IS ROUTINE URINARY TRACT INVESTIGATION NECESSARY FOR CHILDREN WITH MONOSYMPTOMATIC PRIMARY NOCTURNAL ENURESIS?

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ABSTRACT

Objectives. To investigate in a prospective study the role of bladder function and to compare the results of urinary tract ultrasonography and urinalysis in children with and without primary nocturnal enuresis because, although this is a common problem in children, the etiology and mechanisms of the disorder have not been elucidated.

Methods. The study included 106 children with monosymptomatic primary nocturnal enuresis and a control group of 57 children with no history of voiding dysfunction, aged 5 to 19 years. All children underwent urinalysis, bladder and upper urinary tract ultrasonography, and uroflowmetry. The bladder capacity, bladder wall thickness, and postvoid residual volume were measured using ultrasonography. The findings were compared between the enuresis and control groups according to age: 5 to 9 years, 10 to 14 years, and 15 to 19 years.

Results. The mean age was 9.6 ± 3.1 years in the nocturnal enuresis group and 9.4 ± 3.3 years in the control group ($P = 0.727$). The mean number of defecations per week was significantly lower statistically in the enuresis group than in the control group in the age categories of 5 to 9 years and 10 to 14 years ($P = 0.038$ and $P = 0.018$, respectively), and the mean number of urinations per day was significantly higher statistically in the enuresis group than in the control group in the age groups of 5 to 9 years and 10 to 14 years ($P = 0.002$ and $P = 0.001$, respectively). The bladder capacity, bladder wall thickness, postvoid residual volume, uroflowmetry maximal flow rate, and average flow rate were not significantly different statistically between the children with primary nocturnal enuresis and the control group in the three age brackets. Urinary infection was detected in 2 children (1.88%) in the nocturnal enuresis group and none of the children in the control group ($P = 0.547$). Upper urinary tract abnormalities detected by ultrasonography were seen in 3 children (2.83%) in the nocturnal enuresis group and 1 child (1.75%) in the control group, revealing no statistical significance ($P = 0.671$).

Conclusions. Our findings show that the ultrasonographic and uroflowmetry findings on bladder function and the upper urinary system and the incidence of urinary infection are similar in children with and without nocturnal enuresis. Obtaining a voiding and elimination diary in conjunction with a good history may be beneficial in children with monosymptomatic primary nocturnal enuresis. In addition, routine urinalysis may be unnecessary in the evaluation of children with monosymptomatic primary nocturnal enuresis after obtaining a careful and complete history of the voiding dysfunction. UROLOGY **58:** 598–602, 2001. © 2001, Elsevier Science Inc.

Although monosymptomatic primary nocturnal enuresis is a common problem in children, the etiology and mechanisms of this disorder have not been elucidated, despite more than 20 years of clinical research.[1] The incidence of primary nocturnal enuresis is 20% in children 5 years old, 11.5% in children 7 to 12 years old, and 1% in adolescents.[2,3]

One of the current treatments of nocturnal enuresis in children has been to increase the functional bladder capacity.[4,5] The bladder capacity has also been shown to be a predictor of the response to medical treatment of nocturnal enuresis.[6–8]

The rate of urinary infection increases by varying

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degrees in children with voiding dysfunction. Urinary tract abnormalities detected by ultrasonography are reported in 3% of children with voiding dysfunction.[9]

In published studies, the bladder capacity, incidence of urinary infection, or findings of urodynamic studies have been included in reports of children with nocturnal enuresis. However, no study has compared all the variables, such as the number of defecations, number of urinations, bladder capacity, bladder wall thickness, postvoid residual volume, uroflowmetry findings, and urinalysis results, in the same population between children with nocturnal enuresis and children with no voiding dysfunction. Should routine urinary tract investigation comprise renal and bladder ultrasonography, urinalysis, and uroflowmetry in children with monosymptomatic primary nocturnal enuresis? The aim of this prospective study was to investigate the role of bladder function in children with primary nocturnal enuresis. We also compared the results of urinary tract ultrasonography and urinalysis in children with and without primary nocturnal enuresis.

MATERIAL AND METHODS

This prospective study was conducted between May 1999 and February 2001. This study included only children with monosymptomatic primary nocturnal enuresis. One hundred thirty-one children were evaluated for their voiding dysfunction in our pediatric urology clinic. Sixteen children (12.2%) with secondary nocturnal enuresis were excluded from the study. Nine children (6.9%) with neurologic or physical abnormalities were also excluded from the study. Thus, the study included 106 children with monosymptomatic primary nocturnal enuresis and 57 children with no history of voiding dysfunction, as a control group, aged 5 to 19 years. Children were divided into three groups according to their age: 5 to 9 years (enuretic 48, control 21), 10 to 14 years (enuretic 40, control 26), and 15 to 19 years (enuretic 18, control 10).

