

Endoscopic treatment of vesicoureteric reflux in paediatric patient: results of a long-term study

Alberto Attilio Scarpa, Carmine Del Rossi, Emilio Casolari, Claudia Gatti, Antonio Giorgio Scarpa

Unit of Paediatric Surgery, University Hospital of Parma, Parma, Italy

Abstract. *Background and aim of the work:* Vesicoureteric reflux is the most common uropathy in paediatric age. It may be treated with open surgery, antibiotic therapy or endoscopic injection. The purpose of this work is to determine outcomes and experiences of parents with children who underwent endoscopic treatment for VUR. *Materials and methods:* In a period of 5 years (from 2004 to 2009) 48 patients (20 boys and 28 girls, mean age 5,5, range 1-17) underwent endoscopic treatment for VUR. Sample included 31 cases of primary reflux (64,6%), 11 complex cases of VUR (6 duplex system, 3 duplex system with ureterocoele, 2 bladder exstrophy) and 6 children (12,5%) with VUR secondary to neurogenic bladder. All procedures were performed by the same surgeon. A questionnaire assessing experiences with endoscopic treatment was administered to all families. *Results:* Follow-up lasted from a minimum of 6 months to 5 years. Overall cure rate was 68,7% (33/48) per child after a single injection, a second injection performed in cases with VUR recurrence raised it to 81,2% (39/48 patients). Overall cure rate per grade of VUR was 60% (3/5) for grade I, 94,1% (16/17) for grade II, 86,9% (20/23) for grade III, 64,7% (11/17) for grade IV and 85,7% (6/7) for grade V. Minimal postoperative complications were recorded: 2,1% urinary tract obstruction, 12,5% macrohaematuria, 6,2% lumbar pain, 4,1% urinary retention or strangury. The results of the survey given to families were encouraging. *Conclusions:* Endoscopic treatment for VUR seems to be a feasible procedure as primary intervention. (www.actabiomedica.it)

Key words: Vesicoureteric reflux, endoscopic treatment, Deflux, VCUG, echocontrast cystosonography, questionnaire

Introduction

Vesicoureteric reflux (VUR) is a common affection in paediatric age with a prevalence of 1% in healthy population (1), a mild predominance in whites (2) and is present in approximately 30-50% of children with diagnosis of urinary tract infections (UTI) (1).

This uropathy predisposes to UTI, pyelonephritis, development of scars and ultimately renal damage, which can impair renal function and produce hyper-

tension, reflux nephropathy, until the condition of renal failure (3) [renal nephropathy is the main cause of 25% of cases of chronic renal failure (5) and accounts for approximately 5% of the paediatric end-stage renal disease population (5)].

In most cases we diagnose VUR during further examinations for UTI; 80% of these patients are female and the mean age at diagnosis is 2-3 years.

Primary VUR can be found earlier, during diagnostic investigations for pre-natal hydronephrosis; in this population 80% of children are boys (6).

The treatment of VUR is controversial; it is agreed that treatment of VUR should be performed to minimize the risk of febrile UTIs and consequently prevent pyelonephritis and renal damage with the relating sequelae.

Until the 80s feasible methods to treat VUR were antibiotic prophylaxis as initial therapy and surgical repair for patients with persistent VUR.

Since the early 80s, the endoscopic method was introduced as a further possibility for treatment of VUR and injection techniques, injectable agents and consequently treatment success rates have considerably improved (7). Initially the role of endoscopic treatment, such a minimally invasive procedure, was to substitute for antibiotic prophylaxis in the management of mild cases of VUR (grades I-III) and initial bulky agents demonstrated a moderate reliability and were associated with safety issues such as immunological reactions and clinically significant migration of the material (8).

With approval, in 2001, of Dextranomer/Hyaluronic acid Copolymer (Deflux®) for the treatment of VUR we recorded a gradual change in the perspective on the use of chronic antibiotics, repetitive invasive catheterization for voiding cystourethrogram (VCUG) and the invasiveness of open surgical correction of VUR. A recent multicentric study carried out in the US between 2002 and 2004 by Mitchell et al. and which involved 37 hospitals demonstrated a 288% increase in the number of endoscopic injections with the use of Dextranomer/Hyaluronic acid Copolymer (Deflux®) while the number of open reimplantations remained stable. The number of antireflux procedures increased of 55% over this period (9).

