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REVIEW ARTICLE

Long-term results of endoscopic treatment of vesicoureteric reflux with different tissue-augmenting substances

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Abstract *Objective:* To review the current literature regarding the outcome of endoscopic treatment of vesicoureteric reflux (VUR) using different tissue-augmenting substances, with special emphasis on long-term efficacy.
Material and methods: The current literature, including our own experience, on long-term results after endoscopic treatment was reviewed by MEDLINE/PubMed search.
Results: The short-term results are similar in the majority of series to those of open surgery, but there is a high recurrence rate with use of dextranomer/hyaluronic acid (Deflux) as a tissue-augmenting material.
Conclusions: There is a significant shortage of evidence-based literature on long-term follow-up after endoscopic correction of VUR utilizing dextranomer/hyaluronic acid. The high recurrence rate that has been reported after Deflux injection highlights a need for close observation beyond routine protocols and appropriate parental counseling upon endoscopic correction, and also the need to search further for alternative tissue-augmenting substances. The algorithm for treating VUR is yet to be finally determined.

Introduction

Since the introduction of STING (subureteric Teflon injection) two decades ago, and since the approval by the Food and Drug Administration (FDA) of the dextranomer/hyaluronic acid (Dx/HA) copolymer (Deflux, Q-Med Scandinavia, Uppsala, Sweden) for the treatment of VUR, over the last 7 years endoscopic management has emerged as a first-line treatment for all grades of reflux in some centers [1—5]. The overall success rates reported by the different groups range between 68% and 92%, depending mainly on VUR grade [1—3,6]. Complications following this procedure are infrequent and relate mainly to obstruction of the

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Table 1 Long-term results of endoscopic treatment of VUR.

Published report	Bulking agent	Longest follow-up (years)	Follow-up success rate (%)	
			Initial	Long-term
Chertin et al.	PTFE	17	98.2	95
Chertin et al.	PTFE	10	100	91
Haferkamp et al.	Collagen	3	95	9
Reunane	Collagen	4	93.9	81.8
Dodat et al.	Macroplastique	7	93.3	79.4
van Capelle et al.	Macroplastique	10	84 (77)	unknown
Caldamone and Diamond	Autologous chondrocytes	3	83	70
Mevorach et al.	Coaptite	2	72	72

ureterovesical junction and the development of new contralateral reflux following treatment of unilateral VUR [5]. UTI is a common problem in children and occurs in up to 5% of girls and 1—2% of boys. VUR is present in 25—70% of children with febrile UTI and acute pyelonephritis. The combination of VUR and UTI may predispose children to progressive renal scarring and chronic renal failure. The concept of the endoscopic correction of VUR offers a minimally invasive treatment in the management of UTI or renal parenchymal damage associated with reflux. A recent meta-analysis of injection therapy, considering outcomes from injection with Dx/HA, polytetrafluoroethylene, collagen, polydimethylsiloxane and chondrocytes, suggested fewer subsequent UTIs than previously noted with open surgery or antibiotic prophylaxis, with an overall incidence of 6% (range 2.74—14.15%) and febrile infection observed in only 0.75% of patients [7].

Since endoscopic treatment of UTI has enjoyed a high rate of success in the short-term, it is extremely important to address the issue of long-term efficacy. In this review, we aimed to summarize the worldwide long-term experience of the different bulking agents utilized for endoscopic correction of VUR (Table 1), with special emphasis on UTI incidence and efficacy of the Dx/HA copolymer (Table 2) as the ultimate tissue-augmenting substance for endoscopic injection in the majority of pediatric urology centers.

Polytetrafluoroethylene (PTFE)

PTFE is one of the most widely used biomaterials in medicine. Medical applications include vascular grafts, heart valves and tissue replacement patches. PTFE was one of the first commonly used tissue-augmenting substances for endoscopic correction of reflux [4]. Since the published experience of PTFE spans more than 20 years of follow-up, it is interesting to observe and compare the incidence of UTI and long-term durability with currently used biomaterials for injection therapy.

