



## Enuresis: Is bedwetting really isolated or not?

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### ABSTRACT

It is aimed to evaluate the clinical and laboratory characteristics of children applied to nephrology outpatient clinic with the complaint of bedwetting. The records of all patients who applied to Pediatric Nephrology outpatient clinic with the complaint of bedwetting between January 2006 and June 2012 were evaluated retrospectively. A total of 364 patients, 207 male (56.9%) and 157 female (43.1%), aged between 5 to 17 years were enrolled in the study. Three hundred twenty-six patients (89.6%) had primary and 38 patients (10.4%) had secondary enuresis. Non-monosymptomatic enuresis was determined in 143 (39.3%) of the cases. The most common finding of 34 patients who underwent urodynamic study was low bladder capacity and overactive bladder. In conclusion, voiding disorders are frequently encountered but generally overlooked problems during childhood. By distinguishing monosymptomatic enuresis from non-monosymptomatic enuresis, it would be possible to determine bladder disorders earlier and give the appropriate treatment.

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### 1. Introduction

Nocturnal enuresis (NE), commonly called bedwetting, is involuntary urination during sleep after the age at five which bladder control usually occurs and it is one of the most prevalent problems of childhood. With the rising awareness that children with bedwetting differ regarding pathogenesis, treatment response and co-morbidity, diverse subgroups have been proposed (Watanabe and Azuma, 1989; Neveus et al., 2000; Aceto et al., 2003). NE is considered primary when a child has never had a dry period for at least 6 months whereas it is considered as secondary nocturnal enuresis (SNE) when child has experienced a dry spell of at least 6 months (Neveus et al., 2006; Özkaya, 2008). Monosymptomatic nocturnal enuresis (MNE) means that there are no daytime symptoms suggestive of the lower urinary tract (LUT) malfunction. Children with day time LUT symptoms are defined as having non-monosymptomatic enuresis (NMNE). Although NE is generally considered as benign, it can lead to emotional distress, self perception of and worry in affected children and their parents. In this study, we aimed to evaluate the demo-

graphic, clinical and laboratory findings of patients' applied to our pediatric nephrology department with the only complaint of bedwetting.

### 2. Materials and methods

All records of the patients who applied for the first time to Ondokuz Mayıs University (OMU) between January 2006 and June 2012 with only complaint of bedwetting were evaluated retrospectively and those aged between 5 and 17 were enrolled in the study. All children were evaluated with a complete medical history, comprehensive physical examination and were questioned about voiding habits. Three-day bladder diary about the frequency and volume of urine was obtained from patients. Etiological factors such as emotional stress, family history, and constipation were also investigated. Causes of emotional stress were investigated with conversations with the family and the patient one by one at outpatients' clinic. Family history of enuresis was questioned by physician for genetic susceptibility. Constipation was evaluated according to Rome III diagnostic criteria for functional gastrointestinal

disorders (Douglas and Drossman, 2006). We used Pediatric Lower Urinary Tract symptom score (PLUTSS) which is a questionnaire composed of items regarding daytime symptoms, nighttime symptoms, voiding habits, bowel habits and quality of life and had been previously described by Akbal et al. (2005). All patients' urinary calcium excretions were evaluated and calcium/creatinine ratios above 0.21 was considered as high and it was confirmed by 24 hours urine collection.

Videourodynamic work-up was performed if patients had complex incontinence complaints with poor response to voiding education which includes timed voiding and bladder training. Treatment failure to education was defined if PLUTSS score did not change or still it's greater than 9. All the urodynamic studies were performed and interpreted with MMS solar urodynamic device in OMU Urology Department. After performing uroflowmetry, cystometry was done. These procedures were carried out in a specific room for videourodynamic investigations in urology department. Peeing time, maximum peeing time, flow time, maximum flow rate, mean flow rate and volume of urine were evaluated. After all procedures were ended, residual urine amount was measured with ultrasonography.

The ambience during cystometry procedures was tried to be as possible as stress free, the child lying and one of the parents standing by his side. No sedation was given. Cystometry was performed with double lumen 8F and 6F cystometry catheters (TDOC, Utah/USA). Rectal balloon catheter (Stericom Ltd-UK) was placed for abdominal pressure measurements. Before the procedure, the device was calibrated and bladder was emptied with a catheter. Symphysis pubis level was assumed as zero point for calibration. Transducers were connected to cystometry catheter and rectal catheter after calibration. The bladder was filled retrogradly with sterile 0.9% NaCl at room temperature. The rate of the perfusion pump was set as the 10% of bladder capacity per minute would release. Recording began synchronously with infusion and the system was checked by asking the patient to cough. The procedure was terminated when the child came urgency to pee.

