

**An Observational Assessment of Vesicoureteral Reflux in Children****Sunil Kumar Singh<sup>1</sup>, Anil Kumar<sup>2</sup>**<sup>1</sup>Senior Resident, Department of Pediatrics, GMCH, Bettiah, Bihar, India<sup>2</sup>Professor and HOD, Department of Pediatrics, GMCH, Bettiah, Bihar, India

Received: 14-11-2023 Revised: 19-12-2023 / Accepted: 20-01-2024

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Conflict of interest: Nil

**Abstract****Aim:** The aim of the present study was to assess the vesicoureteral reflux in children.**Methods:** The present study was conducted in the Department of Pediatrics. 100 children with history of UTIs and VUR were included in the study.**Results:** The efficacy population for analysis consisted of 35 boys and 65 girls, with a mean age of 4.7 years at baseline. Most patients (96%) had reflux grade III or IV. There were no major differences between boys and girls in regard to reflux severity at baseline. The response to treatment varied according to reflux grade at baseline, and the likelihood of failure increased with growing reflux severity at baseline.**Conclusion:** Reflux is resolved by endoscopic treatment with dextranomer/ hyaluronic acid copolymer in a high proportion of children. Patients responding to therapy had no sign of deterioration on a voiding cystourethrogram 2 to 5 years after treatment, and there are no long-term safety concerns.**Keywords:** long-term follow-up, vesicoureteral reflux, children

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**Introduction**

Children suffering from primary vesicoureteral reflux (VUR) are at risk to develop recurrent UTI episodes and consequent kidney damage that may lead to hypertension and/or end-stage renal disease. [1-3] Prolonged administration of antibiotics is a widely accepted practice in children with VUR after the first UTI episode. [3-6] Although this conservative management is preferred by most pediatricians, there are physicians who consider surgical intervention in children in whom reflux fails to resolve after a certain period of time. [7] Two large randomized studies showed no difference in the occurrence of new scar lesions between VUR groups treated either with surgical intervention or long-term antibiotic prophylaxis. [8,9]

According to the Italian Society of Pediatric Nephrology (SiNePe), VUR represents a risk factor for UTI development [9], distinguishing two different entities related to it, "reflux disease" and "reflux symptom"; the first involves predominantly males, with a rare incidence, prenatally or under two years of age, with severe VUR (stage IV-V), abnormal renal parenchyma and urinary tract, and spontaneous resolution in 50% of cases. The second and more common form of VUR is usually assessed in females, with low-grade I-III VUR, associated with normal kidneys and urinary tract, with a high rate of resolution (80-90%). [10,11] A voiding cystourethrogram (VCUG) is the "gold standard" for

VUR detection, allowing grading of the severity from a wisp of contrast just beyond the bladder with no dilatation of the ureter or collecting system (grade I) up to dilatation and tortuosity of the ureters with calyceal clubbing (grade V). This radiologic test is an invasive procedure requiring urethral catheterization, often painful and traumatic for the child, causing UTIs in 1 to 3% of cases. [12,13] Although a diagnostic study can be achieved with a relatively low radiation dose by using careful technique and modern equipment, in practice, the range of doses is extremely wide. [14]

Primary vesicoureteric reflux (VUR) is caused by a maturational abnormality of the vesicoureteric junction and passage of urine in a retrograde manner up the ureter. Although the exact prevalence in the general population is unknown, 30-40% of children with urinary tract infections (UTI) are found to have reflux and urinary tract infections occur approximately in 5-10% of children. [15]

The aim of the present study was to assess vesicoureteral reflux in children.

**Materials and Methods**

The present study was conducted in the Department of Pediatrics, GMCH, Bettiah, Bihar, India and 100 children with history of UTIs and VUR were included in the study. Children 1 to 15 years old with

dilating (grade III or greater, unilateral or bilateral) vesicoureteral reflux were recruited for our open study. In all patients an upper urinary tract infection had been reported at least 1 year previously.

Vesicoureteral reflux was diagnosed by 2 or more separate voiding cystourethrograms at least 6 months apart, the latter at study entry. Antibiotic prophylaxis, including nitrofurantoin or trimethoprim, was administered between these assessments. All patients had normal creatinine levels. Exclusion criteria were neurogenic bladder, Hutch diverticulum, bladder exstrophy, duplicated refluxing ureters, history of surgical or endoscopic treatment of vesicoureteral reflux and serious illness. However, patients with bladder dysfunction, including urinary incontinence, increased urinary frequency, voiding dysfunction or increased urgency, were eligible for analysis. Our study was performed in accordance with the declaration of Helsinki and approved by the local ethical committee. Oral consent was obtained from the parents and, when possible, from the patients. All patients were placed under general anesthesia before undergoing endoscopic treatment of ureters with grade III or greater and contralateral ureters with grade I or II reflux. A 10Fr Storz cystoscope was used to facilitate injection of dextranomer/hyaluronic acid copolymer with a standard, low pressure type prefilled syringe and polytetrafluoroethylene coated, 25 cm. long, 3.5Fr needle.