In the longest follow-up study of primary VUR treated by PTFE injection published so far [3], there were 258 children with a median age of 6 years comprising 393 ureters. VUR was of all grades, while 96% of all injected ureters were Grade III—V. Almost all patients (88.5%) in this group had a routine VCUG 10 years after the successful injection, eliminating the possibility of silent VUR recurrence. This VCUG during follow-up of between 11 and 17 years showed no evidence of VUR in 360 (95%) out of 379 ureters. Of the remaining 19 (5%) ureters, only six recurred at grades III and IV and underwent repeat endoscopic correction. The most significant fact in this study is that none of the patients developed a febrile UTI and 3.6% had an afebrile UTI during follow-up. Similar findings in terms of VUR recurrence and incidence of febrile UTI were demonstrated by other researchers with a follow-up of 10 years after PTFE injection [4].

Although the majority of pediatric urologists have acknowledged the efficacy of endoscopic correction of low-grade VUR, some still question the durability of this treatment in high-grade VUR [8]. Convincing data from long-term follow-up over 17 years after PTFE injection in children with grades IV and V reflux has been published [9]. Of 717 refluxing units, reflux recurred in only nine (1.2%), confirming that with the correct choice of implant for endoscopic correction this procedure can be the first choice in high-grade VUR.

However, in spite of the convincing data regarding the long-term efficacy of endoscopic correction of VUR utilizing PTFE, the worrying information regarding the possibility of PTFE particle migration cannot be brushed aside. For this reason, alternative injectable substances have been sought.

Other tissue-augmenting substances

Over the years, a number of different tissue-augmenting substances have been evaluated in clinical practice.

Table 2 Long-term results of endoscopic treatment of VUR with Dx/HA.

Published report	Longest follow-up (years)	UTI rate after injection (%)	Failure rate (%)
Läckgren et al.[a]	7	8	13
Chertin et al.**	6	2.2	3.9
Chi et al.	4.8	24	12
Sedberry-Ross et al.	7	27	25
Lee at al.	1	None	26
Schmedding et al.	3	Unknown	21

** Follow-up VCUG was not performed on a routine basis after first successful one following surgical examination.

[a] Late VCUG was performed in only 45 of the 334 treated ureters.

Glutaraldehyde cross-linked bovine collagen emerged as a first alternative to PTFE [10—12]. Since the collagen was used very intensively in the medical industry for the manufacture of cardiac valves and hemostatic agents, and causes minimal tissue reaction when locally injected, it appeared a promising substance for VUR correction in the short-term. However, long-term study clearly showed that the initial success rate dramatically decreased during follow-up. Reunane reported his experience with collagen injection in 197 refluxing ureters in 148 children [10]. All underwent direct radionuclide cystography at 1 month, 6 months, 2 years and 4 years following endoscopic correction. The results for the simpler cases were better than previously reported with this tissue-augmenting substance, achieving ureteral cure rates of 93.9% after 1 month and 81.8% after 4 years, but the more complex cases fared significantly worse with a 44.4% cure rate after 1 month and only 21.4% success at 4 years.

These disappointing results received further support. Haferkamp et al. prospectively studied 36 patients treated with a single collagen injection [11]. While they achieved 80% success at 3 months after injection, only 9% of the previously cured ureters were still free of reflux at 37 months after injection.

Polydimethylsiloxane is a solid, silicone, elastomer, soft-tissue bulking agent that has been incorporated into a patented device called Macroplastique (Uroplasty Inc., Geleen, The Netherlands) [13—15]. In spite of the fact that the majority of particles of the agent are greater than 100 μm in diameter, the presence of particles sized 80 μm and less may still cause distant migration. The short-term results of use of Macroplastique as a tissue-augmenting substance were similar to those for the other bulking agents [4]. However, there is a significant shortage of prospective long-term studies that may prove the efficacy of silicon in the treatment of VUR. Van Capelle et al. published a retrospective review of 195 patients who underwent endoscopic correction of VUR utilizing Macroplastique as a tissue-augmenting substance in two institutions [13]. The study period lasted over 10 years. Overall success rates were 84% and 77% in two departments. One of the major drawbacks of this study, as well as others dealing with long-term efficacy of bulking agents, is that the patients were discharged from follow-up after 1 year if they were free of symptoms.