Maximum bladder capacity, maximum bladder pressure, maximum abdominal pressure, maximum detrusor pressure and detrusor compliance were evaluated during cystometry. Detrusor compliance was calculated by dividing the volume change by pressure change. Maximum bladder capacity was compared with primary biliary cirrhosis (PBC) suggested by International Continence Society. Residual urine of 20ml or more was accepted as abnormal. PBC less than 65% defined as low bladder capacity and PBC more than 150% as high bladder capacity (Neveus et al., 2006).

### Statistical analysis

All computations were performed with SPSS software version 15.0 (SPSS Inc., Chicago, IL, USA). Values which followed non-normal distribution are expressed as median and comparisons were evaluated by the Mann-Whitney U-test. Categorical parameters were analyzed using the chi-square test. P value was considered significant if it was less than 0.05.

### 3. Results

Three hundred sixty four children with the median age of 9.4

(9.4±2.8) years were enrolled in the study. Of the patients, 56.9% were male (n: 207) and 43.1% were female (n: 157). None of the patients had pathological physical examination finding. 89.6% (n: 326) of 364 patients had primary nocturnal enuresis (PNE) and 10.4% (n: 38) had SNE. According to the history, of the 326 patients with PNE, 194 (59.5%) were classified as MNE and 132 (40.5%) as NMNE. Of the 38 patients with SNE, 27 (71.1%) were regarded as having MNE and 11 (28.9%) were as NMNE. When causes of emotional stress were evaluated, only 9 patients with SNE were observed to have emotional stress and the rest had none.

Family history was positive in 39.8% (n: 145) of all patients. 41.7% (n: 136) of the PNE and 23.7% (n: 9) of the SNE patients had a family history. Hypercalciuria was found in 8.2% (n: 30) of all patients. There was no statistically significant difference between MNE and NMNE groups regarding frequency of constipation, hypercalciuria and family history (p=0.21, p=0.844, p=0.276 respectively). Significant difference was found between patients with MNE and NMNE in terms of age and gender (p=0.001, p=0.004 respectively) (Table 1).

**Table 1. Demographic features of enuresis groups and comparison of variables**

Variables	MNE (n=221)	NMNE (n=143)	p value
Age (years)	10*(10±2.8)	8*(8.6±2.6)	0.001
Gender (M/F)	139/82	68/75	0.004
Family history	93 (42.1%)	52 (36.4%)	0.276
Hypercalciuria	18 (8.2%)	12 (8.4%)	0.844
Constipation	15 (6.8%)	15 (10.5%)	0.21

MNE; monosymptomatic nocturnal enuresis,  
NMNE; non monosymptomatic enuresis  
\*Age was expressed as median (mean±standard deviation)

The minimum PLUTSS score was 3 and the maximum was 33 (median: 11, mean: 12.6±5). When 34 patients with NMNE who did not respond to standard behavioral therapy (motivation, positive feedback, time voids, double voiding) and with a symptom score of 9-33 were evaluated with urodynamic work-up, 5 (14.7%) had found to have residual urine prior to urodynamic evaluation, 4 (11.8%) have low compliance, 22 (64.7%) have low bladder capacity, 16 (47.1%) have detrusor overactivity (DO) and 8 (23.5%) have normal urodynamic evaluation findings.

### 4. Discussion

PNE and SNE are considered to be separate entities with different pathogenesis. PNE is thought to be caused by reduced nocturnal bladder capacity, nocturnal polyuria, awakening problem or a combination of these factors (Hunsballe et al, 1995; Loening-Baucke, 1997; Wolfish et al., 1997; Lackgren et al., 1999; Kawauchi et al., 2002). Also genetic susceptibility, constipation and hypercalciuria have been attributed to the etiology of PNE whereas psychosocial factors, urinary tract infections, constipation, diabetes, neurogenic bladder are reported as causes of SNE (Pace et al., 1999; Robson and Leung, 2000; Sureshkumar et al., 2000; Raes et al., 2006). In our study, 9 of 27 patients with MNE had a cause for SNE.

