Association of Nocturnal Enuresis With Vesicoureteral Reflux and Renal Cortical Damage

Mitra Naseri 1*

1 Pediatric Nephrology Department, Dr Sheikh Children Hospital, Mashhad University of Medical Sciences, Mashhad, IR Iran

ARTICLE INFO

Article type: Original Article

Article history:
Received: 07 Aug 2011
Revised: 20 Aug 2011
Accepted: 25 Oct 2011

Keywords:
Nocturnal Enuresis
Diurnal Enuresis
Vesicoureteral Reflux

ABSTRACT

Background: The prevalence of vesicoureteral reflux (VUR) is higher in enuretic children than in non-enuretic children. Recent studies have reported VUR in 6–23% of children with enuresis.

Objectives: To clarify the association of nocturnal enuresis with vesicoureteral reflux (VUR) and to identify children who are at risk for VUR.

Patients and Methods: During 2007–2009, neurologically normal children who were referred with a chief complaint of nocturnal enuresis and had abnormal renal ultrasonography (US) results, daytime incontinence, abnormal results in urodynamic studies, urinary tract infection, or a history of VUR in their siblings were prospectively evaluated for VUR by voiding cystourethrography (VCUG).

Results: A total of 60 children (26 boys and 34 girls) aged 5–17 (mean ± SD: 8.46 ± 2.45) years met the inclusion criteria and were enrolled in the study. Twenty-eight (46.7%) patients had mono-symptomatic nocturnal enuresis (MNE), and 32 (53.3%) had non-mono symptomatic nocturnal enuresis (NMNE). VUR was reported in 10 (16.7%) patients and posterior urethral valve (PUV) was found in 1 (1.7%) patient. The prevalence of VUR was significantly higher in patients with daytime incontinence and in girls (\( P = 0.016 \) and 0.003 respectively). We did not find any significant correlations between VUR and the form of enuresis (primary versus secondary), urinary tract infection, or any diurnal urinary symptoms other than daytime incontinence (\( P > 0.05 \) for all). Of 10 renal scintigrams, 5 (50%) showed renal cortical defects.

Conclusions: VUR is uncommon in children with MNE and in those with NMNE who do not wet themselves during the day; however, it is a relatively common finding in enuretic children who have daytime incontinence. We recommend VCUG in all enuretic children who have daytime incontinence.

Please cite this paper as:
Naseri M. Association of Nocturnal Enuresis With Vesicoureteral Reflux and Renal Cortical Damage. Nephro-Urol Mon. 2012;4(2):448-53. DOI: 10.5812/numonthly.2030

Implication for health policy/practice/research/medical education:
The groups that can use the paper are general practitioner, pediatricians and researchers.

1. Background

Nocturnal enuresis often accompanies urological abnormalities (1), and urinary incontinence can be caused by anatomic or neurologic abnormalities, including vesicoureteral reflux (VUR), ectopic ureter, bladder extrophy, myelomeningocele (2), congenital urethral stricture (3), anterior urethral valve (4), and PUV (5). The prevalence of VUR is higher in enuretic children (6) than in other children (9, 10). New studies have noted VUR in 6–23% of children with enuresis (1, 11, 12), while other urological abnormalities have been reported in a few cases (1, 11, 12).

The American Academy of Pediatrics recommends urological evaluation of enuretic children only in cases with a history of urinary tract infection (UTI) (11), while other...
In our series, VUR was found to be associated with abnormal bladder elimination (daytime incontinence, decreased or increased bladder frequency) in 9 out of 32 (28.1%) patients who were in the NMNE group, while in children with normal bladder elimination (the 28 patients in the MNE group) VUR was reported in only 1 patient (3.6%) (Table 3).

