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High success rate with new modified endoscopic treatment for high-grade VUR: A pilot study with preliminary report

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Summary

Purpose
Despite the benefits of the minimally invasive endoscopic treatment for vesicoureteral reflux (VUR) it has a major drawback which is low success rate in high grade VUR. For overcoming this problem, we introduce a new modified technique of endoscopic treatment called periureteral injection technique (PIT).

Materials and methods
In a prospective study a total of 37 ureters in 19 boys and 14 girls were treated, including 3 bilateral cases. Of 37 units, 30 (81.1%) had grade IV and 7 (18.9%) had grade V primary VUR (18 right, 13 left and 3 bilateral units). Subureteral injection of Vantris® was done at the 5-o'clock and 7-o'clock positions in which the direction of injecting needles were almost parallel. Pre- and post-operative evaluation included urinalysis, urinary tract ultrasonography, voiding cystourethrography (VCUG), dimercaptosuccinic acid scan and urodynamic studies.

Results
The median age was 38 months (range 8–125). At 6 months follow up period confirmed with VCUG, the VUR has been disappeared in 34 (91.8%) units and 3 units [2 (5.4%) grade II and 1 (2.7%) had grade III)] had downgraded VUR. Complications included early fever due to urinary tract infection in 1 children, transient dysuria in 2 patients and low back pain in one patient (Summary Table).

Conclusion
The success rate of PIT for treatment of high grade VUR is high. However, further studies with more patients and longer follow up periods are needed to draw final conclusion.

Table Demographic and clinical characteristics of patients and study results.

Variables	Values	Grade of reflux after PIT	
		Completely disappeared	Downgraded
Mean age, months (range)	38 (8–125)	–	–
Refluxing unit, n (%)	36 (100.0)	–	–
Grade IV	29 (80.6)	27 (93.1)	2 (6.9)
Grade V	7 (19.4)	6 (85.7)	1 (14.3)
Gender, n (%)			
Male	19 (57.6)	–	–
Female	14 (42.4)	–	–
Laterality, n (%)			
Left	12 (36.4)	–	–
Right	18 (54.5)	–	–
Bilateral	3 (9.1)	–	–
Follow-up period, months	6		
Postoperative complications, n (%)			
Fever	1 (2.8)	–	–
Dysuria	2 (5.5)	–	–
Flank pain	1 (2.8)	–	–

PIT, periureteral injection technique.

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Introduction

VUR affects approximately 1−3% of all children [1], making it the most common pediatric anomaly of the urinary tract [2]. Endoscopic periureteral injection of different materials is an accepted treatment for low-grade VUR [3]. Endoscopic technique is non-invasive compared with open surgery. Once the reflux is successfully corrected, there is no need to administer long-term antibiotic prophylaxis. Surgical intervention may be necessary in patients with breakthrough infection despite continuous antibiotic prophylaxis (CAP), non-compliance with the prophylaxis medications [4], high-grade VUR (Grade IV and V) and presence of pyelonephritic changes in kidney or congenital abnormalities [5]. For high-grade VUR, ureteral reimplantation has proven to be the standard therapy [6]. However, open surgery is an invasive method with its own complications, and Grade V VUR has been reported to be resistant to treatment in 20% of cases after ureteral reimplantation [7].

Endoscopic treatment of VUR was introduced in 1981 by Matouschek [8], and popularized in the early 1980s by O'Donnell and Puri [9]. Endoscopic treatment is an effective and minimally invasive approach to treating children with VUR. As the injection evolved, the endoscopic treatment became the first option for the management of VUR [10]. But the most important disadvantage of this procedure, especially in high-grade VUR, was its lower success rates at long-term follow-up [11]. In this pilot study, a new, modified endoscopic treatment method has been introduced for treatment of high-grade (IV and V) VUR — it is called the periureteral injection technique (PIT).

