

ORIGINAL ARTICLE

EFFICACY OF ENDOSCOPIC TREATMENT FOR PRIMARY VESICO-URETERIC REFLUX IN CHILDREN

Muhammad Athar Khawaja, Gul Nawaz, Muhammad Imran Jamil, Shujah Muhammad, Asad ur Rehman, Durre Shohab, Iftikhar Ali Khan, Ijaz Hussain, Waqas Iqbal, Saeed Akhter

Pakistan Kidney Institute, Shifa International Hospital, Islamabad-Pakistan

Background: Vesicoureteral reflux (VUR) is a common anomaly affecting 1–3% of all children and 30–50% of those with urinary tract infection (UTI). In the past febrile vesicoureteric reflux on chronic antibiotic prophylaxis were treated by open surgery. Now a day's endoscopic injection of a bulking material has replaced open surgical procedure in cases of primary VUR. Our objective was to assess the efficacy of endoscopic treatment for primary vesico-ureteric reflux in children.

Methods: This was a descriptive case series. One hundred and five patients with either unilateral or bilateral VUR (181 ureters) underwent endoscopic treatment for primary VUR between January 2011 and January 2014. Children from 1 to 12 years of age with grade-II to IV reflux on preoperative voiding cystourethrogram (VCUG) were enrolled through consecutive non-probability sampling. Efficacy of treatment was evaluated at three months post injection by a standard VCUG. Ureters with no or grade-I reflux were considered successful treatment. **Results:** Out of 105 patients 76 had bilateral while 29 had unilateral reflux. Mean age was 5.7 years (SD±.7). Among 181 refluxing ureters, 116 (64%) were free of reflux, while 49 (27%) showed down gradation and 16 (8.8%) showed no response to treatment on postoperative VCUG. **Conclusion:** Endoscopic treatment for VUR is a viable option for patients with primary VUR and may be considered in management of such cases.

Keywords: Endoscopic treatment, Vesicoureteral reflux, Urinary tract infection

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INTRODUCTION

Vesicoureteral reflux (VUR) is the most common urologic finding in children, occurring in approximately 1–3% of newborns and as high as 30–50% of young children with a urinary tract infection (UTI).¹

It is an anatomical and/ or functional disorder with potentially serious consequences. The uropathy caused by VUR predisposes to UTI and pyelonephritis. Pyelonephritis causes scar formation in kidney which leads to renal damage, impairment of renal function and hypertension.

Fortunately, patients with VUR at presentation have a wide range of severity, and there is good proportion of patients who do not develop renal scars or require any intervention.² The main goal of treatment is preservation of kidney function, by minimizing the risk of pyelonephritis. By defining and analysing the risk factors for each patient [i.e., age, gender, grade of reflux, lower urinary tract dysfunction (LUTD), anatomical abnormalities, and status of kidney function], it is possible to identify the patients with a potential risk of UTIs and renal scarring. Controversy persists over the optimal diagnostics and treatment options available for VUR, particularly the choice of diagnostic procedures, treatment (medical, endoscopic or open surgical), and the timing of treatment.

VUR can resolve spontaneously. The spontaneous resolution of VUR is dependent on age, gender, grade of reflux, laterality, mode of clinical

presentation, and anatomical factors.³ The presence of renal cortical abnormality, bladder dysfunction, and breakthrough febrile UTIs are negative predictive factors for reflux resolution.^{4,6}

The facts that reflux may persist for a number of years provide the rationale for treating VUR. The aims of treatment are to reduce the risk of febrile UTIs affecting the upper urinary tract and, possibly, protect against future renal damage. Treatments for VUR may be classified into three main different types: antibiotic prophylaxis, open, and endoscopic surgery.

Traditionally, if medical management with low-dose antibiotic prophylaxis failed, the only alternative was open surgery.⁷ Since Matouschek's initial description of the sub-ureteral injection technique in 1981 and the first clinical series reported by O'Donnell and Puri in 1984 it has evolved into a therapeutic alternative to open surgery,^{9, 10} and now considered endoscopic sub-ureteral transurethral injection has become a first-line therapy for children with VUR because of its high success rates and a very low incidence of complications.^{1,7,8}

Overall success rates using Dextranomer Hyaluronic Acid ranged between 68–92% depending mainly upon VUR grade.^{8,11,12}

The VUR cure rate has also been shown in a randomized, prospective study to be significantly higher following Dextranomer Hyaluronic Acid than with 12 months of antibiotic prophylaxis.¹³ There is

an apparent learning curve with the treatment procedure. In one study, success rates increased from 60% for the first 20 of 134 patients treated, to 80% for the last 20 cases.¹⁴

Many patients respond to a single treatment: in two studies, about three-quarters of patients were cured (reflux grade 0) at 3 months and, in another study, reflux was corrected in 86% of ureters at 3–12 months' follow-up.^{8,14} Nevertheless, in patients not responding to the first procedure, repeat endoscopic injection is viable. Our aim was to determine the efficacy of endoscopic treatment for grade-II–IV vesicoureteric reflux in children 1–12 years of age.