Autologous chondrocytes were proposed by Caldamone and Diamond for the endoscopic treatment of VUR following successful animal experiments [16]. However, the need for two periods of anesthesia and a significant recurrence rate after 1 year raise a serious question regarding the reliability of this tissue-augmenting substance in the pediatric population.

Calcium hydroxyapatite has been used as a biocompatible implant for orthopedic and dental procedures in humans for more than 25 years. In 1998 the FDA approved a study of Coaptite, which was performed in women to investigate this endoscopic bulking agent in the treatment of stress urinary incontinence. The initial results, safety and durability of the material at 3 years prompted the FDA decision to approve a pilot investigation for VUR in children in 2000. In 2001, given initially favorable results of the pilot study (70% cure in 10 patients/10 ureters at 3 months), a prospective multicenter trial of synthetic calcium hydroxyapatite, a subureteral bulking agent, in children with traditional indications for surgical treatment of VUR was performed at 10 United States centers [17]. At 1 and 2 years, 24 of 74 patients (32%) were cured. Ureteral cure rates were 46% and 40% at 1 and 2 years, respectively. With 35 patients treated and 85% compliance with the required 2-year VCUG, the primary center achieved 2-year cure rates of 66% of patients and 72% of ureters. Although the initially cured ureters did not show recurrence of reflux at 2 years of follow-up, the small study cohort and relatively short follow-up indicate that multicenter clinical trials with longer follow-up are required.

Dextranomer/hyaluronic acid (Deflux)

The overall success rate reported by different groups of authors for use of Deflux ranged between 68% and 92% depending mainly on the VUR grade [1—3]. Recently, Kirsh et al. have demonstrated that by utilizing their technique of hydrodistention implantation (HIT) the short-term results of endoscopic correction may be close to those after open surgery, and in the case of a low degree of reflux even similar to those following open reimplantation [1]. Therefore, only the question of Deflux long-term durability remains the subject of interest and parental concern. However, long-term follow-up is lacking, as well as strict criteria for what is considered a 'success'. It seems that long-term success should be defined on the basis of prospective studies where all patients will be required to undergo a VCUG even after first postoperative negative on VUR imaging, strict registration of all incidences of febrile and afebrile UTIs following injection, and recording of all possible renal parenchymal changes during follow-up. One meta-analysis that examined all types of injections, including Dx/HA, demonstrated a primary success rate of 78.5% for grades I and II, 72% for grade III, 63% for grade IV and 51% for grade V reflux [7]. Many of the studies in this meta-analysis had limited follow-up, with only one VCUG within the first 3—4 months postoperatively.

The early report on 7.5 years of follow-up after successful reflux correction with Deflux from a Swedish group, who pioneered the use of this tissue-augmenting substance, showed very low reflux recurrence [18]. The overall success rate of 84% following first VCUG decreased to 74% in the long-term follow-up. However, in only 45 (13.4%) out of 334 treated ureters was a later VCUG performed. Moreover, the authors defined the resolution of VUR as 'nondilating' reflux. In those patients who had a later VCUG 96% still showed resolution of VUR at 2 and 5 years. Recently, some intriguing data regarding the very high incidence of VUR recurrence were presented by Lee et al. [19]. They retrospectively studied later VUR recurrence verified by VCUG, which was performed 1 year after successful Deflux injection. The initial experience with Dx/HA was similar to previous studies, with a postoperative VCUG success rate of 73%. At further evaluation with VCUG 1 year after endoscopic treatment, 39 of 150 ureters exhibited VUR, resulting in a recurrence rate of 26% and an overall cumulative failure rate of 54% (130 of 241 ureters). These results, which show an overall success rate of only