Although bladder elimination symptoms were more common in VUR+ children, the difference was not significant (P > 0.05 for all) (Table 3). We noted that constipation was more common in the VUR group, while encopresis
Table 1. US and VCUG Findings in the VUR+ and VUR- Groups

| Clinical Parameter | US a Bladder Findings | VCUG a Findings (Other Than VUR) |
|--------------------|------------------------|----------------------------------|
|                    | All Patients, No. (%)  | VUR+ Group, No. (%)              |
|                    |                        | VUR- Group, No. (%)              |
| Normal             | 7 (100)                | 0 (0)                            |
| Increased bladder wall thickness | 43 (100)            | 8 (18.6)                         |
| Irregularity of bladder wall | 37 (100)            | 5 (13.5)                         |
| Post void urinary residue | 14 (100)            | 3 (21.4)                         |
| Increased bladder volume | 1 (100)              | 0 (0)                            |
| Widening of bladder neck | 2 (100)              | 1 (50)                           |
| Decreased bladder volume | 2 (100)              | 0 (0)                            |
| Total number       | 60 (100)               | 10 (16.7)                        |

a Abbreviation: VUR, vesicoureteral reflux

Table 2. Clinical Findings in VUR+ Children and VUR- Children with Enuresis

| Clinical Parameter | Patients, No. (%) | VUR+, No. (%) | VUR-, No. (%) | P-Value Measurement |
|--------------------|-------------------|---------------|---------------|---------------------|
| Age                | 1                 |               |               |                     |
| ≤10 y              | 46 (100)          | 8 (17.4)      | 38 (82.6)     |                     |
| >10 y              | 14 (100)          | 2 (14.3)      | 12 (85.7)     |                     |
| Gender             |                   |               |               | 0.003               |
| Female             | 34 (100)          | 10 (29.4)     | 24 (70.6)     |                     |
| Male               | 26 (100%)         | 0 (0)         | 26 (100%)     |                     |
| Positive family history b | 37 (100)    | 4 (10.8)      | 33 (89.2)     | 0.609               |
| Negative family history | 11 (100)      | 2 (18.2)      | 9 (81.8)      |                     |
| Daytime incontinence | 32 (100)       | 9 (28.2)      | 23 (71.8)     | 0.016               |
| Daytime continence | 28 (100)         | 1 (3.6)       | 27 (96.4)     |                     |
| Abnormal defecation | 15 (100)        | 4 (26.7)      | 11 (73.3)     | 0.25                |
| Normal defecation  | 45 (100)          | 6 (13.3)      | 39 (86.7)     |                     |
| Positive history of UTI | 22 (100)      | 5 (22.7)      | 17 (77.3)     | 0.494               |
| Negative history of UTI | 36 (100)      | 4 (11.1)      | 32 (88.9)     |                     |
| Primary enuresis c | 50 (100)          | 10 (20)       | 40 (80)       | 0.333               |
| Secondary enuresis | 9 (100)           | 0 (0)         | 9 (100)       |                     |
| UTI at presentation d | 10 (100)       | 4 (40)        | 6 (60)        | 0.055               |
| Sterile urine at presentation e | 49 (100)    | 6 (12.2)      | 43 (87.8)     |                     |
| Total e            | 60 (100)          | 10 (16.7)     | 50 (83.3)     |                     |

a Abbreviation: VUR, vesicoureteral reflux
b In 12 cases, the parents were unsure of their family history.

Nephro-Urol Mon. 2012;4(2):448-453
was more common in VUR+ patients. Five of 18 (27.7%) patients with abnormal bowel symptoms had VUR (Table 3). A Tc-99m-DMSA scan was done in all cases with VUR, and 5 of 10 (50%) renal scintigrams showed unilateral or bilateral renal cortical defects.

5. Discussion

VUR has been reported in enuretic patients with different incidence rates (24, 25). Shinsuke et al. (12) reported VUR in 31 of 135 (23%) of the children with enuresis who underwent VCUG, while Yasuyuki (11) found VUR in 86 KUU in 70 (6.4%) of 1088 patients, and Kawauchi (1) noted urological abnormalities on VCUG in 7.1% of 695 enuretic children. Although different studies have suggested that VUR is more common in enuretics than in the normal population, there is no general consensus on the groups of enuretic children who should be evaluated for lower urinary tract abnormalities, especially VUR (13-17).

