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Original Article

Primary Vesicoureteral Reflux in Children in Southern Iran

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Abstract

Background: Experience with vesicoureteral reflux (VUR) differs in different centers and there is plenty of controversies.

Objective: To evaluate the outcome of primary VUR complications and the rate of recurrence of UTI.

Methods: In a retrospective study, the medical charts of all infants and children with primary VUR who were followed up by one nephrologist were reviewed. During 16 years, 271 patients (226 females, 45 males) with 401 refluxing ureters were followed up as primary VUR.

Results: The patients' age at diagnosis was 4 days to 16 years (Mean: 4.4 years) and the mean duration of follow-up was 4.2 years. Urinary tract infection (UTI) was the presenting symptom in 97% and fever was recorded in 30% of cases. Frequencies of different grades of VUR at initial investigation were 6.5%, 52%, 23.4% and 18.1% for grades I to IV, respectively. The responsible microorganism in 90% of the first episodes of UTI was *E. coli*. Scarring or small size kidney was present in 63 patients. Recurrence of UTI in VUR of grades I to IV, were 68.7%, 51%, 60.1% and 46.8%, respectively. Follow-up voiding cystourethrogram revealed resolution of VUR in 52%, improvement in 31%, no change in 11%, and deterioration in 6%. Complications such as chronic renal failure, hypertension and renal tubular acidosis were observed in 11, 10 and 9 patients, respectively.

Conclusion: Symptomatic primary VUR is more common and has better prognosis in girls. Recurrence of UTI is not related to the grade of VUR.

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Keywords • Vesicoureteral reflux • urinary tract infection • sex • complications

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Introduction

Vesicoureteral reflux (VUR) is defined as the retrograde flow of urine from the bladder to the ureters. Primary VUR is usually detected during radiological evaluation of infants and children with urinary tract infection (UTI). It can also be identified in the uninfected siblings or offspring of the index patients.[1]

Table 1: Number of patients using prophylactic antibiotics, and recurrence of UTI in different grades of VUR

VUR Grading	No. of patients (%)	Patients on prophylactic antibiotics	Patients with recurrent UTI
I	17 (6.5)	16 (93.7)	12 (68.7)
II	135 (52)	131 (97)	69 (51)
III	61 (23.4)	56 (92)	37 (60.1)
IV	47 (18.1)	35 (74)	22 (46.8)
Total	260 (100)	238 (91.5)	140 (53.8)

With prenatal diagnosis of hydronephrosis, it is possible to identify a further subset of patients with VUR in the neonatal period.[2] Complications such as renal scarring, chronic renal failure and hypertension are well known in patients with VUR and UTI. Antireflux surgery offers no short-term advantages other than abolishing the reflux.[3] It also does not result in improved renal function or renal growth, and does not affect the rate of new scar formation or the incidence of hypertnsion.[4] To evaluate the outcome of primary VUR, complications and the rate of recurrence of UTI, we reviewed the charts of 271 patients with VUR who were treated and followed at a university center in Shiraz.

Patients and Methods

The medical charts of all the patients with primary VUR who were followed by one pediatric nephrologist at a referral center during the last 16 years in Shiraz, Southern Iran were reviewed. Patients with VUR secondary to lower urinary tract obstruction, neurogenic bladder, bladder diverticulum or non-neurogenic neurogenic bladder were excluded from the study.

Of the 271 children with primary VUR, 260 who had conventional voiding cystourethrogram (VCUG) were included in this study. Follow-up urine cultures were done within an interval of 1-3 months or at any time when a fever of unknown origin or urinary symptoms appeared. Ultrasonography was performed in all, dimercaptosuccinic acid (DMSA) renal scan in 112 and follow-up VCUG (with a mean interval of 2.1 years) in 117. Antireflux surgery was done in 37 (14.2%) of the patients (24 with grade IV, 7 with grade III and 6 with grade II). About 91 % of the patients received prophylactic antibiotics.(Table 1)

Renal scarring was defined as an area of photon deficiency or small size hypofunctioning kidney on DMSA scan or renal parenchymal thinning on renal sonogram. UTI was defined when two consecutive cultures showed a growth of more than 100,000 colony-forming units/ml in clean-catch midstream specimens, or urine collected by sterile bags. Investigations for renal tubular acidosis was done in patients with poor weight gain of unknown cause.

Statistical analysis was done using χ^2 and the Student's t-tests.

Results

There were 401 refluxing ureters in 271 patients, and around 50% had bilateral VUR. The age at diagnosis ranged from 4 days to 16 years (mean: 4.4 years) and the male-to-female ratio was 0.2 (p=0.002). Follow -up duration ranged from 1 month to 16 years (mean: 4.2 years). In 97% of the patients VUR was documented during the investigation for UTI and 3% following investigation for prenatal or postnatal hydronephrosis or work-up because of positive family history. The presenting symptoms of the first episode of UTI comprised dysuria, enuresis or urinary frequency (33%), fever (30%), poor weight gain (10.6%), flank or abdominal pain (9.7%) and irritability (9.1%). In 90% of the patients the isolated microorganism in the first episode of UTI was E. coli. The initial grading of VUR, prophylactic antibiotic administration and the rate of recurrence of UTI in different grades of reflux are illustrated in Table 1. Recurrence of UTI was not statistically significant in different grades of VUR with or without surgery.