46%, are extremely sobering, especially since only 74% of the initially successful cases remained so at 1 year. These findings led the authors to believe that other studies, if re-evaluated beyond the initial VCUG, would yield similar findings. Because of this data, it is the authors' belief that Dx/HA is more appropriate for lower grades of reflux. Recently, the working group on pediatric urology of the German Association of Pediatric Surgeons published results of a multicenter prospective trial, which aimed to evaluate the long-term efficacy of endoscopic treatment of VUR utilizing Dx/HA [20]. A total of 284 patients (424 renal reflux units, RRU) were treated endoscopically with Deflux injection. The reflux was corrected in 68% of RRU. Forty-six percent of the patients completed 3 years of follow-up. In 21% of RRU a recurrence of VUR was diagnosed between 6 months and 3 years. Based on this data, the authors strongly recommended continuing to follow patients, even after a successful injection, beyond the first 3 years after surgery.

Renal parenchymal damage and UTI incidence following successful endoscopic correction of VUR

It has been shown that open surgical correction of VUR offers reasonable kidney protection [21—24]. Recent data published by many researchers clearly demonstrate that STING is an option for surgical correction of VUR. However, the question as to whether the surgical correction of VUR utilizing an endoscopic approach will prevent further renal damage and UTI development still needs to be answered [25—27]. Since we have been using the endoscopic approach over the last two decades in VUR patients, we recently published our data regarding the changes in renal function and incidence of UTI in children who underwent successful endoscopic correction of VUR utilizing different tissue-augmenting substances [27]. We retrospectively evaluated 507 patients, 169 males and 338 females (696 RRU), with a median age of 3.7 years, who underwent successful endoscopic correction of primary VUR from 1988 to 2007 with a median follow-up period of 13 years. Endoscopic correction was performed utilizing polytetrafluoroethylene (Teflon) and Dx/HA copolymer. Reflux was Grade 1 in 36 RRU (5.2%), Grade II in 178 (25.6%), Grade III in 298 (42.7%), Grade IV in 163 (23.4%), and Grade V in 21 (3.1%). DMSA scan and renal ultrasound were performed in all patients preoperatively. Renal ultrasound was performed in all patients following surgery and a technetium 99 m DMSA scan was performed in 509 (73%) of the 696 RRU postoperatively. The preoperative scan demonstrated renal scarring in 543 (78%) of the 696 RRU. Renal deterioration was demonstrated in 11 of the 26 RRU with initial severe renal scarring (uptake on DMSA less than 20%). The remaining RRU from this group demonstrated an insignificant change of 2.3% in relative renal function after successful correction of VUR ($P > 0.005$). Those patients who demonstrated downgrading of VUR did not show new renal scars. Twenty-seven RRU (6.1%) of the remaining 446 RRU demonstrated a greater than 5% decrease in relative renal function without new scarring. Eleven children (2.2%) (eight in the Teflon and three in the Dx/HA copolymer group) developed febrile UTIs following successful endoscopic correction, which drove re-evaluation resulting in the diagnosis of VUR recurrence in eight (72.7%) patients; 28 (5.6%) children suffered afebrile UTIs without VUR recurrence.

It has been shown that sterile reflux does not cause renal scars unless extreme hydrodynamic conditions exist in the affected kidney [28—30]. VUR-associated bacteriuria which leads to a protracted inflammatory reaction is a major cause of exudative pyelonephritis and kidney damage. In our series, only 2.2% of the children developed recurrent pyelonephritis in the long-term follow-up. However, eight of those 11 children showed VUR recurrence on follow-up VCUG. These data are similar to those previously published [29,30]. Sedberry-Ross et al. and Chi et al. have evaluated the incidence of febrile UTI following successful endoscopic correction of VUR. The Dallas group clearly demonstrated that in 159 patients, of whom 95% had preoperative UTIs, and all of whom had demonstrated a complete resolution of reflux after Dx/HA injection, 40 patients (25%) had recurrent UTI, of which half were febrile [30]. Re-imaging was done in 15 patients with recurrent febrile infections, and seven had recurrent reflux. The study by the Washington group of 45 patients who had undergone successful Dx/HA injection demonstrated that 12 (27%) had recurrent UTIs. On re-imaging with VCUG 10 of these patients (83%) showed recurrence of VUR [29].

