A Comparison Between Dextranomer/ Hyaluronic Acid and Polyacrylate Polyalcohol Copolymer as Bulking Agents for Treating Primary Vesicoureteral Reflux

Farshid Alizadeh[1], Iman Omidi[1], Saeid Haghdani[2]*, Mohammad Hatef Khorrami[1], Mohammad Hossein Izadpanahi[1], Mehrdad Mohammadi Sichani[1]

Purpose: In recent years, endoscopic subureteral injection has gained popularity as a therapeutic alternative to open surgery because of its high success rates and low morbidity. We compared the success and complication rates of Polyacrylate polyalcohol copolymer (PPC) and Dextranomer/Hyaluronic acid (Dx/HA) in the endoscopic treatment of VUR.

Materials & Methods: We retrospectively reviewed the patients who underwent endoscopic correction of their VUR by subureteric injection of PPC or Dx/HA from Jan 2010 to April 2016. The injection technique was STING (subureteric), distal HIT (intraureteric), and double HIT according the hydrodistention (HD) grade. The success rate, injection technique, injection volume, VUR grade, and obstruction rate were evaluated and compared between two groups.

Results: 107 renal refluxing units (RRU) with a mean age 55.23 ± 36.58 months and 64 RRU with a mean age 52.13 ± 31.66 months were treated in Dx/HA and PPC groups, respectively. The PPC group showed a more successful outcome in comparison to the Dx/HA group (92.2% versus 75.7% of the RRU with $P < .001$) at 3 months follow up. The injection technique was not significantly different between two groups. In PPC group the success rate was decreased significantly with increasing reflux grade but this reduction was not statistically significant in Dx/HA group. The injected volume was significantly more in PPC group; in addition, there was statistically significant correlation between injected volume of the bulking agent and obstruction rate. However, the obstruction rate did not establish significant difference between the two groups ($P = .83$), however it was earlier in Vantris (4 months versus 22 months).

Conclusion: Our investigation approved PPC as a more effective material, regardless of other confounding variables such as reflux grade, learning cure, and technique of injection, in endoscopic treatment of VUR. In addition, the other remarkable point is this effectiveness is not accompanied by more post-operation obstruction.

Keywords: vesicoureteral reflux; Dextranomer/ hyaluronic acid; polyacrylate polyalcohol copolymer; endoscopic treatment

INTRODUCTION

Vesicoureteral reflux (VUR), the abnormal flow of urine from the bladder into the ureters or kidneys, is the most common urological anomaly in children[1]. The primary goal of therapy in VUR is to prevent pyelonephritis which can lead to long-term sequelaes such as renal scarring, hypertension, reduced somatic growth, renal insufficiency and end-stage renal disease [2,3]. Treatment routes for VUR include observation, antibiotic prophylaxis, and surgical intervention[4,5]. Ureteroneocystostomy is the gold standard of surgical therapy with the success rate of greater than 95%[6]. In recent years, endoscopic subureteral injection has been introduced as a therapeutic alternative to open surgery because of its high success rates about 80-95%, low incidence of complications, its minimally invasive nature and short hospital stay [7-9]. This technique was initially described by Matouschek in 1981[10] and the first case series was reported by O'Donnell and Puri in 1984 [11]. Since then, different materials have been used in subureteral injection which include: collagen, polytetrafluoroethylene (Teflon®)[12], polydimethylsiloxane (Macroplastique®) [13], calcium hydroxyapatite (Coaptite®) [14], Dextranomer/Hyaluronic acid copolymer (Dx/HA, Deflux)[8] and recently, Polyacrylate polyalcohol copolymer[15].

In 2001, the Food and Drug Administration approved Dextranomer/Hyaluronic acid copolymer (Deflux; Q-Med Scandinavia, Uppsala, Sweden) for subureteral injection and thereafter, the endoscopic management of VUR has emerged as a first line treatment of VUR worldwide[8].

