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Clinical Course of Children and Adolescents with Primary Vesicoureteral Reflux: A retrospective study of 958 patients

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Abstract

Introduction. Vesicoureteral reflux (VUR) is the most common pediatric urologic abnormality and since it can predispose to urinary tract infection and resultant kidney scar it is an important issue in pediatric nephrourology.
Methods. A retrospective chart review and follow-up of 958 patients with primary VUR was performed in the Children's Medical Center, Tehran, Iran.
Children with primary vesicoureteral reflux were included in the study and these parameters were studied: age, sex, clinical presentation, VUR grade, sonographic findings, DMSA changes, treatment modality (medical, surgical or endoscopic) and response to treatment, hypertension (presence/absence), urinary tract infection recurrence and development of new kidney scars in patients under medical treatment.
Results. VUR was more prevalent in girls. Sonography was unable to detect VUR in many cases. Presence of renal scars was strongly associated with degree of reflux. Medical management was effective in a substantial percentage of patients and they experienced full resolution of reflux. This was especially true for lower degrees of VUR. 17.6% of patients developed new kidney scars on follow-up which was associated with higher degrees of VUR. Hypertension and breakthrough urinary tract infection was an uncommon finding in our patients.
Conclusion. Medical management, which means using prophylactic antibiotics for prevention of urinary tract infection, is effective in many cases of VUR especially in cases with lower degrees of VUR. Surgical and endoscopic procedures must be reserved for patients with higher degrees of VUR unresponsive to conservative management or in whom new scars may develop.

Keywords: vesicoureteral reflux, pediatric, urinary tract infection

Introduction

Vesicoureteral reflux (VUR) is one of the most common pediatric urologic abnormalities which affects 1-2% of children [1]. VUR is defined as the retrograde flow of urine from the bladder into the ureters and renal pelvis [2]. It is a congenital anomaly which can result in significant sequels like repeated pyelonephritis and the resultant renal scarring, hypertension and renal insufficiency [3]. It is still one of the most common causes of renal failure in children [4]. VUR is classified as primary or secondary to a concomitant condition [5]. Primary vesicoureteral reflux is the result of anatomical defect of the vesicoureteric junction.
Many advances have been made over the past two decades in understanding the pathophysiology and management of VUR in children.
The aim of the present study was to evaluate the clinical course of children and adolescents with primary vesicoureteral reflux.

Materials and methods

This was a retrospective chart review of 958 children and adolescents 1 day to 14 years old, diagnosed with primary VUR who were admitted to the Pediatric Nephrourology Unit of the Children's Medical Center in Theran, Iran between 1993-2007. This hospital is affiliated with Tehran University of Medical Sciences (TUMS). Patients with secondary VUR and those with incomplete follow-up were excluded from the study.
Patients were diagnosed by voiding cystoureterography (VCUG) in the majority of cases and radionuclide cystography in some patients. VUR grade was classified

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according to the International Reflux Study Committee's system [6]. In patients with radionuclide cystography, VUR was graded as mild (corresponding to grade I, II), moderate (corresponding to grade III), and severe (corresponding to grade IV, V).
The following parameters were analyzed in the study: age, sex, clinical presentation, VUR grade, sonographic findings, DMSA changes, treatment modality (medical, surgical or endoscopic) and response to treatment, hypertension (presence/absence), urinary tract infection recurrence and development of new kidney scars in patients under medical treatment.

Statistical analysis

All statistical analyses were performed using SPSS 16 statistical software. The Chi Square test was used for the comparison of proportions.
The study was approved by the Ethics Committee of TUMS.

Results

A total of 958 patients were analyzed in this study. Main baseline data are shown in Table 1.
VUR was bilateral in 310 patients (32.3%). Ultrasound was performed in all patients but it was unable to detect VUR in 548 (57.2%) patients which shows that it is not a reliable modality for detecting VUR in children. This is true especially for lower grade VURs. The prevalence of different grades of VUR in our study population was as follows: I (28.9%), II (24.7%), III (27.3%), IV (9.9%) and V (8.9%).