Different studies have been conducted to define the risk of congenital lower urinary tract anomalies in enuretic children without considering the type of enuresis or their response to treatment (1, 6, 8). They have found VUR in 6.4–16% of patients, an incidence similar to that in our series (16.7%). We selected patients according to the recommendations of previous studies (13-17). Therefore, it should be considered that the overall incidence of VUR in enuretic patients might be lower than that found.

Our findings are consistent with Kajwara’s study, which showed VUR more frequently in children with NMNE than in children with MNE (26). In contrast to our study, which noted VUR only in cases with primary enuresis, Abrams et al. stated that secondary enuresis is more likely to be associated with an organic cause (27), while the study by Robson et al. noted that the prevalence of VUR did not differ significantly between cases of primary and secondary enuresis (28). Similar to Husman’s study (29), we noted some significant urological abnormalities in a minority of children with primary MNE.

In contrast to the studies by Shinsuke and Yasuyuki (11, 12), which reported low-degree VUR in the majority of affected cases, in our series, the grade of VUR was moderate in most patients and severe in 3 patients.

Nocturnal enuresis can cause renal damage, especially when recurrent UTI or VUR exists (30). Due to the moderately high incidence of renal parenchymal damage in patients with enuresis and UTI, McDermott et al. recommended considering infection as an indication for further investigation (performing VCUG) (25). In our series, 5 of 10 patients with VUR had a UTI. Two patients without history of infection and 3 patients with UTI showed renal cortical damage on renal scintigram. We did not obtain a Tc-99m-DMSA scan for all cases with a history of UTI, and in our series, only a few patients were evaluated for renal damage, so the results showing the correlation between UTI and renal damage are not statistically valid. In contrast to previous studies (14-17), we did not find a correlation between VUR and UTI, secondary enuresis, or any daytime symptoms except for incontinence (P > 0.05 for all). It is surprising that Nielsen’s study suggested enuresis as a protective factor against nephropathy in patients with VUR (24).

Dysfunctional elimination syndrome (DES), which refers to an abnormal pattern of bowel and bladder elimination with unknown etiology, usually presents in toilet-trained children without underlying anatomic or neurologic abnormalities. It has been reported that VUR

| Table 3. Urinary and Bowel Symptoms in VUR+a Children and VUR - Children With Enuresis |
|-----------------------------------------------|-----------------|--------------------|-----------------|-----------------|-----------------|-----------------|
| Symptom                                      | All Patients, No. (%) | VUR+ Group, No. (%) | VUR- Group, No. (%) | P value        |
| Daytime urinary leakage                      | 29(48.3%)         | 6(60%)             | 23(46%)          | 0.5            |
| Incontinence urinary                         | 10 (16.7)         | 4 (40)             | 6 (12)           | 0.052          |
| Increased voiding frequency                  | 10 (16.7)         | 3 (30)             | 7 (14)           | 0.347          |
| Straining                                    | 1 (1.7)           | 0 (0)              | 1 (2)            | 1              |
| Dribbling                                    | 2 (3.3)           | 0 (0)              | 2 (4)            | 1              |
| Giggle incontinence                          | 2 (3.3)           | 0 (0)              | 2 (4)            | 1              |
| Urge incontinence                            | 12 (20)           | 3 (30)             | 9 (18)           | 0.43           |
| Holding maneuver                             | 7 (11.7)          | 1 (10)             | 6 (12)           | 1              |
| Wetting during nap                           | 2 (3.3)           | 0 (0)              | 2 (4)            | 1              |
| Interrupted urinary stream                   | 2 (3.3)           | 0 (0)              | 2 (4)            | 1              |
| Constipation                                 | 8 (13.3)          | 1 (10)             | 7 (14)           | 1              |
| Encopresis                                   | 10 (16.7)         | 4 (40)             | 6 (12)           | 0.052          |
| Decreased voiding frequency                  | 3 (5)             | 0 (0)              | 3 (6)            | 1              |
| No daytime urinary or bowel symptom          | 19 (31.7)         | 1 (10)             | 18 (36)          | 0.148          |
| Total                                        | 60 (100)          | 10 (100)           | 50 (100)         |                |

\*Abbreviation: VUR, vesicoureteral reflux
and DES are associated (31, 32). Two kinds of elimination disorders are associated with VUR, pure bladder elimination disorder and combined bladder and bowel elimination disorder. DES is always a factor that worsens prognosis of VUR, increase the risk of infections complications and renal damage (33).