Dextranomer/Hyaluronic acid Copolymer (Deflux®) is nonmutagenic, nonimmunogenic, easy to inject, biodegradable with stable implant volume and its relatively large particle size prevents distant migration and embolism (10, 11) furthermore it has been shown to be well tolerated and to have long-term efficacy in the endoscopic treatment of VUR (13, 14).

Currently more and more common is the choice of the endoscopic treatment as primary therapy for VUR. A greater reliability and efficacy of injectable agent and the advances in injection techniques have

changed indications for endoscopic treatment extending its application to complex cases and high-grade (IV-V) VUR.

The aim of this study is to determine the efficacy of endoscopic injection for treatment of VUR in a population of young patients treated at our centre and, at the same time, to investigate patients' experiences and parental satisfaction about the same treatment approach for VUR.

Materials and methods

In a period of 5 years (2004-2009) 48 patients, 20 boys (41,7%) and 28 girls (58,3%) with a mean age of 5,5 years (range 1-17), underwent endoscopic treatment for VUR.

Twenty-one children (43,7%) had bilateral and 27 (56,3%) had unilateral VUR, 9 (33,3%) on the right side and 18 (66,6%) on the left, for a total of 69 renal units treated. In 8 children (17%) the uropathy was suspected in pre-natal diagnosis (ultrasound report of pyelectasis or hydronephrosis). In 28 cases (58%) VUR was diagnosed during investigations for UTI, in the last 12 children (25%) with an ultrasound screening for other conditions (eg bladder exstrophy, usual evaluation for Bifid Spine).

In all patients a diagnostic voiding cystourethrogram (VCUG) or echocontrast cystosonography (ECS) was performed and it made us able to define, for every child, the grade of reflux and other aspects that could be associated to it.

The reflux was primary in 31 cases (64,6%): in one case a "horseshoe" kidney malformation coexisted, in two cases renal agenesis (on the right side in both cases) was observed. Eleven children (22,9%) showed complex cases of VUR associated with more important anomalies of the ureterovesical junction (UVJ): 6 cases with a duplex system, 3 cases with a duplex system with ureterocoele and 2 cases with bladder exstrophy. The remaining 6 children (12,5%) showed VUR secondary to neurogenic bladder (NB).

At diagnosis reflux was grade I in 5 patients (7,2%), grade II in 17 (24,6%), grade III in 23 (33,3%), grade IV in 17 (24,6%) and grade V in 7 (10,1%) (Fig. 1).

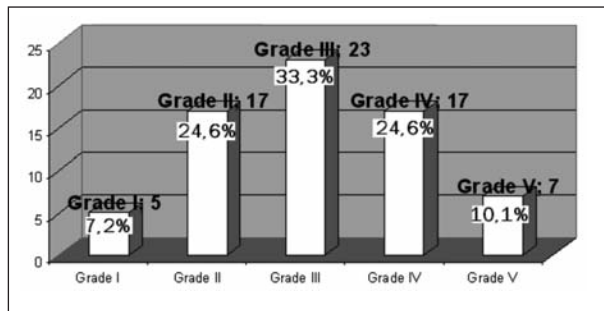


Figure 1. Bar chart representing the subdivision of the sample per grade of reflux

VUR grades II to IV represented the main indication for endoscopic treatment; grade I has been treated for superior contralateral VUR.

Forty-two (89,3%) out of the 48 patients, received antibiotic prophylaxis as first therapeutic approach for VUR (average term of the treatment 4 years and 3 months).

All 48 patients underwent endoscopic treatment to correct VUR and the procedure was performed in the operating room with the patient under general anaesthesia.

At the time of indication for endoscopic injection the parents of all patients were informed with a detailed explanation of all currently accepted management options for VUR including observation, antibiotic prophylaxis, endoscopic injection and open ureteroneocystostomy. Also, patients and parents were informed about the characteristic aspects of the endoscopic treatment: minimal invasivity compared with open technique, short hospitalization, possibility of treatment failure and of its repeatability.

Most of treatments were performed with the STING technique (Fig. 2). Since 2008 all cases of high-grade VUR (IV-V), with wide dilatation of ureteral orifice and/or associated more complex anomalies of the UVJ, were treated with the HIT (hydrodistention implantation technique) single or duplex (Figs. 3, 4) in order to produce complete coaptation of the ureteral tunnel (the intramural tract of the ureter).