Bedwetting is frequently associated with a family history (Chiozza et al., 1998; Kanaheswari, 2003). A previous study from Turkey reported that 32.1 % of children with nocturnal

enuresis had a positive family history (Gunes et al., 2009). In our study, positive family history for enuresis was 39.8% and significant difference was not found for the frequency of family history between patients with MNE and NMNE ( $p=0.276$ ).

Several studies have suggested that hypercalciuria might be responsible for enuresis in some patients. Kamperis et al. (2006) reported that hypercalciuria was equally distributed among MNE, NMNE and healthy children, indicating that hypercalciuria did not play a significant role in enuresis. In our study hypercalciuria was detected in 8.2% of cases. Since there was not a healthy control group in this study, we could not compare hypercalciuria frequency statistically, but in a study from Turkey, the idiopathic hypercalciuria frequency was reported as 12.5% in healthy children between ages of 7-14 (Koyun et al., 2007).

There is evidence that children with enuresis who have concomitant symptoms of LUT malfunction such as increased/decreased frequency, daytime incontinence, urgency, hesitancy, straining, weak stream, intermittency, holding maneuvers, feeling of incomplete emptying, post-micturition dribble and genital and LUT pain differ clinically, therapeutically and pathogenetically from children without such symptoms and those children are accepted as having NMNE (Butler and Holland, 2000; Nevés et al., 2006). Therefore, a comprehensive history and physical examination are very important in assessing a child with bedwetting problem. The detailed history, physical examination and bladder diary will easily differentiate primary from secondary enuresis, MNE from NMNE. Although all the children enrolled in our study were brought by their parents or referred us because of bedwetting, only 221 (60.7%) were diagnosed as MNE. Rest of these children had LUT malfunction symptoms and diagnosed as having NMNE. Furthermore, all of these patients had been treated as MNE and referred to us because of unresponsiveness to the treatment and 143 (39.3%) patients' parents were not aware of their child's daytime symptoms.

When we compared the patients with MNE and NMNE, we did not find statistically significant difference in terms of family history, hypercalciuria and constipation. However, significant difference in terms of age and gender was found between patients with MNE and NMNE. In MNE group ages were statistically higher than NMNE group ( $p=0.004$ ). This may be due to the underestimation of MNE by the parents

because of lack of daytime symptoms.

Misculin et al. (2010) reported that MNE is more frequent in boys than girls at the age of 6 to 7. In a cohort analysis, Butler et al. (2006) reported that MNE/NMNE ratios were 2:1 and there was no significant difference in terms of gender between MNE and NMNE patients. In present study, whereas MNE was found more frequently in boys than girls, girls' predominance was observed in NMNE group.

Identification of urological causes such as diurnal storage dysfunction, or diurnal voiding dysfunction in patients with NMNE is of paramount importance. In the majority of cases, examination with non-invasive tools (urinalysis, questionnaires, uroflowmetry and post-voiding residual urine assessment) will lead to diagnosis of LUT dysfunction.

However, findings in some children may be unclear to make diagnosis and an urodynamic evaluation may be required. The PLUTSS symptom score used in this study was reported to have 90% sensitivity and specificity (Akbal et al., 2005). In our clinical practice, the use of this symptom scoring as a first line diagnostic tool has assisted us to separate pathological voiding abnormalities and has significantly decreased the need for urodynamic studies. Naseri and Hradfar (2012) reported that there were abnormal urodynamic findings in 37% of patients with MNE and the most frequent findings were DO and low bladder capacity (63% and 80% respectively). In a study by Seghal et al. (2007), 116 cases with enuresis were evaluated and uninhibited contraction in 43.1%, low bladder capacity in 17.2% was determined. In this study, urodynamic evaluation was performed only in the patients with NMNE who had PLUTSS score  $\geq 9$ . DO and low bladder capacity were the leading findings in our study with a frequency of 47.1% (n:16) and 64.7% (n:22) respectively.

In conclusion, despite the fact that only patients with the complaint of bedwetting were enrolled in this study, with a careful questioning, physical examination and using PLUTSS, 40.5% of the patients were found to be NMNE. It may be said that enuresis is not an isolated bed wetting. It is therefore important to take thorough history and perform a complete physical examination to make the distinction between MNE and NMNE in order to choose the right therapy options.

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