Dx/HA is a viscous biocompatible gel consisting of dextranomer microspheres of 80 to 120 µm in diameter and non-animal hyaluronic acid. The overall success rate, depending on the VUR grade, stated in the literature ranges between 68 and 92% [9,16]. In these conclusions, the long term recurrence rate of 10% to

[1]Department of Urology, Isfahan University of Medical Sciences (IUMS), Isfahan, Iran.
[2]Department of Urology, Hasheminejad Kidney Research Center (HKRC), Iran University of Medical Science, Tehran, Iran.
*Correspondence: Hasheminejad Kidney Research Center (HKRC), Iran University of Medical Science, Tehran, Iran.
Postal address: Hasheminejad Kidney Center, North Valiasr street, Vanak Square, Tehran, Iran.
Tel: +989133154014. Fax: +983136284154. Email: Saeed_haghdani@yahoo.com.
Received September 2017 & acceted May 2018

26% with Dx/HA propel researchers into another tissue-augmenting substance in order to reach better long-term efficacy in the endoscopic treatment of VUR[16-19]. Some have recommended that the biodegradable nature of Dx/HA is responsible for the concluding VUR recurrence [17]. Therefore, Polyacrylate polyalcohol copolymer (PPC, Vantris, Promedon, Cordoba, Argentina) as a new non-biodegradable tissue-augmenting substance was developed. Polyacrylate Polyalcohol Copolymer is a biocompatible agent with an average diameter of 300µm made of microparticles of PPC in glycerol and physiological solution [20]. The overall success rate of PPC in the literature was reported to be between 83.6% and 94.9% in the short-term follow-up[15,20,21]. In addition, one study with over three years follow up showed no VUR recurrence with PPC[21]. The comparative studies between these two agents in literature are rare[22-24]. There are controversial results in short term observations. While some studies presented PPC as the more successful substance, Pogorelic et al.[25] study showed no significant difference in cure rates between the Vurdex and PPC. In this study, we compared the success rate of PPC and Dx/HA in the endoscopic treatment of VUR with considering other suggested variables such as the injection technique and volume.

MATERIALS AND METHODS

We retrospectively reviewed the records of patients under the age of 15 years who fulfilled inclusion criteria of the study and underwent endoscopic correction of their VUR by a single pediatric urologist (FA) from Jan 2010 to April 2016. Before the April 2013, patients were treated by subureteric injection of PPC (43 patients, 64 RRU) and after that time, by Dx/HA injection (65 patients, 107 RRU).

Inclusion criteria included patients with diagnosis of unilateral or bilateral primary VUR grades II–V with breakthrough UTIs despite prophylactic antibiotics, persistent VUR after a period of observation, poor compliance with prophylactic antibiotics, and evidence of new renal scarring on a 99-m technetium dimercapto-succinic acid (DMSA) renal scan. Grade I VUR were treated only if accompanied by a contralateral higher grade reflux.

The first evaluation of patients after UTI or finding of hydronephrosis on ultrasound study was with voiding cystourethrography (VCUG) and reflux grading was performed according to the International Classification System (International Reflux Study Committee). The preoperative work-up included a detailed history and physical examination, a VCUG, a urinalysis and culture. Before surgery, all patients were evaluated for the presence of neurologic deficits, dysfunctional voiding and/or constipation. If any symptoms of enuresis, nocturia, urgency, frequency (documented by a voiding diary), postponement, holding maneuvers, urinary and/or fecal incontinence or constipation existed, a flowmetry/pelvic floor electromyography (EMG) was performed to check for the presence of dysfunctional voiding (DV). This test was also performed if increased bladder wall thickness (>3 mm with full bladder) or increased post-void residual urine were observed on ultrasound in the absence of active UTI or bladder outflow obstruction. A formal pressure-flow study was performed in patients with significant bladder wall trabeculation on VCUG or documented neurological abnormalities. All patients with proven DV were first treated by biofeedback-assisted pelvic floor muscle training.

We considered the VUR to be secondary if it was accompanied by a known neurologic deficit, severe form of DV (Hinman syndrome) or documented urethral obstruction (e.g. posterior urethral valve). Exclusion criteria were isolated grade I VUR, active UTI at the time of surgery, past history of open ureteroneocystostomy or subtrigonal injection of bulking agents, anatomical anomalies of the urinary tract (concomitant ureteropelvic junction obstruction, double urinary collecting system, ectopic ureter, posterior urethral valve) and alterations in bladder dynamics (untreated DV and neuropathic bladder).

The Committee of Ethics approved the protocol, and parents signed a written informed consent before operation.

