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Spontaneous vesicoureteral reflux resolution in children: A ten-year single-centre experience

Peer Wildbrett, Mandy Schwebs, Jürgen Abel[1], Holger Lode[1], Winfried Barthlen

ABSTRACT

Background/Aim: To evaluate the spontaneous resolution rate in infants and young children with vesicoureteral reflux (VUR). **Patients and Methods:** Paediatric patients with VUR treated in our hospital from January 2000 to December 2010 were retrospectively analyzed. Only patients with pretreatment and follow-up voiding cystourethrogram were included into the study. Treatment success was defined as complete VUR resolution. **Results:** The resolution rate for infants less than 1 year of age was 38.6% (17 of 44 renal units). Renal units with mild-moderate VUR (I-III) had a resolution rate of 40% (12 of 30 renal units) compared to 35.7% (5 of 14 renal units) with severe grade (IV-V) VUR. The resolution rate for children over 1 year of age was 39,1% (9 of 23 renal units). Renal units with mild-moderate VUR (I-III) had a resolution rate of 42.9% (9 of 21 renal units) compared to 0% (0 of 2 renal units) with severe grade (IV-V) VUR. **Conclusion:** Infants less than 1 year of age with nonsymptomatic, mild, moderate or severe VUR have a spontaneous resolution rate of more than 35% and therefore should receive a primary conservative therapy. Children over 1 year of age with nonsymptomatic mild-moderate VUR (I-III) have a spontaneous resolution rate of about 40% and should receive primary conservative treatment as well.

Keywords: Children, spontaneous resolution, vesicoureteral reflux

INTRODUCTION

Vesicoureteral reflux (VUR) is the retrograde flow of urine from the bladder into the ureter. Two mechanisms of primary VUR one passive and one active have been discussed. Impaired passive valve function may result from an abnormally short intravesical tunnel at the ureterovesical junction.[1] Spontaneous resolution of reflux in children could be explained by the growth of the bladder, during which the intravesical tunnel elongates.[2] In addition, refluxing ureters are characterized by reduced and degenerated muscle fascicles of the distal ureteric wall. This might lead to an insufficient contraction of the muscular conduit to close the ostium impairing an active valve mechanism. Spontaneous reflux resolution might also be the result of maturation or remodeling of atrophic smooth muscle fibres at the very distal ureteric ending.[3,4]

VUR is assumed to be a risk factor for urinary tract infection (UTI) and thus it might cause pyelonephritis, renal scaring, reflux nephropathy and hypertension. UTI occurs in about 5-10% of children but only one-third of children under the age of 5 years who develop a UTI have VUR.[5,6] On the other hand VUR was found in normal kidneys without history of UTI in 17.2%.[7]

Treatment of VUR is aimed to prevent reflux nephropathy and hypertension.[8] Reflux nephropathy accounts for 7-17% of end-stage renal disease worldwide but the protective effect of surgical treatment of vesicoureteric reflux is not known.[9] A recent Cochrane review concluded that eight children would require combined surgical and antibiotic treatment to prevent one additional child developing febrile UTI by 5 years, but it would not cause fewer children developing renal damage.[10] These data indicate a possible overtreatment of VUR by antireflux surgery in some paediatric patients and it is important to identify the population that would not benefit from surgery.

The rates of resolution of VUR depending on the grade of reflux have been reported up to 37.5%.[11,12] It is assumed that these particular patients do not benefit from surgery. The aim of this study was defining the rates of spontaneous resolution for children with VUR in our centre.

Departments of Pediatric Surgery and [1]Pediatrics, University Children's Hospital Greifswald, Germany

Address for correspondence:
Dr. Peer Wildbrett,
Department of Pediatric Surgery, University Hospital Greifswald, Ferdinand-Sauerbruch-Strasse, D-17475 Greifswald, Germany.
E-mail: peer.wildbrett@uni-greifswald.de

PATIENTS AND METHODS

From January 2000 to December 2010, all conservative treated patients with primary VUR were retrospectively analyzed. Standard work up included ultrasonography, diuretic renography using ^{99m}Tc-MAG3 and VCUG. Only patients with initial and follow-up VCUG were included in the study.

All VCUG examinations were performed and interpretated by two board-certified paediatric radiologists with 7 years experience each in reading paediatric VCUG. The main endpoint of this study was to assess the rate of spontaneous VUR resolution in children referring to age and reflux grade. VUR was reported using the International Reflux Study Committees classification for radiographic grades of reflux.[13]

RESULTS

During a 10-year study period, 62 paediatric patients with VUR received conservative treatment for one or both renal units. Thirty percent were detected by postnatal work-up of hydronephrosis, 45% were diagnosed after a UTI and 25% underwent VCUG due to voiding dysfunction or other organ anomalies.

Twenty-one patients (34%) had unilateral and 41 patients (66%) bilateral reflux. Twenty-one of 41 patients (51%) with bilateral reflux received primary conservative treatment for both renal units. Twenty of 41 patients with bilateral reflux received primary conservative treatment for one side. The other side was primarily treated by antireflux surgery.

Each renal unit was separately monitored. Eighty-three renal units were primarily conservatively treated. Twenty-two percent (18 of 83 renal units) received antireflux surgery after failed conservative treatment.