The University of Mersin and the local governmental ethics committee approved the protocol. Informed consent was obtained from all children and their parents. All children were evaluated with a complete medical history and physical examination, and all underwent urinalysis, bladder ultrasonography, and uroflowmetry. Primary nocturnal enuresis was defined as bedwetting two or more times per week. Ultrasound examinations were performed to evaluate bladder capacity, bladder wall thickness, and postvoid residual volume of the bladder and the abnormalities of the upper urinary tract, using a 3.5-mHz curved array and 5 to 7.5-mHz linear array transducers of a Siemens system (Siemens Sonoline Versa Plus). The bladder capacity was calculated when the children had a sensation of fullness. At that time, the bladder wall thickness was also detected using the anterior bladder wall. After urination, the residual bladder volume was measured. The bladder capacity was also confirmed by calculating the total urinated volume plus the postvoid residual volume, as determined ultrasonographically. The largest volume calculated for each person was considered their bladder capacity. Any abnormalities of the upper urinary tract detected by ultrasonography were recorded.

The uroflowmetry study was performed using an apparatus of Life-Tech urodynamic equipment (Janus 4, Life-Tech, Houston, Tex). Urinalysis was performed using microscopic examination of the urinary sediment for leukocytes and red blood cells. If the microscopic examination of the urinary sediment was positive for leukocytes, urine culture was performed to confirm urinary infection.

The findings were compared between the enuresis and control groups for each age category (5 to 9, 10 to 14, and 15 to 19 years). All statistical analyses were performed using a commercially available statistical program (Statistical Package for the Social Sciences, version 9.0). The chi-square test was used to compare two proportions for the incidence of upper urogenital tract abnormalities and the results of urinalysis. The independent *t* test was used to compare bladder capacity, bladder wall thickness, and postvoid residual volume in the same three age brackets. Probability values of less than 0.05 were considered statistically significant. The values are presented as the mean ± SD.

RESULTS

Of the 106 children with primary nocturnal enuresis, 55 were boys (51.9%) and 51 were girls (48.1%). The mean age of these children was 9.6 ± 3.1 years. Of the 57 in the control group without nocturnal enuresis, 30 were boys (52.6%) and 27 were girls (47.4%); the mean age was 9.4 ± 3.3 years. There was no significant difference between the boys and girls included in this study ($P = 0.903$ for boys, $P = 0.932$ for girls). The difference in the mean ages between the two groups was also not statistically significant ($P = 0.727$). The mean number of bed-wetting episodes per month in children with primary nocturnal enuresis was 25.3 ± 7.6 days (range 10 to 30). The mean height and weight of the children in the two groups in the three age brackets were not different. Table I shows the mean number of defecations per week, mean number of urinations per day, bladder capacity, bladder wall thickness, postvoid residual volume, uroflowmetry maximal flow rate, and average flow rate between the children with primary nocturnal enuresis and the control group. The mean number of defecations per week was significantly lower statistically in the enuresis group than in the control group in the age categories of 5 to 9 years and 10 to 14 years ($P = 0.038$ and $P = 0.018$, respectively), but the difference was not significant between the enuresis and control groups for those 15 to 19 years old ($P = 0.205$). The mean number of urinations per day was significantly higher statistically in the enuresis group than in the control group for those 5 to 9 years and 10 to 14 years old ($P = 0.002$ and $P = 0.001$, respectively); however, this difference was not significant between the enuresis and control groups for those 15 to 19 years old ($P = 0.158$).