An association between bowel and urinary symptoms has been reported, and chronic constipation has been suggested as a risk factor for urological problems (21, 33). Kawauuchi et al. (1) suggested that the risk of UTI and urgency is increased in chronic functional constipation; however, only pollakiuria (severely increased voiding frequency) was statistically more frequent in patients with urological abnormalities than in patients without them. In our series, abnormal urinary and bowel elimination symptoms, such as urinary incontinence, increased voiding frequency, urge incontinence, and encopresis were common findings in patients with VUR (P > 0.05 for all), while the majority of patients with constipation did not have urological abnormalities (P > 0.05) (Table 3).

We found renal cortical damage in 5 of 60 (8.3%) enuretic children. This finding differs from the general belief of a favorable course of childhood enuresis. We did not find any significant correlation between a family history of enuresis and the absence of congenital anomalies of the urinary tract (VUR). In fact, 4 (40%) of the children with VUR and the single child with PUV had a family history of enuresis. This finding suggests that a family history of enuresis in close relatives does not guarantee the absence of urological abnormalities.

While VUR is uncommon in children with MNE and those with NMNE who do not wet themselves during the day, it is a significantly common finding in enuretic children with daytime incontinence. Our study suggests that VUR might be more frequent in females. As few studies have evaluated the relation between gender and VUR in enuretic children, we believe that additional studies are needed to prove or disprove this association. We noted that children with NMNE who have daytime incontinence are at increased risk for VUR; thus, VCUG is recommended for this group of enuretic children.

Acknowledgments

The author would like to acknowledge the help of Dr. Mehran Hirafar (pediatric surgeon), Dr. Alamdaran and Dr. Hebrani (radiologists), and Ms. Olomi and Ms. Vafa, the technicians in the urodynamic office.

Financial Disclosures

None declared.

Funding/Support

No special source of support.