For the injections we used two different kind of injectable agents: 15 treatments (31,2%) were performed using Silicone (Macroplastique®), the remain-

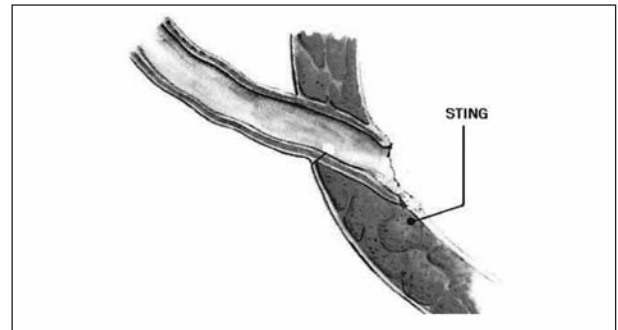


Figure 2. Injection site of the bulking agent using the STING technique

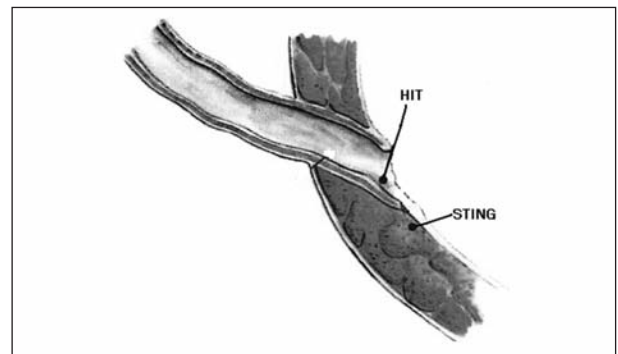


Figure 3. Injection site of the bulking agent using HIT technique

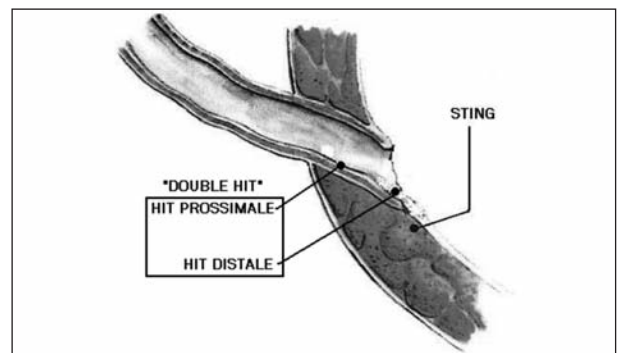


Figure 4. Injection sites in accordance with the procedure named "DOUBLE HIT". In same cases a third injection using STING technique for better occlusion of the ureteral meatus is associated

ing 33 (68,7%) using Dextranomer/Hyaluronic acid Copolymer (Deflux®). Since 2008 all procedures were performed using the dextranomer (Deflux®). The mean injected volume was 1,2 ml.

All procedures were performed by the same surgeon and in one-day surgery without complications. All patients received preoperative antibiotic prophylaxis, which continued for one week after surgery. At the end of the injection an ECS was intraoperatively performed in all patients in order to demonstrate the implant and evaluate the persistence of VUR.

Patients are then followed with a postoperative (1-1,5 months after surgery) renal ultrasound to show possible urinary tract obstruction due to the ureteral implant, and, at the same time, its stability. In all patients a VCUG or ECS was performed between 6-12 months after endoscopic injection in order to demonstrate a recurrence or a worsening of VUR. All patients underwent clinical follow-up with physicochemical and cultural urine analysis (monthly during the first year) and ultrasound to diagnose UTI.

Long-term follow-up has been carried out using annual renal ultrasound and DMSA renal scan for children with reflux nephropathy documented before the endoscopic treatment.

Patients with persistence or recurrence of VUR documented at VCUG/ECS were treated with a second endoscopic injection while in one case only a third injection was performed.

During follow-up we intended to assess patients' and parental compliance with endoscopic treatment and in general with the management of VUR using a standard questionnaire containing 13 questions (Fig. 5).