Urinary infection was detected in 2 (1.88%) of the 106 children with primary nocturnal enuresis and none of the children in the control group; the

TABLE I. ***Mean number of defecations per week, mean number of urinations per day, bladder capacity, bladder wall thickness, postvoid residual volume, uroflowmetry maximal flow rate, and average flow rate between primary nocturnal enuresis and control groups***

Group	Defecations/wk (n)	Urinations/ day (n)	Bladder Capacity (mL)	Bladder Wall Thickness (mm)	Postvoid Residual Volume (mL)	Maximal Flow Rate (mL/s)	Average Flow Rate (mL/s)
5–9 years							
Enuresis (n = 48)	6.48 ± 1.3	7.38 ± 2.72	165.3 ± 87	2.51 ± 1.4	14.5 ± 20.5	21 ± 8	10.9 ± 4.4
Control (n = 21)	7.33 ± 1.87	5.23 ± 1.72	168.3 ± 75	2.31 ± 0.5	6.4 ± 9.9	22.4 ± 7.2	12.1 ± 4
P value	0.038	0.002	0.892	0.724	0.093	0.559	0.318
10–14 years							
Enuresis (n = 40)	6.62 ± 1	6.47 ± 2.54	287 ± 128	2.83 ± 0.72	31.6 ± 36.8	28.1 ± 6.9	13 ± 4
Control (n = 26)	7.65 ± 2.34	4.69 ± 1.19	308.1 ± 160.5	2.86 ± 0.58	23.7 ± 30.4	31.6 ± 12.5	15.7 ± 6.1
P value	0.018	0.001	0.565	0.797	0.364	0.29	0.102
15–19 years							
Enuresis (n = 18)	6.3 ± 3.2	6.5 ± 3	366.3 ± 197.5	2.91 ± 0.62	19.8 ± 26.4	25.6 ± 1.8	11.6 ± 7.3
Control (n = 10)	8.11 ± 3.67	5.11 ± 1.99	373.2 ± 194	2.82 ± 0.58	7.3 ± 10.1	29.6 ± 10	12.5 ± 4.3
P value	0.205	0.158	0.468	0.182	0.084	0.539	0.757

difference was not statistically significant (P = 0.547). Microscopic hematuria was seen in 1 (0.94%) of the 106 children in the enuresis group and none of the children in the control group; again, the difference was not statistically significant (P = 0.762).

Upper urinary tract abnormalities detected by ultrasonography were seen in 3 children (2.83%) in the nocturnal enuresis group and in 1 child (1.75%) in the control group. The difference in the incidence of urogenital tract abnormalities was not statistically significant (P = 0.671). These abnormalities included unilateral ureteropelvic junction obstruction (n = 2) and decreased echogenicity of the parenchyma (n = 1) in the enuresis group and decreased echogenicity of the parenchyma (n = 1) in the control group.

As shown in Table I, the differences in bladder capacity, bladder wall thickness, postvoid residual volume, uroflowmetry maximal flow rate, and average flow rate were not statistically significant between the children with primary nocturnal enuresis and the control group in the three age brackets. The bladder capacity was 165.3 ± 87 mL in the enuresis group and 168.3 ± 75 mL in the control group for children 5 to 9 years old (P = 0.892), 287 ± 128 mL and 308.1 ± 160.5 mL, respectively, for children 10 to 14 years old (P = 0.565), and 366.3 ± 197.5 mL and 373.2 ± 194 mL, respectively, for those 15 to 19 years old (P = 0.468).

COMMENT

Although the etiology and mechanisms of nocturnal enuresis have not been well elucidated, a possible cause of this disorder is a hereditary developmental delay in the maturation of the somatic mechanisms that cause a reduction in nocturnal urine production and a normal arousal to a full bladder.[10] Anal sphincteric dysfunction is also seen in children with developmental delay.[11] The dysfunctional elimination syndrome (which includes bladder instability, Hinman's syndrome, and constipation) has gained attention in recent reports discussing enuresis.[12] In our study, the mean number of defecations per week was significantly lower statistically in the enuresis group than in the control group for children 5 to 9 years and 10 to 14 years old. This significant difference in the number of defecations in these two groups may have been due to an element of dysfunctional elimination in some of the children with nocturnal enuresis. We also found a significantly higher mean number of urinations per day in the enuresis group than in the control group for children aged 5 to 9 and 10 to 14 years. However, this difference was not significant between the enuresis and control groups in those 15 to 19 years old. This significant difference in the number of urinations may have been because some enuretic children had smaller functional bladder capacities or because of an element of dysfunctional elimination syndrome in some of these children. Obtaining a voiding/elimination diary in conjunction with a good history and physical examination may be beneficial and represents the main approach in treating children with monosymptomatic primary nocturnal enuresis.

Different therapies and drugs have been proposed for the treatment of nocturnal enuresis. Although daytime functional bladder capacity correlates well with bladder capacity during sleep, opinions in published reports conflict as to whether enuretic children have a normal or reduced functional bladder capacity.