Table 1. Baseline characteristics of patients (n=958)

	Number (%)
Gender	
Male	441(42%)
Female	607(58%)
Clinical Presentation	
Urinary tract infection	893(86%)
Fetal hydronephrosis	114(11%)
Positive family history	26(2%)
Others	15(1%)
Age	
Mean	2.8
Median	2.1
Range	1 day -14 years

DMSA scan showed renal damage in 41.2% of patients at admission. We found a strong association between severity of VUR and renal damage. Of the 151 patients with severe VUR, 126 (83.4%) showed renal damage on DMSA scan whereas 269 of 556 patients with mild to moderate reflux (48.3%) showed renal damage.
The mean follow-up of patients was 14 months (range 6-36 months). Many patients were lost to follow-up because this was a retrospective chart review and many phone numbers and addresses were changed. Finally 638 patients were followed-up. Of these 386(60.5%) patients were managed medically; 49(7.6%) were submitted to surgical procedures and 203(31.8%) were submitted to endoscopic procedures. Reflux resolution was seen in 63% of patients submitted to medical management. Medical management consisted of prophylactic antibiotic therapy for prevention of urinary tract infection in patients. Reflux resolution was defined as absence of VUR on control VCUG or radionuclide cystography. Reflux resolution with medical management was more signifycant in patients with lower degrees of VUR: 84% in grade I and 78% in grade II. Forty-nine patients were treated surgically of whom 37(67.2%) responded to the surgical treatment.
A total of 203 patients were submitted to endoscopic procedure, of whom 108(53.2%) responded to this mode of treatment and their VUR resolved on follow-up.
Blood pressure was recorded for 834 patients. Fourteen patients (2%) showed blood pressure above the 95th percentile for age, sex and height.
Urinary tract infection during follow-up in patients under conservative management was 11% and 10% in patients submitted to endoscopic management.
At the end of the follow-up period 68(17.6%) of patients submitted to medical management developed new scars on DMSA scans. New scar formation was strongly associated with higher degrees of VUR.

Discussion

In this study we have reported the clinical course of a group of children and adolescents with primary VUR. VUR was slightly more prevalent in girls similar to previous reports [7,8]. Mean age at diagnosis was 2.8 years and was also similar to previous reports [9,10].
41.2% of patients showed renal damage and decreased uptake on DMSA renal scans and this was higher in children with severe degrees of VUR. The association of renal damage with VUR degree has been reported in previous studies, too [8-13].
Our study showed that ultrasound is not a suitable radiologic modality for detecting VUR as it was unable to detect VUR in 57.2% of patients. Elder JS in his study reported the imaging modalities for VUR [14].
The goal of treatment in patients with VUR is to reduce renal parenchymal injury [10]. In our study treatment modalities consisted of medical management, surgery or endoscopic intervention.
Medical therapy is the administration of low-dose antibiotic to prevent urinary tract infection and thus formation of renal scars. Resolution of VUR was observed in 63% of patients who were managed medically. Previous studies have also shown that VUR tends to resolve spontaneously [15,16].
We identified that reflux resolution was more signifycant in patients with lower degrees of VUR. This was also shown in a study by Silva *et al* [10].

Breakthrough UTI was seen with a lower incidence in our study in comparison with previous studies. Perhaps this is due to the retrospective nature of the study. However, the true incidence of UTI could be underestimated. Some studies have reported 57.6% [10], 33% [11], 50% [17] rate of breakthrough UTI in patients with VUR.

Hypertension was observed in 2% of our patients. Reflux nephropathy is one of the leading causes of hypertension in children [18] and studies with longer duration of follow-up have reported a greater prevalence of hypertension among people with VUR.

Smellie *et al.* reported a hypertension prevalence of 6.6% in 226 adults with VUR detected in childhood.[11] Wallace *et al.* followed-up 166 patients with VUR for more than 10 years and found an incidence of hypertension in these patients to be 12.8% [19].

In our study 17.6% of patients developed new scars on DMSA renal scans at the end of the follow-up period, which is similar to previous studies [7,20].

There are some limitations to this study. The most important is the retrospective nature of the study.

But its large sample size and use of different treatment modalities increase the strength of the study.

Conclusion

Ultrasound is not a suitable radiologic modality for detecting VUR in children. Medical treatment by using prophylactic antibiotics alone for prevention of urinary tract infection is effective in many cases of VUR and reflux resolution is detected in many cases under medical management alone. Surgical or endoscopic procedures should be reserved for patients unresponsive to supportive therapy or in whom new scars develop.