All parents answered the questions during a verbal communication with us. Particularly, patients' parents were asked about the first therapeutic approach for VUR in their child, if antibiotic prophylaxis was carried out before endoscopic treatment and for how long. We also asked them how many times their child underwent endoscopic injection. In order to determine long-term outcome of our treatments, parents were asked if their child had experienced UTIs since treatment, and if necessary, how many times. Patients' micturition patterns before and after treatment were analyzed in order to determine whether any associated voiding dysfunction had solved. Patients or their parents were asked to state their frequency of voiding and if urgency, incontinence or difficulty in voiding were experienced. Par-

VUR Questionnaire	
1.	Before your child were treated, did he/she show signs/symptoms of voiding dysfunction? ➤ Frequency/urgency/dysuria ➤ Urinary incontinence (daytime and/or nocturnal) ➤ Urinary retention
2.	When indication to endoscopic treatment was placed, have you been well informed about the main features of this approach to treat VUR? ➤ Minimally invasivity ➤ Greater acceptability by the little patient and his/her parents ➤ Short hospitalization ➤ Possibility of treatment failure ➤ Repeatability of the treatment ➤ However possibility of using open surgery if VUR relapse
3.	After your child were treated, did he show signs/symptoms of voiding dysfunction or other? ➤ Frequency/urgency/dysuria ➤ Urinary incontinence (daytime and/or nocturnal) ➤ Urinary retention ➤ Abdominal or flank pain ➤ Emesis ➤ Macrohaematuria
4.	How did your child experience the treatment (comfort, fear, safety)?
5.	Which has been, in your experience, the worst aspect of VUR management? ➤ Endoscopic treatment ➤ Long-term antibiotic prophylaxis ➤ VCUG/CSG
6.	Are you satisfied, in your experience, with the endoscopic treatment of VUR (yes/no)?

Figure 5. Questions asked parents of our little patients in order to assess compliance to endoscopic treatment

ents were also asked about the experience of endoscopic injection for their child (how comfortable he/she found the procedure, how afraid he/she was and how safe he/she felt) and their attitudes towards different aspects of VUR management and treatment were assessed by asking them to select the worst (between endoscopic injection, long-term antibiotic prophylaxis and VCUG) and the better aspect (between antibiotic prophylaxis discontinuance after endoscopic injection, its minimal invasivity and the short hospitalization) of VUR.

Results

Patients were followed from a minimum of 6 months to a maximum of 5 years.

The number of endoscopic treatments performed in order to correct VUR, like the trend observed in the United States (3), at our centre gradually increased under 5 years (Fig. 6).

Controls with VCUg or ECS showed that 33 (68,7%) out of the 48 patients were cured (absence of VUR) with a single injection. In 8 children, between those with persistence or relapse of the reflux in spite of a stable implant seen at a sonographic control (fig. 7), a second injection has been performed, it resolved the uropathy in other 6 cases and led us to an overall cure rate of 81,2% (39/48 patients).

The cure rate per renal unit treated was 68,1% (47/69) with a single injection, while the second treatment raised it to 81,1% (56/69).

Primary reflux was cured in 22/31 (71%) children with a single injection and in 25 (80,6%) after the second one. Between the 11 patients with complex cases of VUR associated with other anomalies of the UVJ (duplex collecting system, ureteral duplication with ureterocele and bladder exstrophy) 7 (63,6%) were cured with a single injection while in other 3 pts. (91%) a second treatment was necessary in order to correct VUR. At last, cure was achieved with a single injection in 4/6 (66,6%) patients with VUR secondary to NB. The injection was never repeated in this cluster of patients.

In one case only a third injection was performed and it was unsuccessful.



Figure 7. Echocontrast cystosonography. The image on the right shows, on the bladder, a stable and bulky implant (circle) in site of the right UVJ. Despite this fact, the examination demonstrates, on the left side, the persistence of VUR shown by the slope of the contrast agent to ipsilateral kidney

Endoscopic treatment was successfully performed in one paradigmatic case of VUR relapsed after ureteroneocystostomy.

After a single injection the cure rate per grade of VUR was 60% (3/5 of renal units) for grade I, 82,3% (14/17) for grade II, 69,6% (16/23) for grade III, 52,9% (9/17) for grade IV and 71,4% (5/7) for grade V.