Technique

In the operation room, cystoscopy was performed by a 8-9.8 Fr offset lens, Wolf cystourethroscope and if the ureteral orifice was in the extravesical position (not diagnosed on VCUG), the patient was considered ineligible for endoscopic surgery.

The injection technique was STING (subureteric) in the absence of hydrodistention (HD) of the ureteral orifice, distal HIT (intraureteric) when the HD was grade 1 or 2, and double HIT in the presence HD grade 3. A combination of HIT and STING was used whenever a slit-like orifice and disappearance of HD was not achieved by HIT alone. The material was injected until complete coaptation of the ureter was achieved and the type and volume of injected agent was recorded. The patient was discharged the evening of the day of surgery if no fever or significant hematuria was observed. After discharge from hospital, prophylactic oral cephalexin 15mg/Kg at bed time was prescribed until post-operative imaging showed reflux resolution or down-grading to Grade A on RNC.

Follow up study

Follow-up radionuclide cystography (RNC) was performed 3 months after the operation or after any episode of febrile UTI in patients who had been cured of their reflux. According to the protocol, repeat RNC in cured patients was performed only in the presence of febrile UTI or new-onset hydroureteronephrosis (HUN). Renal and bladder ultrasound was performed at the post-operative month one, every 3 months during the first year, every 6 months during the next 2 years and then, yearly. If a new-onset HUN or exacerbation of the previous one was observed, a repeat RNC and a Lasix renogram was requested. We devided post-operative ureteral obstruction into early and late. Early-onset obstruction presents with renal colic in the early post-operative period and resolves spontaneously, while late-onset obstruction presents with urinary tract infection, creatinine rise (in bilateral cases) or as an incidental finding on post-operative imaging.

Success was defined as complete VUR resolution. In patients with bilateral reflux, if resolution occurred in one side, the operation was considered to be failed.

Data were entered into the SPSS software (IBM Corporation, New York, United States), version 22. Fisher's exact test, Mann-Whitney *U* test, *t*-test and one-way ANOVA were used for analyzing the data.

Table 1. Demographic data and patients' characteristic in both groups.

Characteristics	PPC group	Dx/HA group	*P* value
Mean Age (months)	52.13 ± 31.66	55.23 ± 36.58	0.57
Sex			
Male	10(15.6%)	22(20.6%)	0.54
Female	54(84.4%)	85(79.4%)	
Laterality of VUR			
Left	35(54.7%)	53(49.5%)	0.53
Right	29(45.3%)	54(50.5%)	
Hx of UTI	60(93.8%)	81(75.7%)	0.003
pre-operative renal cortical scar	47(74.6%)	45(48.9%)	0.001

RESULTS

One hundred and seven RRU and 64 RRU were treated in Dx/HA and PPC groups, respectively. The demographic data and patients' characteristic are presented in **Table 1**. The success was achieved in 92.2% (59) RRU in PPC group and 75.7% (81) RRU in Dx/HA group ($P < .001$).

By Mann-Whitney test, in reflux grade in PPC group the success rate was decreased significantly with increasing reflux grade ($P = .04$) but this reduction was not statistically significant in Dx/HA group ($P = .30$). In post-operative period, early-onset obstruction was observed in 3 (4.7%) and 4 (3.7%) RRU in PPC and Dx/HA groups, respectively while late-onset ureteral obstruction occurred in 2 (3.1%) and 2 (1.9%) of RRU in PPC and Dx/HA groups, respectively. The obstruction rate did not establish significant difference between the two groups ($P = .83$). However, in patients with late-onset obstruction, the mean time from injection to obstruction was longer in Dx/HA group (22 moths vs. 4 months).

The Spearman analysis showed statistically significant correlation between injected volume of the bulking agent and obstruction rate in PPC group ($r=0.24$, $P = .04$); however, the Dx/HA group failed to confirm this relationship ($P = .52$).

During the follow-up, 4 patients (10.2%) in the PPC group and 7 patients (18.4%) in the Dx/HA group who had been cured of their VUR, developed febrile UTI that underwent repeat RNC. One patient (25%) in the former group showed recurrence of VUR while this figure was 4 (57%) in the latter group.

