

Endoscopic treatment of vesicoureteric reflux with dextranomer/hyaluronic acid copolymer (Deflux): Single-surgeon experience with 48 ureters

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ABSTRACT

Purpose: VUR is a common urologic problem in children. Cystoscopic injection of bulking agents (most commonly Deflux) has gained popularity as the first line treatment in the west. However, primarily due to cost factors, it has not gained much popularity in our country. We present our initial experience with cystoscopic Deflux injection for VUR.

Materials and Methods: We reviewed our 3-yr experience with the use of Dx/HA (Deflux) for correction of VUR in children and adolescents. All children were evaluated with Ultrasound, MCUG and DMSA renal cortical scan. The indications for surgical correction of VUR included breakthrough infections while on antibiotic prophylaxis, persistent high-grade VUR beyond 3 yrs of age, and presence of significant renal damage on DMSA at diagnosis (in those children presenting with UTI). All children underwent cystoscopic Deflux injection using the standard technique of subureteral injection (0.4-1 ml per ureter). All children received antibiotic prophylaxis for 3-6 months after the injection. USG was done at 1 month and MCUG at 3-6 months after the injection.

Results: 33 patients (48 ureters) underwent cystoscopic Deflux injection for correction of VUR. Mean age was 4.5 yrs (1-17 yrs); there were 12 boys and 21 girls. Thirteen children had antenatally diagnosed HDN, while 20 children presented with febrile UTI. All children had primary VUR except one child with persistent VUR 4 yrs after PUV fulguration. The VUR was grade 1-2 in 8, grade 3-4 in 37, and grade 5 in 3 ureters. Every child had at least one ureter with dilating reflux (grades 3,4 or 5). When present, low grade VUR (grade 1 or 2) was always on the contralateral side. Only one child received a 2nd injection after 6 months. Follow-up MCUG was done in 28 children (41 ureters). Complete reflux resolution was achieved in 27 ureters (65%), and the reflux was downgraded in 2 (5%). There were no complications of Deflux injection.

Conclusions: Endoscopic correction of VUR in children is a safe and effective minimally invasive treatment for VUR. It stops or downgrades VUR in 70% of ureters. At present, we recommend it as a first-line treatment for grades 1-4 VUR requiring surgical management. Cost is the major factor limiting its use in our country.

Key words: Child, deflux, endoscopy, urinary tract infection, vesicoureteric reflux

INTRODUCTION

Vesicoureteric reflux (VUR) is a common problem encountered by pediatricians and pediatric urologists

and is seen in 1-3% in healthy children. The most common presenting symptom is urinary tract infection (UTI). VUR is seen in 30-50% of children presenting with febrile UTI; recurrent UTI with VUR can lead to renal scarring and subsequent chronic renal failure.^[1,2] The mechanism of renal damage is related to the reflux of infected urine with interstitial inflammation, although sterile urine may also cause renal damage by mechanical and immunological mechanisms. Current treatment options for these children include long-term antibiotic prophylaxis to prevent pyelonephritis while awaiting spontaneous resolution of VUR. However, high grade reflux has a low rate of spontaneous resolution and patient's compliance to medication may become a problem.^[3,4] Surgical correction of VUR, which can be done by either open or laparoscopic approach, is another option; these procedures, though they have good success rates, are invasive and are not without complications. Over the last

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few decades, endoscopic subureteric injection with bulking agents has gained popularity in the treatment of VUR. It was first reported in 1984 on pig models^[5] and human subjects^[6] using Teflon (PTFE) as the bulking agent. The principle of endoscopic treatment (ET) is to create a solid support behind the intravesical ureter and elongate the intramural length of the ureter. Subsequently, various agents, including teflon, silicon, and bovine collagen, have been used for this purpose. The most popular and widely used agent currently is dextranomer/hyaluronic acid copolymer (Deflux). Various centers have published results of Deflux injections over the past years; most were able to achieve an overall success rate of 70% with a single injection, with better outcomes in the low-grade group.^[7-10] For the past 3 years, we have been offering ET by cystoscopic Deflux injection as a treatment option for children with grades 2-4 VUR, where surgical correction of VUR is indicated. We do not offer ET routinely for grade 5 VUR, but do it only when the parents insist on ET.