A second injection raised the cure rate to 94,1% (16/17) for grade II, 86,9% (20/23) for grade III, 64,7% (11/17) for grade IV and 85,7% (6/7) for grade V. We did not treat grade I VUR for a second time (Fig. 8).

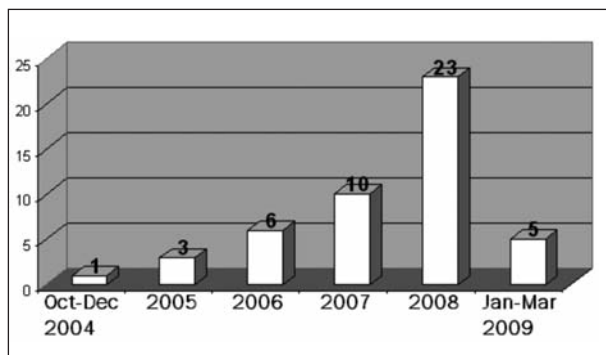


Figure 6. Bar chart representing the distribution per years of endoscopic procedures performed at our centre

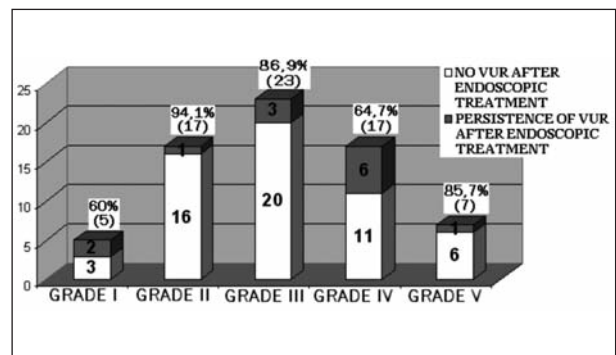


Figure 8. Bar chart representing the cure rate per grade of VUR

No significant differences were found with reference to the two different injectable agents used to treat VUR.

In one case (2,1%) only an urinary tract obstruction was observed as a consequence of the implant and de novo hydronephrosis was diagnosed with renal ultrasound. In 6 cases (12,5%) events of gross haematuria were observed during 2-3 days following endoscopic treatment and only 3 (6,2%) patients experienced lumbar pain postoperatively. Two children (4,1%) presented voiding dysfunctions such as urinary retention or strangury directly after endoscopic treatment, in all probability due to traumatic catheterization. Sixteen children (33,3%), except those with NB, showed voiding dysfunctions before treatment, only 3 pts. (6,2%) still presented these problems (urinary incontinence, urgency) after treatment. We observed no other complications or adverse events like a quick reabsorption and therefore vanishing of the implant, its migration or embolization, with none of the two different bulking agents used for treatments. Even in the case of an unsuccessful endoscopic injection and relapse of VUR after treatment, the ultrasonic control showed a stable and bulky implant in place of the UVJ.

In our experience 10 (20,8%) patients developed febrile UTIs (with cultural urinary test positive).

We also analyzed the information obtained using the questionnaire proposed to the families. The totality (100%) of parents claimed that they were well informed about prognostic and therapeutic aspects of endoscopic treatment: less invasive compared with open technique, a greater acceptance to the child, short hospitalization, a lower risk of complications postoperatively, possibility of treatment failure and of its repeatability that does not exclude recourse to open surgery for the correction of reflux. In 40 (83,3%) cases parents have reported seeing their child comfortable and at ease during his/her hospitalization, the remaining 8 (16,7%) patients have had the experience of treatment with discomfort and fear (Fig. 9).

When asked about the worst aspect of the diagnostic and therapeutic management of VUR parents of 30 (62,5%) of our patients indicated examination by VCUG or ECS (both invasive and bothersome as they require catheterization) for diagnosis and follow-up of

the uropathy. Fifteen (31,25%) other parents answered to the same question indicating long-term antibiotic prophylaxis. Parents of only 3 (6,2%) patients considered the endoscopic treatment as the less favourable aspect in the approach to VUR (Fig. 10). For the parents of 37 (77,1%) children the most favourable and acceptable aspect of endoscopic treatment for VUR was the least invasive surgery, for other 6 pts. (12,5%) the brief hospitalization. The remaining 5 (10,4%) parents preferred the choice of endoscopic approach to treat VUR for the consequent possibility of interrupting the antibiotic prophylaxis (Fig. 11).