DISCUSSION

In our study the PPC group showed a more successful outcome (92.2% of the RRU and 90.6% of the patients) in comparison to the Dx/HA group (75.7% of the RRU and 58.4% of the patients). These results were in accordance with previous investigations. Karakus et al.[22] compared these two agents which revealed PPC promises higher resolution rate than Dx/HA (88.6% vs 70.3%), although the former group had markedly higher ureterovesical junction obstruction. In another comparative study, reflux resolved after the first Deflux injection in 63% of RRU and Vantris injection in 92.7% of RRU[24]. However, in Turk et al. study[23] the overall treatment success rate was 79% in Dx/HA group and 81% in PPC group which was not significantly different.

The overall success rate reported with use of Dx/HA ranged between 68–92% based on the VUR grade [8,16,24,26]. One study that examined Dx/HA, demonstrated a success rate of 78.5% for grades I and II, 72% for grade III, 63% for grade IV and 51% for grade V reflux which revealed this hypothesis that increasing the grade of reflux decrease the success rate of treatment with this material[27]. Although our result did not demonstrate any significant decrease in success rate in grade IV and V VUR in the Dx/HA group.

PPC comes from the family of Acrylics, particles of polyacrylate polyalcohol copolymer immersed in a glycerol and physiological solution carrier. When injected in soft tissues, it causes a bulkiness that remains stable[28]. A multicentric study comprising 88 renal units treated with PPC showed the overall success rate about 83.6%[20]. In Sencan study[29], the accumulative success rate after the injection of PPC at the end of the first year was 98.1%. Chertin et al. reported the success rate of PPC after a single injection as 94.9% [15]. They

Table 2. Procedural detail in both groups.

Variables	PPC group	Dx/HA group	*P* value
Injection technique			0.36
HIT	16 (25%)	40 (37.4%)	
Double HIT	6 (9.4%)	11 (10.3%)	
STING	20 (31.2%)	25 (23.4%)	
HIT+STING	22 (34.4%)	31 (29%)	
Injected volume(mL)	0.78 ± 0.39	0.58 ± 0.30	0.001
VUR Grade (RRU)			
I	2 (3.1%)	6 (5.6%)	0.93
II	11 (17.2%)	13 (12.1%)	
III	21 (32.8%)	42 (39.3%)	
IV	20 (31.2%)	27 (25.2%)	
V	10 (15.6%)	19 (17.8%)	
Follow up (months)	17.17 ± 12.81	18.81 ± 11.92	0.4

also demonstrate cure of reflux with a single injection in 92.1% of all patients in one year follow up. In Warchol study, reflux resolved in 93% of all treated RRUs after first procedure, and in 100% after the second procedure. For high grade VUR, that is IV and V, success was achieved in almost 90% after the first injection and 100% after the second injection[24]. Chertin et al. evaluated prospectively the long term efficacy of PPC in children with VUR which showed no VUR recurrence in 3 years of follow-up, while recurrence rate with Dx/HA ranges from 10% to 26% in long term follow up [21,30]. Radiographic investigation in the Sedberry-Ross et al. and Swedish Reflux Study also demonstrated high radiographic recurrence (27%-38%) that was attributed to biodegradable nature of Dx/HA[31,32].

The use of PPC to correct grades IV and V is also very efficient with an overall success rate achieved of over 80% [33,34]. But in our study the success rate decreased in PPC (but not the Dx/HA) group significantly with increasing reflux grade.

Technique of injection is suggested as another variable for success rate of materials in recent literature. Single subureteral transurethral injection (STING) technique was used first time in 1984 for the endoscopic treatment of pediatric VUR[35]. The suggested injection site is 2 to 3 mm below the affected ureteric orifice, at the 6 o'clock position. Hydrodistention Implantation Technique (HIT), which entails inserting the needle into the submucosal tunnel of the ureter via hydrodistention has been introduced in 2004 [16]. Kirsh et al. by using Hydrodistention Implantation Technique injection (HIT), showed the short-term results with the endoscopic correction close to those results after open surgery. A success rate of 92% using the HIT procedure compared with the 79% using the STING procedure was reported[16]. Yucel et al.[36] and Watters et al.[37] found no differences on VUR resolution rate between the two techniques. Double Hydrodistention Implantation Technique was also described by these researchers [38]. Double HIT, included two intraluminal ureteric tunnel injections which involves both proximal and distal intraureteral injections. Kalisvaart et al. revealed 96% clinical success with double HIT after 1 year of follow-up[38]. Akin et al.[39] observed a higher success rate with double HIT treatment compared to HIT. However, our data did not show significant difference between HIT and double HIT technique in either study groups. Another important factor, predicting the success rate of the procedure, is learning curve. In our study groups this variable was omitted because the same surgeon did the procedure in both groups after passing the learning curve during the fellowship training program. In fact, although Dx/HA injection was done after PPC injection, this group had lower success rate. Therefore, the effect of surgeon's experience as the cause of difference in success rate is precluded.