MATERIALS AND METHODS

We reviewed our 3 year experience with the use of Dx/HA(Deflux) for correction of VUR in children and adolescents. All children were evaluated with ultrasound, MCUG (micturiting cystourethrogram), and DMSA renal cortical scan. The diagnosis and grading of VUR were made based on the findings on MCUG. The indications for surgical correction of VUR included breakthrough infections while on antibiotic prophylaxis, persistent high-grade VUR beyond 3 years of age, and presence of significant renal damage on DMSA at diagnosis (in those older than 1 year presenting with UTI). All children were evaluated for dysfunctional elimination which when present was conservatively managed before the ET. All injection procedures were done under general anesthesia with the patient in lithotomy position. A single dose of intravenous ceftriaxone was given immediately before the procedure for prophylaxis. During the procedure, rigid cystoscopy was performed to locate the ureteric orifices. A 3F metal needle (supplied with the Deflux injection) was then introduced via the cystoscope and Deflux was injected into the subureteric space at 6 o' clock position until a volcano appearance was achieved with a slit-like ureteric orifice on top of it [Figure 1]. Hydrodistention of the orifice was done before and after injection, and an orifice that remained closed at the end of injection was taken as the end point of injection. Multiple punctures were avoided where possible. The amount of injection for a single ureter ranged from 0.4 to 1 ml. All children received antibiotic prophylaxis for at least 3 months after the injection which was generally continued until reflux resolution was achieved. Follow-up USG was done at 1 month and MCUG at 3-6 months after the injection.

RESULTS

A total of 33 patients (15 bilateral for total of 48 ureters) underwent ET with cystoscopic Deflux injection for

correction of VUR. Mean age was 4.5 years (range 1-17 years); there were 12 boys and 21 girls. 13 children had antenatally diagnosed HDN, while 20 children presented with febrile UTI. All children had primary VUR except one child with persistent bilateral VUR 4 years after PUV fulguration. One child each had a Hutch diverticulum, an incomplete duplication and previous open surgery for VUR on the contralateral side. The VUR was grade 2 in 8, grade 3-4 in 37, and grade 5 in 3 ureters. Every child had at least one ureter with dilating reflux (grades 3, 4, or 5). When present, low-grade VUR (grade 2) was always on the contralateral side. Follow-up MCUG was done in 28 children (41 ureters). Complete reflux resolution [Figure 2] was achieved in 27 ureters (65%), and the reflux was downgraded in 2 (5%). Five children are awaiting postinjection MCUG. In three of them, antibiotic prophylaxis was stopped after 3 months and the parents are not keen on getting a repeat MCUG done since the children are asymptomatic and follow-up USG had documented good Deflux mounds in the bladder. Two children were lost to follow up. With a mean follow



Figure 1: Typical appearance of ureteric orifice at the end of Deflux injection. This appearance along with a closed orifice on hydrodistention marks the endpoint of injection

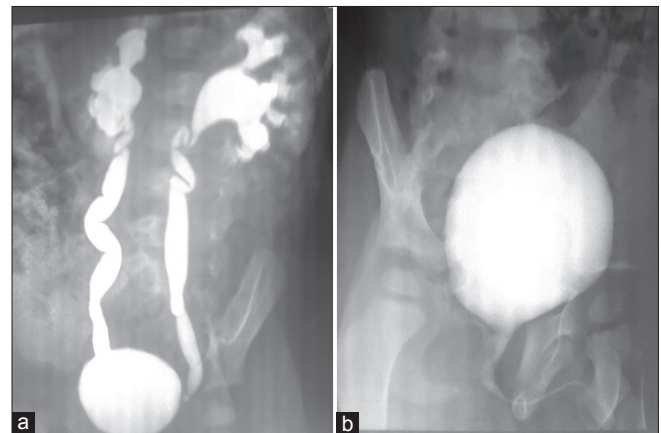


Figure 2: (a) MCUG of 1-year-old boy with bilateral grade 4 VUR and recurrent febrile urinary infections. (b) MCUG of the same child 6 months after bilateral Deflux injection showing complete resolution of VUR

up of 12 months (3-36 months), only one child (a 3-year old girl) out of 33 (3%) developed febrile UTI 1 year after documented reflux resolution on MCUG. A second follow-up MCUG in this child did not show any recurrence of VUR, and the child is on conservative management for constipation and dysfunctional voiding. Of the children with persistent VUR post-ET, two underwent open ureteric reimplantation (including the child with Hutch diverticulum), while one child received a second Deflux injection after 6 months. There have been no complications related to Deflux injection.