MATERIAL AND METHOD

This descriptive case series was conducted at the department of urology, Shifa International Hospital as day care procedure and patients were followed in OPD for 12 months post injection.

A total 105 patient with either unilateral or bilateral VUR (181 ureters) who underwent endoscopic treatment for primary VUR between January 2011 and January 2014 were included in the study. Patients were selected through consecutive non-probability sampling. All patients of 1–12 year of age of either gender with grade-II to IV VUR on preoperative voiding cystourethrogram (VCUG) were enrolled. Patients with grade-I and grade-V reflux and patients with abnormal urinary tract e.g., dysplastic kidney on sonography, secondary VUR, exstrophy bladder, neurogenic bladder and urethral stricture were excluded.

Efficacy was measured in terms of success rate by doing VCUG at three months after injection. Patients with no or grade-I reflux were considered a success. Approval from ethical committee was taken. Out of patients 105 met the inclusion criteria.

A written informed consent was got signed from parents or caretakers of every child. Detailed history regarding the demographic data and clinical presentation was recorded. Detailed systematic examination was done. Blood samples were drawn for

serum creatinine, Urine sample for Urine culture and sensitivity and a voiding cystourethrogram (VCUG) was done to assess grade of reflux.

As reflux can be unilateral or bilateral that is involving both ureters in one patient each of which can have different response to endoscopic treatment so patient with bilateral involvement was considered as two cases to see the end result, i.e., efficacy.

In our study 76 patients were having bilateral while 29 were with unilateral reflux hence a total of 181 ureters. All procedures were performed by consultant paediatric urologist. One ml of Dextranomer Hyaluronic Acid copolymer was injected sub-mucosally into the bladder wall below the ureteral orifice.

Urine analysis and cultures were done in all patients two weeks after injection therapy and subsequently to look for any break through UTIs in symptomatic patients. All patients were kept on prophylaxis antibiotics for 3 months after injection therapy. Patients were regularly followed in OPD for clinical assessment and laboratory tests. VCUG was done at 3 months post-injection to assess the end result. The data was recorded on *pro forma* and analysed using SPSS-16.0.

RESULTS

Of the total 105 patients having either unilateral or bilateral VUR (a total of 181ureters) underwent endoscopic treatment. Out of them 59 (56.2%) were male and 46 (43.8%) female with a male to female ratio of 1.2:1. Mean age was 5.77±3.79 with a range of 1–12 years.

Preoperative grade-III was the most prevalent grade observed in 54.14% followed by grade-IV 33.7% and grade-II 12.15%.

VUR was successfully resolved in 64% (116/181) while treatment was not effective in 36% (65/181).(Table-1) Postoperative complications were observed in 23 (22%) patients including febrile UTI (17%), ureteric obstruction (0.5%) and no response to treatment (8.8%).

Table- 1: Outcome of Endoscopic Treatment in Term of Grade of VUR

Preoperative VUR on VCUG		Efficacy on postoperative VCUG at 3 months		
Grade of reflux	Numbers of ureters (n %)	Successfully resolved (grade I or no reflux)	Downgraded (Reflux reduced to lower grade)	No response on grade of reflux
II	22 (12.15%)	21/22 (95%)	00	1/22 (4.5%)
III	98 (54.14%)	76/98 (77%)	15/98 (15%)	7/98 (7%)
IV	61(33.7%)	19/61 (31%)	34/61 (56%)	8/61 (13%)
Total	181	116/181 (64%)	27 % (49/181)	16/181(8.8%)

Table-2: Comparison of efficacy based on grade of reflux

Grade of reflux	Success rate in grade-II reflux	Success rate in grade-III reflux	Success rate in grade-IV reflux
Our study	95%	77%	31%
Seibold J <i>et al</i> ²⁷	87%	77%	67%
Chertin B <i>et al</i> ²⁸	100%	100%	93%
Coletta R <i>et al</i> ²⁶	94%	81%	56%