Complications following endoscopic injection are rare and including mainly obstruction of the vesicoureteric junction and development of a new contralateral VUR. In our Dx/HA group and PPC group 5.6% and 7.8% of patients developed obstruction respectively, with no statistically significant difference between them. Although several variables involve in the likelihood of obstruction, the amount of injection material was not related to obstruction frequency in our data. There is not unanimous result in this field and controversial observations have been presented up to now[40]. One difference was the mean time to obstruction that was longer in the Dx/HA group (22 vs. 4 months). This finding suggest that long-term follow-up should be rigorous, especially in patients who receive Dx/HA.

This study has some limitations such as small sample size of groups, lack of follow-up RNC after reflux resolution in all patients, non-randomized nature of the study and different inclusion criteria which contained more UTI history and scar formation in PPC group. These problems demand more studies with detailed date and longer follow up.

CONCLUSIONS

Our investigation approved PPC as a more effective material, regardless of other confounding variables such as reflux grade, learning cure, and technique of injection, in endoscopic treatment of VUR. In addition, the other remarkable point is this effectiveness is not accompanied by more post-operation obstruction.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Savage DC, Wilson MI, McHardy M, Dewar DA, Fee WM. Covert bacteriuria of childhood. A clinical and epidemiological study. Arch Dis Child. 1973;48:8-20.
2. Jacobson SH, Hansson S, Jakobsson B. Vesico-ureteric reflux: occurrence and long-term risks. Acta Paediatr Suppl. 1999;88:22-30.
3. Shaikh N, Ewing AL, Bhatnagar S, Hoberman A. Risk of renal scarring in children with a first urinary tract infection: a systematic review. Pediatrics. 2010;126:1084-91.
4. Al-Sayyad AJ, Pike JG, Leonard MP. Can prophylactic antibiotics safely be discontinued in children with vesicoureteral reflux? J Urol. 2005;174:1587-9; discussion 9.
5. Fanos V, Cataldi L. Antibiotics or surgery for vesicoureteric reflux in children. Lancet. 2004;364:1720-2.
6. Arant BS, Jr. Vesicoureteral reflux and evidence-based management. J Pediatr. 2001;139:620-1.
7. Capozza N, Caione P. Vesicoureteral reflux: surgical and endoscopic treatment. Pediatr Nephrol. 2007;22:1261-5.
8. Puri P, Chertin B, Velayudham M, Dass L, Colhoun E. Treatment of vesicoureteral reflux by endoscopic injection of dextranomer/hyaluronic Acid copolymer: preliminary results. J Urol. 2003;170:1541-4; discussion 4.
9. Chertin B, Kocherov S, Chertin L, et al. Endoscopic bulking materials for the treatment of vesicoureteral reflux: a review of our 20 years of experience and review of the literature. Adv Urol. 2011;2011:309626.
10. Matouschek E. [New concept for the treatment of vesico-ureteral reflux. Endoscopic application of teflon]. Arch Esp Urol.

1981;34:385-8.

