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The use of polyacrylate-polyalcohol copolymer hydrogel in the endoscopic treatment of primary vesicoureteral reflux in children

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ABSTRACT

Background/purpose: It is still under discussion which is the best tissue augmenting substance for the endoscopic treatment of children with vesicoureteral reflux (VUR). We describe our preliminary experience (September 2009–November 2011) with polyacrylate-polyalcohol copolymer hydrogel (PPCH).

Methods: This is an observational, descriptive, prospective study which included 81 female and male patients (age 1–14 years) diagnosed with unilateral (n = 45) and bilateral (n = 36) primary VUR comprising a total of 117 refluxing renal units (RRU). Complex cases were excluded from the study. All patients were clinically and radiologically evaluated and those who met the inclusion criteria were treated endoscopically with a single subureteral injection of PPCH by a single surgeon. 11 patients (13.5%) had a pathological 99mTc-DMSA before treatment. The volume of injected product was measured in all cases. Results were considered successful if 6 months postinjection, conventional voiding cystourethrogram (VCUG) revealed VUR was cured (Grade 0). Follow-up ranged from 7 to 32 months.

Results: The overall resolution rate based on the number of RRUs studied was 92.3% (108/117). The mean injected volume of PPCH per patient was 0.6 ml. One patient with obstructive anuria required vesicoureteral reimplantation. Other complications were persistent, self-limiting hematuria (n = 2); lumbar pain (n = 4) and urinary tract infection with normal VCUG (n = 4).

Conclusions: Our short term data show PPCH provides a high level of reflux resolution in selected patients. Long term follow-up is required.

Vesicoureteral reflux (VUR) is characterized by backflow of urine from the bladder toward the kidney, increasing the risk of infection of the upper urinary tract, renal scarring and in the long-term, kidney damage and hypertension [1].

Since the introduction of STING two decades ago and US FDA approval in 2001 of dextranomer hyaluronic acid (Dx/HA) (Deflux®, Q-Med Scandinavia, Uppsala, Sweden) as a tissue augmenting substance for subureteral injection, the endoscopic treatment of VUR has become a widely accepted, first line therapy in numerous centers worldwide [2,3].

However, despite the overall high success rates reported by different authors, there are concerns about the short term follow-up of most series, in addition to recently intriguing data regarding the very high incidence of VUR recurrence following successful Dx/HA treatment. These results led us to investigate whether another tissue augmenting substance could achieve long term efficacy, or in other words, definitive correction of VUR [4].

In 2008, the emergence of a new tissue-augmenting substance, polyacrylate-polyalcohol copolymer hydrogel (PPCH), was published in *Archivos Españoles de Urología*. The characteristics of this biocompatible, synthetic, nonbiodegradable, easy to inject product were described [5].

Namely, Vantris® (Promedon, Córdoba, Argentina) belongs to the family of acrylics: particles of polyacrylate-polyalcohol copolymer immersed in a glycerol and physiological solution carrier (40%), which is eliminated by the reticular system through the kidneys without being metabolized. It has a pH of 6 and a very high molecular mass. When injected into soft tissues, it produces a bulkiness that remains stable through time. Once implanted, the particles are covered by a fibrotic capsule of up to 70 μm. Since particles are anionic with high superficial electronegativity, a low cellular interaction and fibrotic growth are promoted. Also since particles are highly deformable by compression, the material can be injected using a 23-Gauge needle [5].

In 2010, the same authors published their experience with PPCH in a multicenter prospective study including 83 patients with 88.6% efficacy (78 renal units) and an overall success rate of 83.6% [6].

The general objective of this study is to present our preliminary experience with PPCH and to evaluate its efficacy in the management

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of primary VUR in children. The specific objectives are: to report VUR resolution rates (according to radiological criteria) and the complications associated to its application.

1. Patients, materials and methods

This is an observational, descriptive, prospective study reviewed and approved by the institution's Research and Ethics Committee, which included 81 pediatric patients diagnosed with unilateral (n = 45) and bilateral (n = 36) primary VUR comprising a total of 117 refluxing renal units (RRUs). Signed informed consent was obtained from the parents or guardians of all of the patients.

Complex cases were excluded from the study (see list of exclusion criteria below) because this was the authors' first experience with the product; eventual and undesirable complications, as for example, the development of an obstruction in a patient with ureterohydronephrosis wanted to be prevented.

25 patients were male and 56 were female. The mean age at treatment was 4.95 years (range 1–14 years).

All patients were clinically and radiologically evaluated. Those who met the inclusion criteria were treated endoscopically with a single subureteral injection of PPCH.