Materials and methods

Between February 2010 and May 2013, 33 consecutive children (19 boys and 14 girls) with high-grade primary VUR were studied in a prospective manner. A total of 36 ureters, including three bilateral cases (Grade IV VUR in 29 and Grade V VUR in seven cases), were treated with polyacrylate polyalcohol copolymer (Vantris®, Promedon, Cordoba, Argentina) injection using the PIT. The indication for treatment was recurrent UTI despite CAP. All of the subjects had high-grade VUR and febrile UTI while they were receiving CAP. Febrile UTI was defined as rectal fever $\geq$38 °C associated with a positive urine culture and biological inflammatory syndrome (leucocyte count $\geq$15,000/mm^3 and/or C-reactive protein (CRP) $\geq$15 mg/l). Urine cultures with $>10^5$ colony forming units/ml were regarded as UTI. In children who were not toilet trained, urine specimens were collected via sterile bags. Reflux was graded according to the International Reflux Study grading system [12].

A single surgeon treated all patients. The presence of VUR was confirmed by VCUG. In addition to VCUG, pre-operative evaluation consisted of blood chemistry, urinalysis and culture, urinary system ultrasonography, DMSA scan, and urodynamic studies. Only patients with primary VUR were included. Patients with PUV, bladder and bowel dysfunction, and anatomic abnormalities such as ureteral duplication and bladder diverticula were excluded from the study.

In toilet-trained children, bladder and bowel function were assessed only. Bladder and bowel dysfunction was defined as a score of >6 for toilet-trained girls and >9 for toilet-trained boys, based on a dysfunctional voiding scoring system [13]. Furthermore, children with a history of ureteral or endoscopic injection were excluded. Patients with treatment failures were not offered reinjection. Success was defined as the elimination of VUR (Grade 0) with a single injection. The parents were well informed about the study protocol and all of them gave their informed consent before commencement of the study. The Medical Ethics Committee of Guilan University of Medical Sciences approved the study protocol.

The endoscopic technique

Periureteral injection was performed under general anesthesia using a 10-French (F) cystoscope and double hydrodistention implantation technique (HIT), with some modification. In the classic double-HIT injection method, the needle is passed into the ureteral orifice (UO) and inserted at the mid-ureteral tunnel at the six o'clock position. Sufficient bulking agent is injected to produce a bulge, which initially coapts the detrusor tunnel, while a second implant within the most distal intramural tunnel leads to coaptation of the UO (double-HIT method).

In the modified technique, the needle was passed into the UO at two different positions (five and seven o'clock positions). The direction of the inserted needle in these two positions was parallel to each other. This direction was carefully controlled during needle insertion and bulking agent injection. In other endoscopic techniques the injection is usually being done in 6 o'clock, but in PIT, the injection is being done in two sites (5 and 7 o'clock), and a coapted and narrowed ureteral tunnel similar to a nonrefluxing ureter is achieved. It results in satisfactory caoption and narrowing of ureteral orifices. All patients received 50 mg/kg cephalotin intravenously as the pre-operative antibiotic prophylaxis. Half of or two-thidrs of the bladder's capacity was filled. Through a 23-gauge needle, Vantris® was injected submucosally below the ureteral orifice at the five and seven o'clock positions to create a prominent bulge and raise the distal ureter and ureteral orifice. The injection needles were in parallel, flat and did not cross over each other, nor were they at an acute angle. The injection was carried out slowly, while the entire length of the needle was advanced and held for 30 s. The injection made the ureteral orifice appear completely coapted and narrowed (see video as supplementary material). This technique included two injection sites in one session. No second endoscopic injection was performed. The patients were kept on antibacterial prophylaxis for 1 week after the procedure, unless the first ultrasound showed ureteral dilatation.

Supplementary material related to this article can be found online at http://dx.doi.org/10.1016/j.jpurol.2015.07.013.

Follow-up

Urinary tract ultrasonography was performed 1 and 4 weeks after injection to identify hydronephrosis and other complications. In addition, postoperative studies included