Ultimately, parents of as many as 45 (93,7%) children were satisfied with the endoscopic treatment of VUR (Fig. 12). Even in cases where the endoscopic

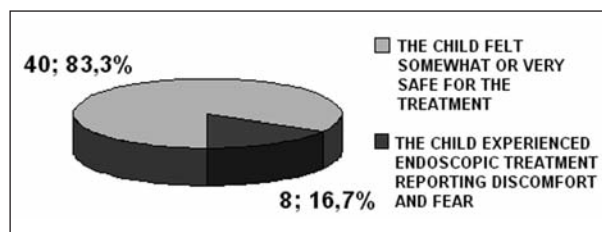


Figure 9. Pie chart reporting how patients' parents remembered their child's experience of endoscopic treatment

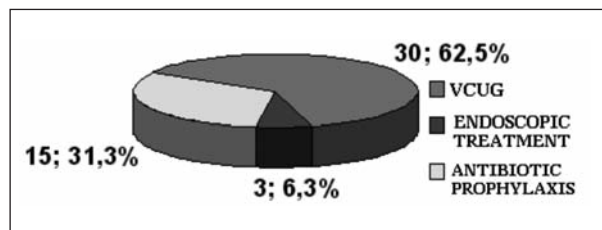


Figure 10. Worst aspect of the diagnostic and therapeutic management of VUR according to our patients' parents

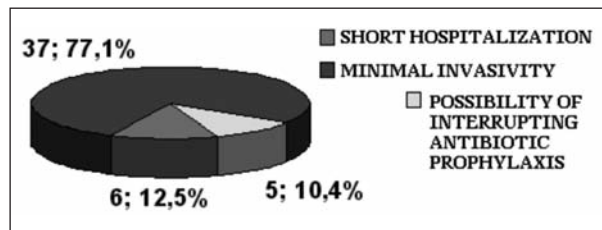


Figure 11. More favourable aspect of the endoscopic approach to treat VUR according to our patients' parents

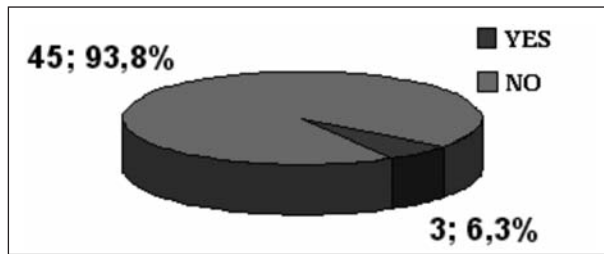


Figure 12. Pie chart showing the rates of families satisfied or not with the endoscopic treatment of VUR

procedure was not successful after the first injection (15 cases) and a second injection was necessary to achieve the correction of the uropathy, parents of 11 (73,3%) patients said they were, however, satisfied with having chosen the endoscopic procedure as a first approach to VUR.

Conclusions

Optimal treatment of VUR is still controversial despite this uropathy is most common in children and despite the significant number of clinical research in this area. As mentioned, the main goal is to treat reflux in order to reduce the risk of UTI, related to it, with the potential sequelae. From this point of view quick and permanent treatment of VUR means avoiding daily administration of antibiotics, in the long run often poorly appreciated by the patient and/or parents, and the need to refer the child to invasive examinations (VCUG/ECS) every year.

According to our survey, referral of the patient to check regularly with VCUG/ECS was considered by the parents the most unfavourable aspect. Conservative treatment of reflux with antibiotic prophylaxis, unwelcome and often inconclusive, requires regular monitoring of the uropathy. Furthermore, antibiotic prophylaxis may contribute to the selection of bacterial strains with drug resistance, a major cause of recurrent infections (14). Most recent studies have also shown that long-term antibiotic prophylaxis may be safely interrupted in patients with low grade VUR and without voiding dysfunction, hydronephrosis or renal scars and urinary tract malformations. Indeed this type of treatment offers no advantage over intermittent antibiotic

therapy of UTI in terms of prevention of a recurring infection and new onset renal damage (15).