Hamano *et al.*,[6] Eller *et al.*,[7] and Rushton *et al.*[8] reported a lower bladder capacity in some children with nocturnal enuresis, and medical therapy of childhood nocturnal enuresis with desmopressin was less effective in children with a low functional bladder capacity than in children with a normal bladder capacity. Therefore, it was suggested that the daytime bladder capacity is a valuable predictor of the response to medical therapy. Kosar *et al.*[13] reported the effectiveness of oxybutynin hydrochloride in the treatment of nocturnal enuresis. They found that oxybutynin hydrochloride was a much more effective treatment in patients with inadequate bladder storage function than in the patients with normal bladder function. However, such studies did not specifically compare prospectively whether the bladder capacity differs between children with and without nocturnal enuresis. In our prospective controlled study, no significant difference was found in the bladder capacity between the children with nocturnal enuresis and the children without voiding dysfunction. If the bladder capacity had been low and the bladder wall thickness increased in children with nocturnal enuresis, the best response to medical therapy would be achieved with an anticholinergic drug such as oxybutynin.

Medel *et al.*[14] investigated the possible effect of desmopressin on the detrusor in patients with urodynamically confirmed bladder instability. They found that clinically undetected bladder instability was unrelated to the results of treatment, and no urodynamic changes were noted during desmopressin treatment. Weerasinghe and Malone[15] suggested that urodynamic investigations are required to identify the underlying cause of wetting and to guide the appropriate treatment in neurologically normal children with enuresis. Although we did not perform cystometry in this study, the uroflowmetry findings were similar between the two groups.

In a study by Kawauchi *et al.*,[16] the incidence of urologic abnormalities in patients with nocturnal enuresis was 1.8% on intravenous urography, 7.1% on voiding cystourethrography, and 11.5% on cystometry, and no abnormalities were observed on renal ultrasonography. However, pollakiuria was statistically more frequent in the patients with urologic abnormalities than in the patients without abnormalities. Parekh *et al.*[9] reported upper urinary system abnormalities in 3% by ultrasonography and no abnormalities by intravenous urography in children with voiding dysfunction. Urodynamic studies were performed in children who did not respond to standard treatment and detected 75% of the abnormalities in varying degrees. In the present study, the incidence of urogenital abnormalities and the urinalysis findings were similar between the children with nocturnal enuresis and those with no history of voiding problems.

Approximately 1% of boys and 3% of girls have at least one symptomatic urinary tract infection during their first 10 years of life.[17,18] Our results also suggest that the incidence of urinary tract infection is not different between the two groups.

CONCLUSIONS

Our findings show that the ultrasonographic and uroflowmetry findings on bladder function and the upper urinary system were similar in the children with and without nocturnal enuresis. No differences were noted between the two groups with respect to bladder capacity, bladder wall thickness, or postvoid residual volume. Obtaining a voiding/elimination diary in conjunction with a good history may be beneficial in children with monosymptomatic primary nocturnal enuresis. In addition, routine urinalysis may be unnecessary in the evaluation of children with monosymptomatic primary nocturnal enuresis after obtaining a careful and complete history of the voiding dysfunction.

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EDITORIAL COMMENT

The authors have presented a comprehensive review of the role of advanced diagnostic modalities in the evaluation of patients with primary nocturnal enuresis. The authors found no significant differences between their control group and the primary nocturnal enuresis group for uroflow, ultrasound postvoid residual volume, urinary system ultrasound findings, and urinalysis. The only differences were noted in the number of bowel movements per week (decreased in primary nocturnal enuresis) and number of voids per day (increased in primary nocturnal enuresis). It was interesting to note the wide standard deviation for the number of voids per day in the enuresis group. I wonder if this represents two distinct populations within the same group—the frequent daytime voiders and the infrequent daytime voiders? Both populations are at risk of nocturnal enuresis, but for vastly different reasons. The infrequent voiding patient may benefit from timed voiding by day to relieve the stress at night, and the frequent voiding patient may have an element of bladder instability. The authors have documented a tendency toward less frequent bowel movements in the primary nocturnal enuresis group. I have noted the same in my patients. Unfortunately, I have been disappointed in my ability to detect constipation on the history or physical examination and have resorted to a one-view abdominal film.

The conclusions of this paper appropriately point to the limitations of diagnostic studies. As the authors allude, primary nocturnal enuresis may represent the mildest form of a pervasive elimination disorder. The symptoms by day are subtle; the results at night are obvious. Even today, our best diagnostic instrument remains an extensive history and physical examination, with further diagnostic studies reserved for those for whom the initial management fails.

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