References

1. Kawauuchi A, Kitamori T, Imada N, Tanaka Y, Watanabe H. Urological abnormalities in 1,328 patients with nocturnal enuresis. Eur Urol. 1996;29(2):231-4.
2. Chen JJ, Mao W, Homayoon K, Steinhardt GF. A multivariate analysis of dysfunctional elimination syndrome, and its relationships with gender, urinary tract infection and vesicoureteral reflux in children. J Urol. 2004;171(3):997-101.
3. Sugimoto M, Kakehi Y, Yamashita M, Matsuki T, Inui M, Takeka S. Ten cases of congenital urethral stricture in childhood with enuresis. Int J Urol. 2005;12(5):558-62.
4. Wu CC, Yang SS, Tsai YC. Anterior urethral valve in an adolescent with nocturnal enuresis. Urolgy. 2007;70(2):1908 e13-5.
5. Kihara T, Nakai H, Mori K, Sato R, Kitahara S, Yasuda K. Variety of congenital urethral lesions in boys with lower urinary tract symptoms and the results of endoscopic treatment. Int J Urol. 2008;15(3):235-40.
6. Tanaka Y, Kawauuchi A, Yoneda K, Naitoh Y, Yamato Y, Iwasaki H, et al. Vesicoureteral reflux detected among patients with nocturnal enuresis. Eur Urol. 2008;53(2):188-91.
7. Cutler C, Middleton AW, Jr., Nixon GW. Radiographic findings in children surveyed for enuresis. Urolgy. 1978;81(5):480-2.
8. Sujka SK, Piedmonte MR, Greenfield SP. Enuresis and the voiding cystourethrogram: A re-evaluation. Urolgy. 1991;98(3):61-4.
9. Gibson H. Ureteral reflux in the normal child. J Urol. 1979;122(2):114-45.
10. Jones BW, Headstream JW. Vesicoureteral reflux in children. J Urol. 1979;121(3):558-62.
11. Kihara T, Nakai H, Mori K, Sato R, Kitahara S, Yasuda K. Variety of congenital urethral lesions in boys with lower urinary tract symptoms and the results of endoscopic treatment. Int J Urol. 2008;15(3):235-40.
12. Tanaka Y, Kawauuchi A, Yoneda K, Naitoh Y, Yamato Y, Iwasaki H, et al. Vesicoureteral reflux detected among patients with nocturnal enuresis. Eur Urol. 2008;53(2):188-91.
13. American Academy of Pediatrics: Committee on Radiology: Excretory urography for evaluation of enuresis. Pediatrics. 1980;65(4):449-56.
14. Gonzales ET, Jr. The wet child. Tex Med. 1976;72(12):47-53.
15. Redman JF, Seibert JJ. The uroradiographic evaluation of the enuretic child. J Urol. 1979;122(2):679-801.
16. Assessment and management of adults with enuresis. Br Med J. 2000;320(7218):124-9.
17. Kendrcy JR, Stewart DA. Enuresis. Pediatr Clin North Am. 1974;21(4):1019-28.
18. Stannard MW, Lebowitz RL. Urography in the child who wets. AJR Am J Roentgenol. 1978;130(5):759-62.
19. Koff SA, Lapides J, Piazza DH. Association of urinary tract infection and reflux with uninhibited bladder contractions and voluntary sphincter obstruction. J Urol. 1979;122(2):373-6.
20. Hunziker M, D’Asta F, Mohanan N, Puri P. High Grade Vescoureteral Reflux in Children Presenting with Urinary Incontinence Without a History of Urinary Tract Infection. J Pediatr Urol. 2010;6:531-8.
21. Kaseria E, Akil I, Yilmaz O, Polat M, Gozmen S, Egenman A. Evaluation of voiding dysfunctions in children with chronic functional constipation. Turk J Pediatr. 2006;48(4):340-3.
22. Neveus T, von Gontard A, Hoebeke P, Hjalmas K, Bauer S, Bower W, et al. 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(2):244-24.
23. Keats T, Sistrom C. Genitourinary system. In: Keats T, Sistrom C, editors. Atlas of radiologic measurement. 7th ed. Missouri: Mosby; 2001. pp. 422-61.
24. Nielsen JB, Norgaard JP, Djurhues C. Enuresis as protective factor in vesicoureteral reflux. Urolgy. 1985;26(5):468-71.
25. McDermott VG, Merrick MV. Isotope renography in childhood enuresis. Clin Radiol. 1994;49(10):705-7.
26. Kajiwara M, Kato M, Mutaguchi K, Usui T. Association of urinary tract infection and reflux with uninhibited bladder contractions and voluntary sphincter obstruction. J Urol. 1979;122(2):373-6.
27. Abrams P, Cardozo L, Khoury S, Wein A. Incontinence. Paris: Health Publicaction; 2002.
28. Robson WT, Leung AK, Van Howe R. Primary and secondary nocturnal enuresis: similarities in presentation. Pediatr. 2005;115(4):395-9.
29. Hjalmas K, Arnold T, Bower W, Caione P, Chiozza LM, von Gontard A, et al. Nocturnal enuresis: an international evidence based management strategy. J Urol. 2004;171(Pt 2):2545-61.
30. Kass EJ, Diokno AC, Monteleger A. Enuresis: principles of man-
management and result of treatment. *J Urol.* 1979;121(6):794-6.

31. Sillen U. Bladder dysfunction and vesicoureteral reflux. *Adv Urol.* 2008:815472.

32. Alova I, Lottmann HB. Vesicoureteral reflux and elimination dis-

orders. *Arch Esp Urol.* 2008;61(2):218-28.

33. Halachmi S, Farhat WA. Interactions of constipation, dysfunc-
tional elimination syndrome, and vesicoureteral reflux. *Adv Urol.* 2008:828275.