These data showed that those patients with initial VUR correction but who developed febrile UTIs in the long-term follow-up require prompt re-evaluation in order to rule out VUR recurrence. Furthermore, in the light of recent reports regarding the low effectiveness of antibiotic prophylaxis in children with VUR, the question is raised as to whether we have an optimal tissue-augmenting substance with durable long-term efficacy and a good safety profile [31—33].

Polyacrylate—polyalcohol copolymer (Vantris)

Biodegradable elements of synthetic origin have a high rate of reabsorption after a year. Non-biodegradable agents of synthetic origin lead to the formation of a fibrotic capsule, giving stability and permanence. Vantris (Promedon, Cordoba, Argentina) is categorized into this last group; it belongs to the family of acrylics: particles of polyacrylate—polyalcohol copolymer immersed in a glycerol and physiological solution carrier. Its molecular mass is very high. When injected into soft-tissues, this material causes a bulkiness that remains stable through time [34].

The carrier is a 40% glycerol solution with a pH of 6. Once injected, the carrier is eliminated by the reticular system through the kidneys, without metabolizing. Particles of this polyacrylate—polyalcohol with glycerol are highly deformable by compression, and may be injected using a 23-gauge needle. The average particle size is 320 mm. Once implanted, particles are covered by a fibrotic capsule of up to 70 μm. Particles of this new material are anionic with high superficial electronegativity, thus promoting low cellular interaction and low fibrotic growth. The new polyacrylate—polyalcohol copolymer with glycerol was tested for biocompatibility according to ISO 10993-1:2003 *in vitro*, showing that it is not mutagenic for the *Salmonella typhi* strains analyzed. The extract turned out to be non-cytotoxic for cell lines in culture and non-genotoxic for mice. In *in-vivo* studies, acrylate did not cause

sensitization in mice. The macroscopic reaction of tissue irritation was not significant in subcutaneous implants and in urethras of rabbits. Seven female dogs were injected transurethrally with Vantris to evaluate short- and long-term migration (13 weeks and 12 months, respectively). No particles or signs of inflammation or necrosis were observed in any of the organs examined 13 weeks and 12 months after implantation. It seems that Vantris is meeting the criteria for the ideal tissue-augmenting substance. The clinical experience with Vantris is still very limited. Eighty-three patients were treated between 2005 and 2006 during a multicenter trial in South America [35]. Sixty-one patients with an average age of 58 months completed a 1-year follow-up. The number of injected ureters was 88 (41 right units and 47 left units). Thirty-two had grade II (36.4%), 41 grade III (46.6%), 12 grade IV (13.6%) and three grade V (3.4%). The injected volume per unit ranged from 0.2 to 1.6 ml, with a mean of 0.76 ml. The average follow-up period was 20 months with a range of 16—24 months. Reflux was eliminated in 78 (88.6%) kidney renal units, decreased to grade I in six (6.8%) units, and persisted in four (4.6%) units.

We have recently started in our institution a prospective trial aiming to investigate the short- and long-term efficacy of Vantris in children with VUR. Our short-term preliminary results are promising. However, more clinical data with longer follow-up are awaited.

Conclusions

There is a significant shortage of evidence-based literature on long-term follow-up after endoscopic correction of reflux utilizing Dx/HA, the FDA-approved tissue-augmenting substance for endoscopic correction of VUR. However, the scanty data available clearly demonstrate high recurrence rates after Dx/HA injection, highlighting a need for close observation beyond the routine protocols and appropriate parental counseling upon endoscopic correction. Moreover, it seems that the algorithm for treating VUR is yet to be finally determined.

Conflict of interest

Dr. Chertin serves as a medical consultant with Promedon.