Implantation was performed below the ureteral orifice at the 6 o'clock position in accordance with the standard STING procedure, as previously used with dextranomer/hyaluronic acid copolymer to create a prominent bulge, and uplift the distal ureter and ureteral orifice.<sup>19, 20</sup> To monitor treatment efficacy, a voiding cystourethrogram was performed at 3 months and 1 year after treatment. A positive response was defined as bilateral grade 0 or I reflux. Patients having this criterion 1 year after therapy did not routinely receive any further medical or endoscopic treatment and did not undergo a follow-up voiding cystourethrogram unless a urinary tract infection was reported. Children attended the local pediatric hospital for a voiding cystourethrogram that was performed with standard protocol, and a second radiologist checked blindly all results before

sending them to us. Patients were allowed to postpone or cancel the voiding cystourethrogram for any reason but those with no voiding cystourethrogram results after the last dextranomer/hyaluronic acid copolymer implantation were excluded from the efficacy population. Treatment with prophylactic antibiotics was continued in all patients until the 3-month voiding cystourethrogram and thereafter only in those with persistent reflux grade III or greater. Children with grade III or greater reflux at 3 months were offered a second implantation, although open surgery was permissible if requested by the patient and parents. A voiding cystourethrogram was also performed 3 months after the second implantation. The majority of patients with persistent reflux in our investigation underwent open surgery, although a third implantation was permitted if requested by the patient and parents. Patient renal status was assessed with ultrasound at 1 day and 1 month after treatment, although the assessment at day 1 was discontinued after the first 3 years of the study. After 1 year ultrasound or excretory urography and, in most patients, a renal function test that included renal scintigraphy with 99m technetium mertiatide was performed in accordance with standard follow-up of children with vesicoureteral reflux. Urine samples were collected at 3 and 12 months after implantation and analyzed for the presence of bacteria. All adverse events were recorded on patient charts during follow-up at the local hospital.

Long-term follow-up of patients to the present time has been done by maintaining contact with the parents and primary care physicians. All children were examined at least annually with urine dipstick or culture, and those with grades II to III vesicoureteral reflux were followed every 6 months. All children in whom clinical signs or symptoms of urinary tract infection or ureteral obstruction developed returned to the clinic for further investigation with a voiding cystourethrogram and ultrasound of the urinary tract. Investigators were also informed of the results of any voiding cystourethrogram performed in study participants for reasons other than symptoms suggesting urinary tract infection or resurgence of vesicoureteral reflux.

## Results

**Table 1: Baseline reflux grade in patients and ureters**

Grade	Male	Female	Total
II	4	8	12 (12)
III	20	44	64 (64)
IV	10	12	22 (22)
V	1	1	2 (2)
Total	35	65	100

The efficacy population for analysis consisted of 35 boys and 65 girls, with a mean age of 4.7 years at baseline. Most patients (96%) had reflux grade III or IV. There were no major differences between boys and girls in regard to reflux severity at baseline.

**Table 2: Reflux grade on voiding cystourethrogram**

Grade after Treatment	Grade before treatment				Total
	II	III	IV	V	
0	5	40	10	1	56
I	2	4	2	1	9
II	5	10	1	0	16
III	0	6	5	0	11
IV	0	4	3	0	7
V	0	0	1	0	1
Totals	12	64	22	2	100

The response to treatment varied according to reflux grade at baseline, and the likelihood of failure increased with growing reflux severity at baseline.

### Discussion

Vesicoureteral reflux is a urinary tract anomaly that affects approximately 1% of children and has a risk of long term renal damage. [15,16] It is frequently associated with urinary tract infection, and subsequent reflux of infected urine can lead to renal scarring and, in the long-term, renal insufficiency and hypertension. [17-20] Vesicoureteral reflux is graded according to the international classification of vesicoureteral reflux, with severity ranging from grades I (mild) to V (severe). [21] A voiding cystourethrogram is the usual method for diagnosing and grading severity. This procedure involves instillation of contrast medium into the bladder, allowing any reflux during instillation and subsequent voiding to be visualized and assessed directly.

The efficacy population for analysis consisted of 35 boys and 65 girls, with a mean age of 4.7 years at baseline. Most patients (96%) had reflux grade III or IV. There were no major differences between boys and girls in regard to reflux severity at baseline. The response to treatment varied according to reflux grade at baseline, and the likelihood of failure increased with growing reflux severity at baseline. Provided that the kidney's anatomy and function is normal on imaging investigation tests, a UTI episode does not usually result in complications. [22] In relation to this, the initially normal kidneys did not develop scar lesions and remained unchanged during the off prophylaxis period in the patients. Surprisingly, none of our children with established renal scarring and persistent VUR developed new scar lesions. It should be noted, however, that the rate of developing new scar lesions may have been underestimated in the present study, due to the fact that not all patients had undergone serial DMSA scans for comparison. Delay in diagnosis and

treatment of UTIs has been shown to contribute to the development of renal scars. [23,24]

Thompson et al [25] analysed data from 196 VUR children while on and off antibiotic prophylaxis and found that re-infection rate was 0.29 and 0.24 per patient per y, respectively. He identified new renal scarring in 5 children while on prophylaxis and in 7 while off prophylaxis and concluded that discontinuing antibiotic prophylaxis is reasonable and safe for children with unresolved reflux. Cooper et al [26] reported the results of discontinuing antibiotic prophylaxis in 51 refluxing children (40 girls and 11 boys) after a mean time period on prophylaxis of 4.8 y. At a mean children's age of 8.6 y, when antibiotics were discontinued, re-infection rate is reported up to 11.8% and no new renal scarring was detected.

### Conclusion

Reflux is resolved by endoscopic treatment with dextranomer/ hyaluronic acid copolymer in a high proportion of children. Patients responding to therapy had no sign of deterioration on a voiding cystourethrogram 2 to 5 years after treatment, and there are no long-term safety concerns.

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