The study was conducted between September 2009 and November 2011. The median follow-up term was 14 months (7–32 months).

The demographic data and patient characteristics are presented in Table 1.

1.1. Clinical and radiological evaluation

All patients underwent the following tests before and after the endoscopic procedure:

1. Renovesical ultrasound to measure prevoid and postvoid residual urine (the latter, for continent patients).
2. Conventional voiding cystourethrogram (VCUG). VUR was classified into Grades I to V, following the International Classification System (International Reflux Study Committee).
1. Renal scintigraphy using technetium 99m–dimercaptosuccinic acid (99mTc-DMSA). This was performed 6 months after the last febrile UTI to assess renal scarring before treatment, and 1 year after treatment. 50% (±5%) of relative renal function (RRF) per renal unit was considered normal. The objective presence of scarring and/or loss of RRF below 40% were considered pathological. Renal units with relative uptake between 40 and 45% were considered normal.
1. Urodynamic/video-urodynamic studies were indicated only in the case of patients with symptoms of bladder and/or voiding dysfunction (n = 7). Only 2 of these 7 patients (28.6%) were included in the protocol as they only had noninhibited contractions treated with anticholinergics.

Table 1
Demographic data and patient characteristics.

Male	25
Female	56
Mean age (years)	4.95 (range: 1–14 years)
Primary VUR cases (RRUs)	117
Unilateral VUR	45
Bilateral VUR	36
VUR Grade (RRU)	
II	14 (11.97%)
III	67 (57.26%)
IV	30 (25.64%)
V	6 (5.13%)
Indications for surgery	
Breakthrough UTI	75 (92.6%)
High grade VUR	5 (7.4%)
Abnormal 99mTc-DMSA	11 (13.5%)
Mean injected volume of PPCH (ml) per patient	0.6 ml (range: 0.3–1.5 ml)
Follow-up (months)	14 (range: 7–32 months)

1.2. Inclusion criteria

1. Pediatric patients with diagnosis of unilateral or bilateral VUR Grades II–V (Table 1) and:
   a. A history of recurrent, breakthrough febrile UTIs;
   b. Adequate bladder and urethral voiding;
   c. Absence of hydronephrosis or ureterohydronephrosis;
   d. RRF per renal unit >15% measured by renal scintigraphy (99mTc-DMSA);
   e. Absence of concomitant pathologies;
   f. Normal renal function;
   g. Antibiotic prophylaxis: use of nitrofurantoin until resolution of VUR.
   h. Nephrological examination.

1.3. Exclusion criteria

1. VUR Grade I;
2. Anatomical anomalies of the urinary tract: double urinary collecting system, ectopic ureter, posterior urethral valve;
3. Hydronephrosis or ureterohydronephrosis/uronephrosis;
4. History of urinary tract surgery;
5. Alterations in bladder dynamics: voiding dysfunction as evidenced on urodynamic or video-urodynamic studies;
6. Neurogenic bladder;
7. Patients with bowel dysfunction;
8. No consent to participate in the study.

1.4. Technique

A single injection of PPCH was administered by a single surgeon. The STING procedure was performed in 79 patients whereas the HIT (hydrodistention injection technique) was carried out only in the first and second patients. In all cases, the volume of injected PPCH was measured.

For the STING procedure, patients received general anesthesia and were placed in the lithotomy position. A right-angled 9.5 Fr cystoscope was used to facilitate the procedure. A metallic needle with a lateral orifice was inserted tangentially to a depth of 2–3 mm, just below the ureteral orifice (6 o'clock position), for injection of the product, until the creation of a prominent bulge. The distal ureter and the ureteral orifice were uplifted, increasing the submucosal length of the ureter.

The HIT procedure was performed similarly to the STING but with the following changes. Pressurized irrigation (hydrodistention) of the ureter was used to facilitate correct positioning of the needle. 0.1 ml of PPCH was injected into the distal ureteral submucosa (6 o'clock position) to confirm implant location. Once confirmed, hydrodistention was stopped and the needle inserted to a depth of 4 mm. The product was then injected until complete coaptation of the ureter was achieved.

1.5. Analysis of results

The endoscopic procedure was considered successful if 6 months postinjection, VCUG revealed VUR was cured (Grade 0). If VUR could not be resolved or was solely downgraded, it was considered a failure. The resolution rate (according to radiological criteria) was calculated for each VUR grade based on the number of RRUs and patients. The overall failure rate was calculated too. The intraoperative and postoperative complications were finally assessed.

2. Results

Before injection of PPCH, VUR Grade II was diagnosed in 14 RRUs, Grade III in 67, Grade IV in 30, and Grade V in 6 (Table 1).