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References

[1] Kirsch AJ, Perez-Brayfield MR, Smith EA, Scherz HC. The modified sting procedure to correct vesicoureteral reflux: improved results with submucosal implantation within the intramural ureter. J Urol 2004;171:2413—6.
[2] Puri P, Chertin B, Murugesh V, Dass L, Colhoun E. Treatment of vesicoureteral reflux by endoscopic injection of dextranomer/hyaluronic acid copolymer (Deflux): preliminary results. J Urol 2003;170:1541—7.
[3] Chertin B, Colhoun E, Velayudham M, Puri P. Endoscopic treatment of vesicoureteral reflux. An eleven to seventeen years follow up. J Urol 2002;167:1443—7.
[4] Chertin B, Puri P. Endoscopic management of vesicoureteral reflux: does it stand the test of time? Eur Urol 2002;42: 598—606.
[5] Elmore JM, Kirsch AJ, Lyles RH, Perez-Brayfield MR, Scherz HC. New contralateral vesicoureteral reflux following dextranomer/hyaluronic acid implantation: incidence and identification of a high risk group. J Urol 2006;175:1097—2001.
[6] Routh JC, Vandersteen DR, Pfefferle H, Wolpert JJ, Reinberg Y. Single center experience with endoscopic management of vesicoureteral reflux in children. J Urol 2006; 175:1889—92.
[7] Elder JS, Shah MB, Batiste LR, Eaddy M. Part 3: endoscopic injection versus antibiotic prophylaxis in the reduction of urinary tract infections in patients with vesicoureteral reflux. Curr Med Res Opin 2007;23:S15—20.
[8] Stehr M, Schuster T, Pepperl S, Wallner CP, Dietz HG. Ureterocystoneostomy (UCN) and subureteral collagen injection (SCIN): combined one-stage correction of high-grade bilateral vesicoureteral reflux (VUR) in children. Eur J Pediatr Surg 2004;14:45—50.
[9] Chertin B, De Caluwé D, Puri P. Endoscopic treatment of primary grades IV and V vesicoureteral reflux in children with subureteral injection of polytetrafluoroethylene. J Urol 2003; 169:1804—7.
[10] Reunane M. Correction of vesicoureteral reflux in children by endoscopic collagen injection: a prospective study. J Urol 1995;154:2156—8.
[11] Haferkamp A, Contractor H, Möhring K, Staehler G, Dörsam J. Failure of subureteral bovine collagen injection for the endoscopic treatment of primary vesicoureteral reflux in long-term follow-up. Urology 2000;55:759—63.
[12] Oberson C, Boubaker A, Ramseyer P, Meyrat BJ, Frey P. Endoscopic and surgical treatment of vesico-ureteral reflux in children. Comparative long-term follow-up. Swiss Med Wkly 2007;137:471—5.
[13] van Capelle JW, de Haan T, El Sayed W, Azmy A. The long-term outcome of the endoscopic subureteric implantation of polydimethylsiloxane for treating vesico-ureteric reflux in children: a retrospective analysis of the first 195 consecutive patients in two European centres. BJU Int 2004;94:1348—51.
[14] Dodat H, Aubert D, Chavrier Y, Geiss S, Guys JM, Lacombe A, et al. Vesicoureteric reflux in children: long-term results of endoscopic treatment by Macroplastique injection. Prog Urol 2004;14:380—4.
[15] Bartoli F, Niglio F, Gentile O, Penza R, Aceto G, Leggio S. Endoscopic treatment with polydimethylsiloxane in children with dilating vesico-ureteric reflux. BJU Int 2006;97:805—8.
[16] Caldamone AA, Diamond DA. Long-term results of the endoscopic correction of vesicoureteral reflux in children using autologous chondrocytes. J Urol 2001;165:2224—7.
[17] Mevorach RA, Hulbert WC, Rabinowitz R, Kennedy WA, Kogan BA, Kryger JV, et al. Results of a 2-year multicenter trial of endoscopic treatment of vesicoureteral reflux with synthetic calcium hydroxyapatite. J Urol 2006;175:288—91.
[18] Läckgren G, Wählin N, Sköldenberg E, Stenberg A. Long-term followup of children treated with dextranomer/hyaluronic acid copolymer for vesicoureteral reflux. J Urol 2001;166:1887—92.
[19] Lee EK, Gatti JM, DeMarco RT, Murphy JP. Long-term followup of dextranomer/hyaluronic acid injection for vesicoureteral reflux: late failure warrants continued followup. J Urol 2009; 181:1869—74.
[20] Schmedding A, Zeeh U, Huebner U, Krause M, Lorenz C. Sx IN — prospective multicenter survey of subureteral injection in children. Presented at international conference on vesicoureteral reflex in children, June 4—6, Goteborg, Sweden; 2009.
[21] Matsumoto F, Shimada K, Harada Y, Naitoh Y. Split renal function does not change after successful treatment in