The 87% of patients who underwent endoscopic treatment for VUR previously had experienced long-term antibiotic prophylaxis (average duration of treatment 4 years and 3 months) as the first therapeutic approach. Our investigation showed that over 30% of the families lived the antibiotic prophylaxis as the most unpleasant experience of the whole course of reflux. Although surgical management with open ureteral reimplantation (ureteroneocystostomy) has long been considered the gold standard to correct VUR, it correlates with a febrile UTI rate of 25–40% in successfully treated patients (3). On the other hand endoscopic treatment has been demonstrated to be associated with a much lower postoperative incidence.

Open ureteral reimplantation (ureteroneocystostomy) on the contrary, offers better guarantees with a success of about 95%, although significantly more invasive (16).

In this study endoscopic treatment has shown an overall cure rate of reflux in the long term of 81,2% and in 79,2% of patients it ended the occurrence of recurring UTI.

The incidence of complications after surgery was mild: urinary tract obstruction and *de novo* hydronephrosis subsequent implantation in 2,1% of cases, abdominal/flank pain in 6,2% and macrohaematuria in 12,5% always limited to the first 2–3 days after treatment.

Voiding dysfunction (e.g. urgent urination, urinary retention, etc.) commonly associated with reflux, in our case were present in 33,3% of the sample. The endoscopic technique was successful in 87,5% (14/16) of children presenting with voiding dysfunction before surgery. In our experience voiding dysfunction does not appear to be a contraindication to the procedure.

Endoscopic treatment has cured primary reflux in 80,6% of cases, complex cases with more severe anomalies associated of the UVJ in 91% of cases, and reflux secondary to NB in 66,6% of cases.

Reviewing the results for classes of VUR grade, it may be concluded that the endoscopic treatment has solved the uropathy in 90% of cases with low-moderate grade VUR (II–III), but the cure rate drops dramatically to 70,8% of cases for high grade VUR (IV–V).

We treated low grade VUR (I) with endoscopic injection only in case of greater grade contralateral reflux; for the isolated forms of low grade VUR (I) the therapeutic approach recommended is conservative which does not require antibiotic prophylaxis (simple clinical observation) in the absence of UTI.

The questionnaire filled to assess children and parents' compliance to this treatment showed that 83% of the young patients has had this experience with ease and without discomfort, while only 6,3% of the families stated endoscopic treatment was unpleasant and traumatic for the child. The most important positive aspect of the endoscopic technique, according to patients and parents, is the low invasiveness of the intervention (77,1% of responses), followed by the short hospitalization (12,5%) and finally (10,4%) the disruption of antibiotic prophylaxis.

As many as 93,8% of the families were generally satisfied for the choice of endoscopic treatment as the first approach to correct VUR.

Ultimately, the endoscopic treatment of VUR offers significant advantages: it is an easy, well codified and minimally invasive procedure, allows immediate correction of the reflux, correlates with a lower risk of postoperative complications, it is associated with a short hospitalization limiting the discomfort of the patient and, at the same time, the cost of treatment in a perspective of health economics.

Our results confirm the long-term efficacy of treatment. Developments in the injection technique along with practice of the operator and the availability of bulking, reliable and safe agents, allowed to achieve high success rates, presenting this procedure as a primary treatment for VUR. Furthermore, this method, as mentioned above, does not preclude open surgery (ureteroneocystostomy) in case of failure.

Its utility is unquestionable as an initial treatment in cases of reflux secondary to NB, due to the technical simplicity of the intervention and the rapid hospitalization.

The presence of complex anomalies of the UVJ (duplex system, duplex system with ureterocoele etc.) not only do not appear to be a contraindication to the treatment of VUR with the endoscopic method, but compared to the data reported in the literature (17),

the results we obtained in these cases have revealed a much higher success rate.

Endoscopic treatment can be taken into account in case of failure of open ureteral reimplantation technique.

We believe that the role of endoscopic technique is as a first-line treatment for low-moderate grade VUR (II-III) associated with recurrent UTI (90% of success in this cluster of patients). The long-term results were, however, unsatisfactory as a percentage (70,8% of success) for treatment of high grade (IV-V) primary VUR. Therefore, open ureteral reimplantation seems to maintain a dominant role for the final correction of VUR grade IV-V and in case of failed repeated endoscopic treatment.