DISCUSSION

VUR is a common disorder seen in children and many treatment options exist. Conservative management consists of long-term administration of prophylactic antibiotics to prevent UTI while waiting for spontaneous reflux resolution. However, prolonged usage of antibiotics is associated with bacterial resistance and breakthrough UTI is not uncommon. Furthermore, there is a low spontaneous resolution rate for high grade reflux.^[11] Surgical correction of VUR is the other option in indicated cases.

Endoscopic correction of VUR with cystoscopic injection of bulking agents has been in use for three decades now. Compared with long-term antibiotic prophylaxis, this treatment modality can offer immediate cure with an acceptable success rate. Yet, it is less invasive and associated with lesser morbidity compared with ureteric reimplantation surgery. Many substances have been tried for this purpose. Polytetrafluoroethylene (PTFE-Teflon) was initially used but fell into disfavor due to reports of distant particle migration and granuloma formation.^[12,13] Silicone has similar problems with a marked local inflammatory response.^[14] With the introduction of Deflux in 1995,^[15] endoscopic correction of VUR became very popular and is now the first-line treatment for VUR in most centers across the world. Deflux is a viscous gel consisting of dextranomer microspheres and stabilized nonanimal hyaluronic acid. Dextranomer microspheres are formed by cross-linking dextran polymers into porous beads 80-250 µm in diameter. Deflux is nonimmunogenic, noncarcinogenic, and biodegradable. When compared to other bulking agents, it has a bigger size and therefore particle migration is less likely.^[16]

Our initial experience with Deflux injection for VUR has been encouraging. The major limitation for Deflux use in our practice is the cost of Deflux itself. The overall costs of treating VUR with ET versus ureteric reimplantation are similar, a phenomenon that has been well documented.^[17] The greatest advantage of ET is that it is largely a day-care procedure with minimal morbidity, compared with the standard technique of ureteric reimplantation. If the first injection fails, a second and even third injection can be tried with increased chance of success. However, it has been

our observation that most of our parents opted for surgical reimplantation after failure of the first injection to cure reflux. Ureteric reimplantation after failed Deflux injection can be done safely and successfully and is no more difficult than primary ureteric reimplantation in terms of operative time, blood loss or length of hospital stay.^[18]

Regarding the injection technique, many variations have been described. The degree of hydrodistension, depth of needle penetration, and the amount of Deflux injected has been evaluated. Many centers regard the final “volcano” appearance, described by Puri *et al.*^[19] as the predictor of success. Lavelle *et al.*^[8] reported an 87% success rate when this morphology was achieved during the injection. Kalisvaart *et al.*^[20] recently reported over 90% success with double HIT technique, and reported the durability of the result on intermediate and long-term follow up. The results from our series are comparable to most of the published data in the literature.^[8-10] We attributed the slightly lower success rate after a single injection to the learning curve. Nevertheless, an overall success of 70% (when considering downgraded reflux also) after a single injection is acceptable for an initial experience.

Similar to other the published reports,^[8-10,19] we did not notice any complications associated with the use of Deflux in our series. We feel that parents should be offered this management option during discussion. Two surveys of informed parental preference have also indicated that ET may be preferred by most parents over the other treatment modalities.^[21,22] Many of our patients had been offered ureteric reimplantation surgery elsewhere before they came to us. The parents were happy that they could avoid a more invasive surgery for their child.

CONCLUSION

Based on this retrospective review, endoscopic injection of Deflux seems to be a safe and effective management option for pediatric patients with VUR.

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