children with primary vesico-ureteric reflux. BJU Int 2003;92: 1006—9.
[22] Nepple KG, Austin JC, Hawtrey CE, Cooper CS. Kidneys with reflux nephropathy maintain relative renal function after ureteral reimplantation. J Urol 2005;174:1606—9.
[23] Webster RI, Smith G, Farnsworth RH, Rossleigh MA, Rosenberg AR, Kainer G. Low incidence of new renal scars after ureteral reimplantation for vesicoureteral reflux in children: a prospective study. J Urol 2000;163:1915—9.
[24] Yu TJ, Chen WF, Chen HY. Early versus late surgical management of fetal reflux nephropathy. J Urol 1997;157:1416—9.
[25] Wadie GM, Tirabassi MV, Courtney RA, Moriarty KP. The deflux procedure reduces the incidence of urinary tract infections in patients with vesicoureteral reflux. J Laparoendosc Adv Surg Tech A 2007;17:353—7.
[26] Traxel E, DeFoor W, Reddy P, Sheldon C, Minevich E. Multivariate analysis of risk factors for urinary tract infections after endoscopic injection of dextranomer hyaluronic acid. Presented at annual meeting of American Academy of Pediatrics, Section on Urology, Boston, Massachusetts; J Urol 2009;132(4):1703
[27] Chertin B, Natsheh A, Fridmans A, Shenfeld OZ, Farkas A. Renal scarring and UTI following successful endoscopic correction of vesicoureteral reflux. J Urol, in press, doi:10.1016/j.juro.2009.03.011.
[28] Elmore JM, Kirsch AJ, Heiss EA, Gilchrist A, Scherz HC. Incidence of urinary tract infections in children after successful ureteral reimplantation versus endoscopic dextranomer/hyaluronic acid implantation. J Urol 2008;179:2367—8.
[29] Sedberry-Ross S, Rice DC, Pohl HG, Belman AB, Majd M, Rushton HG. Febrile urinary tract infections in children with an early negative voiding cystourethrogram after treatment of vesicoureteral reflux with dextranomer/hyaluronic acid. J Urol 2008;180:1605—9.
[30] Chi A, Gupta A, Snodgrass WJ. Urinary tract infection following successful dextranomer/hyaluronic acid injection for vesicoureteral reflux. J Urol 2008;179:1966—70.
[31] Fanos V, Cataldi L. Antibiotics or surgery for vesicoureteral reflux in children. Lancet 2004;364:1720—2.
[32] Garin EH, Olavarria F, Nieto VG, Valenciano B, Campos A, Young L. Clinical significance of primary vesicoureteral reflux and urinary antibiotic prophylaxis after acute pyelonephritis: a multicenter, randomized, controlled study. Pediatrics 2006; 3:626—32.
[33] Pennesi M, Travan L, Peratoner L, Bordugo A, Cattaneo A, Ronfani L, et al. for the North East Italy Prophylaxis in VUR Study Group. Pediatrics 2008;121:e1489—94.
[34] Ormaechea M, Paladini M, Sambuelli R, Lopez S, Rossetti V, deBadiola F, et al. VANTRIS, a biocompatible, synthetic, non-biodegradable, bulking substance, easy to inject. Evaluation of local tissular reaction, localized migration and long-distance migration. Arch Esp Urol 2008;61:263—8.
[35] de Badiola F, Ruiz E, Ormaechea M, Denes E, Pioner G, Griguol O. Multicentric preliminary report for endoscopic treatment of vesico-ureteral reflux using polyacrylate—polyalcohol copolymer particles in glycerol and water (Vantris). J Pediatr Urol 2008;1:s20.