Nineteen percent (16 of 83 renal units) had no follow-up VCUG and therefore were excluded from the study. Renal units were divided into two groups; group 1 less than 1 year of age (44 renal units) and group 2 over one year of age (23 renal units). The median age at diagnosis of group one was 2 months (range 0-9 months) wit a gender distribution of 57% females (25 of 44) and 43% males (19 of 44). The median age at diagnosis of group two was 4 years (range 1-10 years) with a gender distribution of 87% females (20 of 23) and 13% males (3 of 23).

The resolution rate for renal units less than 1 year of age was 38.6% (17 of 44 renal units), with a range of VCUG follow-up times between 11 and 132 months (median: 38.5). When stratified by sex, the resolution rates were 48% (12 of 25 renal units) for females and 26.3% (5 of 19 renal units) for males. Renal units with severe grade (IV-V) VUR had a resolution rate of 35.7% (5 of 14 renal units) compared to 40% (12 of 30 renal units) with mild-moderate(I-III) VUR [Table 1].

The resolution rate for renal units over 1 year of age was 39.1% (9 of 23 renal units), with a range of VCUG follow-up times between 9 and 111 months (median: 28). When stratified by sex, the resolution rates were 45% (9 of 20 renal units) for females and 0% (0 of 3 renal units) for males. Renal units with severe grade (IV-V) VUR had a resolution rate of 0% (0 of 2 renal units) compared to 42.9% (9 of 21 renal units) with mild-moderate (I-III) VUR [Table 2].

DISCUSSION

The current therapeutic management for patients with symptomatic VUR includes antireflux surgery, subureteral injection of bulking materials or long-term antibiotic prophylaxis. Each might be associated with relevant side effects and complications. In the last decade, it became more and more "uncertain whether the identification and treatment of children with VUR confers clinically important benefit".[14]

Table 1: Primary and follow-up VUR grade detected by VCUG for renal units less than 1 year of age

		VUR grade follow-up VCUG					
		no VUR	I°	II°	III°	IV°	V°
VUR grade primary diagnosis	I°	1	3	2	0	1	0
	II°	7	1	0	1	0	0
	III°	4	3	1	6	0	0
	IV°	5	1	2	1	3	1
	V°	0	0	0	0	0	1
Total		17	8	5	8	4	2

Table 2: Primary and follow-up VUR grade detected by VCUG for renal units over 1 year of age

		VUR grade follow-up VCUG					
		no VUR	I°	II°	III°	IV°	V°
VUR grade primary diagnosis	I°	4	0	0	0	0	0
	II°	3	1	2	3	0	0
	III°	2	0	1	4	1	0
	IV°	0	0	0	0	1	0
	V°	0	0	0	0	0	1
Total		9	1	3	7	2	1

Primary and follow-up VUR grade detected by VCUG for renal units over 1 year of age

Main attention should be focused on finding the subpopulation of patients who might or might not benefit from a surgical intervention. It seems to be obvious, that surgery should not be the first therapeutic option for a condition or disease which has the potential to resolve by itself within a short period of time.

Twenty years ago the International Reflux Study in Children showed a resolution of VUR grade III and IV of 16% in the random medical group and 43% in the sideline group where reflux had already improved to grade II or I.[15] A meta-analysis performed by the American Urological Association in 2010 revealed an overall VUR resolution rate in infants less than 1 year of age of 49.9 per 100 patients and 52.0 per 100 renal units, with the range of follow-up times between 12 and 48 months.[16] In children over 1 year of age the overall resolution rate was 53.2 per 100 children with the highest rates occurring between 24 and 36 months (range of 12-71 months).[16] VCUG is the gold-standard exam to assess for VUR.[17] In our study only patients with an initial and follow up VCUG have been included. VUR resolution was defined as complete regression with no reflux even into the distal ureter. The overall resolution rate for renal units less than 1 year of age was 38.6%. Five additional patients with VUR ≥2 showed a spontaneous reduction in reflux severity to grade 1 [Table 1]. In clinical practice reflux grade 1 might be regarded as an innocent finding not requiring reinvestigation.[18] Interestingly, renal units with grade IV-V VUR (35.7) had a similar resolution rate compared to grade I – III (40%). This finding underlines the updated recommendation of the American Urological Association to treat infants less than 1 year of age conservatively even with high grade VUR.[16]

The overall resolution rate for renal units over one year of age was 39.1% and similar to the group <1 year. The resolution rate for VUR grade I-III was high with 42.9%. There were only two patients with grade IV – V reflux and in both of them the reflux severity did not change during follow-up. Over 40% VUR resolution in children over 1 year of age with mild-moderate VUR correlates with recent published data by Sharifian *et al*.[19] and indicates the reservation in terms of surgical intervention in this group.

Current standard therapy for VUR includes the use of continuous antibiotic prophylaxis (CAP) to prevent acute infection.[20] This guidance is heavily debated. It was recently shown in prospective randomized trials that CAP was ineffective in reducing the rate of pyelonephritis recurrence and the incidence of renal damage in children with VUR.[11,21] Furthermore, the clinical significance of VUR becomes more and more questioned because there are no controlled studies among children that support the pathogenic role of VUR in UTI recurrence, pyelonephritis, and formation of renal scars.[22]

In conclusion, every indication for anti-reflux surgery has to be strongly questioned. Generally accepted criteria for surgery are an associated bladder pathology, grade V VUR, recurrent pyelonephritis during antibiotic prophylaxis, progression of VUR grade, new renal scars or patients´ non-compliance. However, this practice probably has to be modified and a more individualized management should take place. Base of this individualized therapeutic approach has to be knowledge about chance and timing of spontaneous reflux resolution.

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