Conflict of interest statement. None declared.

References

1. Fanos V, Cataldi L. Antibiotics or surgery for vesicoureteric reflux in children. *Lancet* 2004; 364: 1720-1722.
2. Wadie GM, Moriarty KP. The impact of vesicoureteral reflux treatment on the incidence of urinary tract infection. *Pediatr Nephrol* 2012; 27: 529-538.
3. Carpenter MA, Hoberman A, Mattoo TK, *et al*. The RIVUR trial: profile and baseline clinical associations of children with vesicoureteral reflux. *Pediatrics* 2013; 132: e34-e45.
4. Hoberman A, Greenfield SP, Mattoo TK, *et al*. RIVUR Trial Investigators. Antimicrobial prophylaxis for children with vesicoureteral reflux. *N Engl J Med* 2014; 370: 2367.
5. Lopez PJ, Celis S, Reed F, Zubieta R. Vesicoureteral reflux: Current management in children. *Current Urology Reports* 2014; 15: 447.
6. Lebowitz RL, Olbing H, Parkkulainen KV, Smellie JM, Tamminen-Mobius TE. International system of radiographic grading of vesicoureteric reflux. International reflux study in children. *Pediatr Radiol* 1985; 15: 105-109.
7. Weiss R, Tamminen-Mobius T, Koskimies O, *et al*. characteristics at entry of children with severe primary vesicoureteral reflux recruitred for a multicenter, international therapeutic trial comparing medical and surgical management. The International reflux Study in Children. *J Urol* 1992; 148: 1644-1649.
8. Nickavar A, Hajizadeh N, Lahouti Haradashti A. Clinical course and effective factors of primary vesicoureteral reflux. *Acta Med Iran* 2015; 53(6): 376-379.
9. Goldraich NP, Goldraich IH. Follow up of conservatively treated children with high and low grade vesicoureteral reflux: A retrospective study. *J Urol* 1992; 148: 1688-1692.
10. Pendio Silva JM, Santos Diniz JS, Parizzoto Marino VS, *et al*. Clinical course of 735 children and adolescents with primary vesicoureteral reflux. *Pediatr Nephrol* 2006; 21: 981-988.
11. Smellie JM, Prescod NP, Shaw PJRidson RA, Bryant TN. Childhood reflux and urinary infection: A follow up of 10-14 years in 226 adults. *Pediatr Nephrol* 1998; 12: 727-736.
12. Abeysekara CK, Yasaratna BM, Abeyanunawardena AS. Long-term clinical follow up of children with primary vesicoureteric reflux. *Indian Pediatr* 2006; 43(2): 150-154.
13. Wang ZI, Xu H, Liu HM, *et al*. clinical analysis of 139 cases of primary vesicoureteric reflux in children. *Zhonghua Er Ke Za Ahi* 2008; 46(7): 518-521.
14. Elder Js. Imaging for vesicoureteral reflux-is there a better way? *J Urol* 2005; 174: 7-8.
15. Schwab CW Jr, Wu HY, Selman H, *et al*. Spontaneous resolution of vesicoureteral reflux: a 15 year prospective. *J Urol* 2002; 168: 2594-2599.
16. Smellie JM, Jodal U, Lax H, *et al*. Outcome at 10 years of severe vesicoureteric reflux managed medically: Report of the international reflux study in children. *J Pediatr* 2001; 139: 656-663.
17. Sjostrom S, Sillen U, Bachelard M, *et al*. Spontaneous resolution of high grade infantile vesicoureteral reflux. *J Urol* 2004; 172: 694-698.
18. Farnham SB, Adams MC, Brock JW 3rd, Pope JCT. Pediatric urological causes of hypertension. *J Urol* 2005; 173: 697-704.
19. Wallace DM, Rothwell DL, Williams DI. The long term follow up of surgically treated vesicoureteral reflux. *Br J Urol* 1978; 50: 479-484.
20. Smellie JM, Tamminen-Mobius T, Olbing H, *et al*. Five-year study of medical or surgical treatment in children with severe reflux: radiological renal findings. The International Reflux Study in Children. *Pediatr Nephrol* 1992; 6: 223-230.