Ultrasonography of the kidneys and urinary tract done in all patients was abnormal in 50% (66% with grades III and IV and 34% with grade I and II). The frequent findings in renal ultrasound were caliectasis (n=69), hydronephrosis (n=27), small size kidney (n=27), cortical thinning (n=4) and renal or bladder stone (n=3).

DMSA scan was performed in 112 patients and the findings were in favor of cortical damage in 60 cases. Follow-up VCUG done in 45% of the patients (mean interval: 2.1 years), showed no VUR in 52%, lower grades of VUR in 31%, higher grades in 6% and no change in 11%.

In 84% of the patients, UTI was treated on outpatient basis and 16% were admitted to the hospital (repeated admissions were required in 5%). Anti-reflux operation was performed in 6, 7 and 24 patients with VUR of grades II to IV, respectively.

Complications of reflux and/or UTI, such as chronic renal failure, hypertension and renal tubular acidosis occurred in 11, 10 and 9 patients, respectively. In Table 2 these complications are compared in the two treatment groups. It must be emphasized that 14 patients had renal scar before the

Table 2: Complications of VUR in the two treatment groups

Patient group	Surgical	Medical
No. of patients	37	223
Bilateral reflux	30 (81%)	100 (45%)
Renal damage (scar)	22 (59%)	41 (18%)
Hypertension	2 (5%)	8 (3.6%)
Chronic renal failure	4 (11%)	7 (3%)
Renal tubular acidosis	1 (0.08%)	8 (3.6%)
Recurrence of UTI	17 (46%)	123 (55%)

operation and surgical treatment was done for higher grades of VUR. Renal stone which developed in 8 patients during follow-up was detected by initial sonography in 3 patients.

Renal scarring was detected by sonography in 19 and by DMSA scan in 60 patients. Totally, 63 patients (45 female and 18 male) with renal scars or small hypofunctioning kidneys were detected. The frequency of grades (I to IV) of VUR in these patients were 4, 11, 26 and 22, respectively. In 13 patients, defect were bilateral. In VUR of grades III and IV the frequency of renal defect was 54% in boys and 41% in girls (p=0.006). Taking all grades together, VUR was present in 43% of boys and 21% of girls (p=0.001).

Discussion

Primary VUR is the most common hereditary disorder of the genitourinary tract and is transmitted in an autosomal dominant fashion.[5] In contrast to the incidence of less than 1% in the general population, primary VUR is found in 29%-50% of children evaluated for UTI.[6] VUR is classified into four grades; nondilated ureters in grades I or II, dilated ureters in grade III, and severe dilatation with tortuousity in grade IV. The grading of VUR is important because the natural history and the risk of renal damage differ in different grades. Patients with high grade VUR are 4 to 6 times more likely to develop scarring than those with low grade VUR and 8 to 10 times more likely to do so as compared to those without VUR.[7,8] In this study, 24% of the damaged kidneys belonged to the patients with low grades of VUR. It is probable that these lesions are the sequel of pyelonephritis. In patients with higher grades of reflux the lesions may be due to both VUR and pyelonephritis or at least in some, associated with congenital defects of the kidney. In one study, severe VUR diagnosed at birth was associated with congenital renal damage and males were affected more often and more severely than females.[9] Our results are similar to this report in many aspects, including the frequency of bilateral lesions. In contrast to several previous reports the male to female ratio in our study is surprisingly different.[9-12] While the rate of renal damage in the present study was lower than that in some previous reports[13,14], it was higher than the rate reported in Chinese children (28% of boys and 11% of girls).[15] We found that the rate of renal damage in boys was at least 43%. We performed DMSA scan usually in the high risk cases, so some patients with minor defect might have been missed. Despite this fact, the high proportion of renal damage in the boys is not explained.

As anticipated, we observed higher rate of renal damage in the surgically treated group. This could be due to the fact that surgical intervention was implemented predominantly in higher grades of VUR. In 14 patients the renal scar was documented before the antireflux operation was performed and in 8 patients it was found after the surgery. So the renal scar in most of the patients is not related to the surgery.

Recurrence of UTI was not increased in the higher grades of VUR, which is at variance to a previous report.[16]

The most common abnormal ultrasonographic finding in the kidneys was caliectasis, followed by hydronephrosis, small size kidney or cortical thinning that were present in nearly 50% of the patients. In at least one half of the patients with VUR the initial renal sonography not predict VUR.[17] This was also in keeping with a previous report which show that caliectasis or hydronephrosis was the most common predictive sign.[18]

Although VCUG was not repeated, in some of the low risk patients in whom resolution of the VUR was more predictable, the total number of cure, improvement or spontaneous recovery was more than 80%. This is significant as compared to the results of other reports.[11,14,19]

In addition to renal failure and hypertension as the most common long term sequel of VUR, renal tubular acidosis (RTA) must also be considered in patients with unexplained growth failure.[20] Although not routinely investigated in our patients, RTA was persumably as prevalent as hypertension or renal failure in VUR.

We can conclude that symptomatic VUR following UTI is more common and less severe in girls and the rate of recurrence of UTI is not directly related to the grade of VUR.

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