DISCUSSION

Many children with VUR may have spontaneous resolution of disease with time and this is mostly seen in younger children. This gave rise to the concept of conservative management (watchful waiting) of VUR, but studies have shown that incidence of development of renal scarring and renal damage in conservatively managed patients ranged from 4.7 to 23%.¹⁵ Although the indication for treatment of primary vesicoureteric reflux has not been changed over the time but advent of endoscopic treatment has changed the management plan of primary Vesicoureteric reflux in children. Endoscopic treatment is a minimally invasive way for correction of VUR. Hence on the basis of high success rate in the cure of patients of VUR Capozza and Caione has proposed it to be the first line treatment in most of the cases of primary VUR describing it a useful alternative to chronic antibiotic prophylaxis in patients with low grade reflux and a better treatment option in patients with high grade reflux.¹⁶

According to the European association of Urology (EAU)/European Society for Paediatric Urology (ESPU) guidelines all the children with Vesicoureteric reflux (irrespective of its grade) and renal scarring should receive chronic antibiotic prophylaxis in their first year of life, while definitive surgical procedure either in form of endoscopic injection or open surgical repair should be limited to patients with recurrent febrile UTIs.¹⁷

In our study the most prevalent grade on preoperative VCUG was grade-III VUR (54.14%) followed by grade-IV (33.7%) and grade-II (12.15%). Similar prevalence for grade-II, III and IV were reported by Puri P. and colleagues (4.8%, 57.3% and 34.9% respectively).¹⁸ Also in a large study by Nicola Capozza and co-workers, the most prevalence grade was grade-III (46%) followed by grade-II (41%) and grade-IV or V (13%).¹⁹

In our study we defined efficacy as having no or grade-I reflux on three months post injection VCUG. Multiple studies used the same criteria for efficacy including the meta-analyses.^{13,18,20,21}

The overall efficacy after first injection was 64% in our study. In a large meta-analysis of 47 full text articles, Routh *et al* reported a success rate of 77% in 7303 ureters treated with Dx/HA²², Rivilla *et al* (74%)²³ and Capozza *et al* (79%)¹⁶.

Others have reported a higher success rate. Puri and Kutasy reported a success rate of 87.1% in large series of 2341 ureters after first endoscopic injection of Dx/HA copolymer.¹⁸ Similar success rate was observed by Neel *et al* (81.8%).²⁴

The overall efficacy results were low in our study as compared to other studies. Possible

explanations to this may be high grade reflux (cumulative % of grade-III+IV was 87%) and less experience (181 ureters) as it is new in Pakistan.

Puri *et al* and Lorenzo *et al* in their articles have proved that higher the grade of reflux lesser will be the outcome especially after first injection.^{18,25}

Success rate was higher for lower grade of reflux as compared to higher grade. In grade-II reflux success rate was the highest 95% followed by 77% for grade-III and 31% for grade-IV. Variable results are reported in different studies.²⁶⁻²⁸ (Table-2)

In our study 49 (27%) ureters showed down gradation of reflux (33 to grade-II and 17 to grade-III) while 16 (8.8%) showed no response to treatment.

Down gradation is not mentioned in most of articles. However many have reported 10-30% down grading rate. Studies have reported a down grading rate of 10%, 16%, 16% and 33% respectively.^{26, 29, 30}

Postoperative complications were observed in 23 (22%) patients. Febrile UTI requiring catheterization and antibiotics were seen in 18 (17%) patients compared to 2.2% reported by Chertin B *et al*.²⁸ Ureteric obstruction evident by progressive hydronephrosis was seen in 1 (0.5%) ureter that resolved in 6 weeks with placement of nephrostomy tube. The reported frequency of ureteric obstruction by Vandersteen DR *et al* and Wolfgang H *et al* were 0.3% and 0.6% respectively.^{31,32}

Sixteen ureters (8.8%) failed to respond and had recurrent febrile UTI. These patients were treated with 2nd injection therapy and half of these were free of reflux while 8 patients were treated by ureteric re-implantation. Gross haematuria, urinary retention, or migration of material has not been observed in our study.

CONCLUSION

Endoscopic treatment with Dextranomer hyaluronic copolymer for VUR is a viable and effective treatment option for patients with primary VUR and may be considered in management of such cases.

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AUTHOR'S CONTRIBUTION

MAK: Literature review. GN: literature review, Data collection and article writing. MIJ, SM,AUR, DS & IAK: Data Collection. WI: Statistical analysis. IH & SA: Critical Review

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Address for Correspondence:

Dr. Gul Nawaz, House No. 558, Street-21, G15/1 Islamabad-Pakistan.

Cell: +92 333 958 7373

Email: drgul2006@yahoo.com