References

1. Jacobson SH, Hansson S, Jakobsson B. Vesico-ureteric reflux: occurrence and long-term risks. *Acta Paediatrica* 1999; 88 (Suppl 431): 22-30.
2. Melhem RE, Harpen MD. Ethnic factors in the variability of primary vesico-ureteral reflux with age. *Ped Radiol* 1997; 27: 750-1.
3. Jacobson SH, Hansson S, Jakobsson B. Vesico-ureteric reflux: occurrence and long-term risks. *Acta Paediatrica* 1999; 88 (Suppl 431): 22-30.
4. Moliterno JA, Scherz HC, Kirsch AJ. Endoscopic treatment of vesicoureteral reflux using dextranomer hyaluronic acid copolymer. *J Ped Urol* 2008; 4 (3): 221-8.
5. Ardissino G, Avolio L, Dacco V, et al. on behalf of the ItalKid Project. Long-term outcome of vesicoureteral reflux associated chronic renal failure in children. Data from the ItalKid Project. *J Urol* 2004; 172: 305-10.
6. Brakeman P. Vesicoureteral reflux. Reflux nephropathy, and end-stage renal disease. *Advances in Urology* 2008; 2008: 1-7.
7. Behrman RE, Kliegman RM, Arvin AM. Nelson - Trattato di Pediatria, XVII ed., Edizioni Minerva Medica.
8. Cerwinka WH, Scherz HC, Kirsch AJ. Endoscopic treatment of vesicoureteral reflux with Dextranomer/Hyaluronic Acid in children. *Advances in Urology* 2008; 2008: 1-7.
9. Stenberg A, Läckgren G. Treatment of vesicoureteral reflux in children using stabilized non-animal hyaluronic acid/dextranomer gel (NASHA/DX): A long-term observational study. *J Ped Urol* 2007; 3: 0-85.
10. Lendvay TS, Sorensen M, Cowan CA, et al. The evolution of vesicoureteral reflux management in the era of dextranomer/hyaluronic acid copolymer: a pediatric health information system database study. *J Urol* 2006; 176: 1864-67.

11. Stenberg AM, Larsson E, Lindholm A, et al. Injectable dextranomer-based implant: histopathology, volume changes and DNA-analysis. *Scand J Urol Nephrol* 1999; 33: 355-61.
12. Stenberg AM, Sundin A, Larsson BS, et al. Lack of distant migration after injection of a 125iodine labeled dextranomer based implant into the rabbit bladder. *J Urol* 1997; 158: 1937-41.
13. Läckgren G, Wahlin N, Skoldenberg E, et al. Long-term follow-up of children treated with dextranomer/hyaluronic acid copolymer for vesicoureteral reflux. *J Urol* 2001; 166: 1887-92.
14. Stenberg A, Läckgren G. A new bioimplant for the endoscopic treatment of vesicoureteral reflux: experimental and short-term clinical results. *J Urol* 1995; 154: 800-3.
15. Moliterno JA, Scherz HC, Kirsch AJ. Endoscopic treatment of vesicoureteral reflux using dextranomer hyaluronic acid copolymer. *J Ped Urol* 2008; 4 (3): 221-8.
16. Bollgren I. Antibacterial prophylaxis in children with urinary tract infection. *Acta Paediatr* 1999; 88: 48-52.
17. Costers M, Van Damme-Lombaerts R, Levchenko E, et al. Antibiotic prophylaxis for children with primary vesicoureteral reflux: where do we stand today? *Advances in Urology* 2008, Article ID 217805.
18. Moliterno JA, Scherz HC, Kirsch AJ. Endoscopic treatment of vesicoureteral reflux using dextranomer hyaluronic acid copolymer. *J Ped Urol* 2008; 4 (3): 221-228.
19. Capozza N, Caione P. Il ruolo del trattamento endoscopico nella cura del reflusso vescico-ureterale – esperienza di 16 anni. *Minerva Pediatrica* 2003; 55: 1-8.
20. Läckgren G, Wahlin N, Skoldenberg E, et al. Endoscopic treatment of vesicoureteral reflux with dextranomer/hyaluronic acid copolymer is effective in either double ureters or a small kidney. *J Urol* 2003; 170: 1551-5.

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Correspondence: Alberto Attilio Scarpa
Unit of Paediatric Surgery
University Hospital
V.le A. Gramsci, 14
43100 Parma, Italy
E-mail: alberto_scarpa@hotmail.com