6. Bower WF, Moore KH, Shepherd RB, Adams RD. The epidemiology of childhood enuresis in Australia. *Br J Urol* 1996;78:602-606.
7. Lewandowska J, Sadowska L, Domanasiewicz M, Matheisel K, Marcinkowska W. Nocturnal enuresis in children with allergy. *Pol Tyg Lek* 1987;42:1474-1476.
8. Yeung CK, Sreedhar B, Sihoe JD, Sit FK, Lau J. Differences in characteristics of nocturnal enuresis between children and adolescents: a critical appraisal from a large epidemiological study. *BJU Int* 2006;97:1069-1073.
9. Akbal C, Genc Y, Burgu B, Ozden E, Tekgul S. Dysfunctional voiding and incontinence scoring system: quantitative evaluation of incontinence symptoms in pediatric population. *J Urol* 2005;173:969-973.
10. Neveus T, von Gontard A, Hoebeke P, Hjalmas K, Bauer S, Bower W, Jorgensen TM, Rittig S, Walle JV, Yeung CK, Djurhuus JC. The standardization of terminology of lower urinary tract function in children and adolescents: report from the Standardisation Committee of the International Children's Continence Society. *J Urol* 2006;176:314-324.
11. Yildirim A, Uluocak N, Atilgan D, Ozcetin M, Erdemir F, Boztepe O. Evaluation of lower urinary tract symptoms in children exposed to sexual abuse. *Urol J* 2011;8:38-42.
12. Schneider D, Yamamoto A, Barone JG. Evaluation of consistency between physician clinical impression and 3 validated survey instruments for measuring lower urinary tract symptoms in children. *J Urol* 2011;186:261-265.
13. Farhad W, Bagli DJ, Capolicchio G, O'Reilly S, Merguerian PA, Khoury A, McLorie GA. The dysfunctional voiding scoring system: quantitative standardization of dysfunctional voiding symptoms in children. *J Urol* 2000;164:1011-1015.
14. Lee T, Suh HJ, Lee HJ, Lee JE. Comparison of effects of treatment of primary nocturnal enuresis with oxybutynin plus desmopressin, desmopressin alone or imipramine alone: a randomized controlled clinical trial. *J Urol* 2005;174:1084-1087.
15. Kajiwara M, Inoue K, Kato M, Usui A, Kurihara M, Usui T. Nocturnal enuresis and overactive bladder in children: an epidemiological study. *Int J Urol* 2006;13:36-41.
16. Pennesi M, Pitter M, Bordugo A, Minisini S, Peratoner L. Behavioral therapy for primary nocturnal enuresis. *J Urol* 2004;171:408-410.
17. Robson WL, Leung AK. Re: behavioral therapy for primary nocturnal enuresis. *J Urol* 2004;172:1546-1547.
18. Elsayed ER, Abdalla MM, Eladl M, Gabr A, Siam AG, Abdelrahman HM. Predictors of severity and treatment response in children with monosymptomatic nocturnal enuresis receiving behavioral therapy. *J Pediatr Urol* 2012;8:29-34.
19. Mark SD, Frank JD. Nocturnal enuresis. *Br J Urol* 1995;75:427-434.
20. Hjalmas K, Arnold T, Bower W, Chiozza LM, von Gontard A, Han SW, Husman DA, Kawauchi A, Läckgren G, Lottmann H, Mark S, Rittig S, Robson L, Walle JV, Yeung CK. Nocturnal enuresis: an international evidence based management strategy. *J Urol* 2004;171:2545-2561.
21. Hjalmas K, Arnold T, Bower W, Caione P, Chiozza LM, von Gontard A, Han SW, Husman DA, Kawauchi A, Läckgren G, Lottmann H, Mark S, Rittig S, Robson L, Walle JV, Yeung CK. Clinical perspectives in primary nocturnal enuresis. *Clin Pediatr (Phila)* 1998;37:23-29.
22. Tauris LH, Andersen RF, Kamperis K, Hagstroem S, Rittig S. Reduced anti-diuretic response to desmopressin during wet nights in patients with monosymptomatic nocturnal enuresis. *J Pediatr Urol* 2012;8:285-290.
23. Kwak KW, Lee YS, Park KH, Baek M. Efficacy of desmopressin and enuresis alarm as first and second line treatment for primary monosymptomatic nocturnal enuresis: prospective randomized crossover study. *J Urol* 2010;184:2521-2526.
24. Lottmann H, Baydala L, Eggert P, Klein BM, Evans J, Norgaard JP. Long-term desmopressin response in primary nocturnal enuresis: open-label, multinational study. *Int J Clin Pract* 2009;63:35-45.