11. O'Donnell B, Puri P. Treatment of vesicoureteric reflux by endoscopic injection of Teflon. Br Med J (Clin Res Ed). 1984;289:7-9.
12. Merckx L, De Boe V, Braeckman J, Verboven M, Piepsz A, Keuppens F. Endoscopic submucosal Teflon injection (STING): an alternative treatment of vesicoureteric reflux in children. Eur J Pediatr Surg. 1995;5:34-6.
13. Dodat H, Aubert D, Chavrier Y, et al. [Vesicoureteric reflux in children: long-term results of endoscopic treatment by Macroplastique injection]. Prog Urol. 2004;14:380-4.
14. Merrot T, Ouedraogo I, Hery G, Alessandrini P. [Preliminary results of endoscopic treatment of vesicoureteric reflux in children. Prospective comparative study of Deflux vs. Coaptite]. Prog Urol. 2005;15:1114-9.
15. Chertin B, Arafeh WA, Zeldin A, Kocherov S. Preliminary data on endoscopic treatment of vesicoureteric reflux with polyacrylate polyalcohol copolymer (Vantris(R)): surgical outcome following single injection. J Pediatr Urol. 2011;7:654-7.
16. Kirsch AJ, Perez-Brayfield M, 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.
17. 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; discussion 74-5.
18. Lackgren G, Wahlin N, Skoldenberg E, Stenberg A. Long-term followup of children treated with dextranomer/hyaluronic acid copolymer for vesicoureteral reflux. J Urol. 2001;166:1887-92.
19. Chertin B, Kocherov S. Long-term results of endoscopic treatment of vesicoureteric reflux with different tissue-augmenting substances. J Pediatr Urol. 2010;6:251-6.
20. Ormaechea M, Ruiz E, Denes E, et al. New tissue bulking agent (polyacrylate polyalcohol) for treating vesicoureteral reflux: preliminary results in children. J Urol. 2010;183:714-7.
21. Chertin B, Arafeh WA, Zeldin A, Ostrovsky IA, Kocherov S. Endoscopic correction of VUR using vantris as a new non-biodegradable tissue augmenting substance: three years of prospective follow-up. Urology. 2013;82:201-4.
22. Karakus SC, User IR, Kilic BD, Akcaer V, Ceylan H, Ozokutan BH. The comparison of dextranomer/hyaluronic acid and polyacrylate-polyalcohol copolymers in endoscopic treatment of vesicoureteral reflux. J Pediatr Surg. 2016;51:1496-500.
23. Turk A, Selimoglu A, Demir K, Celik O, Saglam E, Tarhan F. Endoscopic treatment of vesicoureteral reflux with polyacrylate polyalcohol copolymer and dextranomer/hyaluronic acid in adults. Int Braz J Urol. 2014;40:379-83.
24. Warchol S, Krzemien G, Szmigielska A, Bombinski P, Brzewski M, Dudek-Warchol T. Comparison of results of endoscopic correction of vesicoureteral reflux in children using two bulking substances: Dextranomer/hyaluronic acid copolymer (Deflux) versus polyacrylate-polyalcohol copolymer (Vantris). J Pediatr Urol. 2016;12:256 e1-4.
25. Pogorelic Z, Gudelj K, Budimir D, et al. Comparison of dextranomer/hyaluronic acid based bulking agents in the treatment of vesicoureteral reflux in children: Deflux versus Vurdex. Can J Urol. 2016;23:8312-7.
26. Chertin B, Colhoun E, Velayudham M, Puri P. Endoscopic treatment of vesicoureteral reflux: 11 to 17 years of followup. J Urol. 2002;167:1443-5; discussion 5-6.
27. 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 Suppl 4:S15-20.
28. Ormaechea M, Paladini M, Pisano R, et al. Vantris, a biocompatible, synthetic, non-biodegradable, easy-to-inject bulking substance. Evaluation of local tissular reaction, localized migration and long-distance migration. Arch Esp Urol. 2008;61:263-8.
29. Sencan A, Ucan B, Evciler H, Serdaroglu E, Hosgor M. Early results of endoscopic treatment of vesicoureteral reflux with polyacrylate polyalcohol copolymer. Urol Int. 2014;92:219-22.
30. Chertin B, Abu Arafeh W, Kocherov S. Endoscopic correction of complex cases of vesicoureteral reflux utilizing Vantris as a new non-biodegradable tissue-augmenting substance. Pediatr Surg Int. 2014;30:445-8.
31. 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; discussion 10.
32. Holmdahl G, Brandstrom P, Lackgren G, et al. The Swedish reflux trial in children: II. Vesicoureteral reflux outcome. J Urol. 2010;184:280-5.
33. De Badiola FI, Soria R, Vagni RL, Ormaechea MN, Moldes JM, Benmaor C. Results of Treatment of Grades IV and V Vesicoureteral Reflux with Endoscopic Injection of Polyacrylate Polyalcohol Copolymer. Front

Pediatr. 2013;1:32.

34. Kocherov S, Ulman I, Nikolaev S, et al. Multicenter survey of endoscopic treatment of vesicoureteral reflux using polyacrylate-polyalcohol bulking copolymer (Vantris). Urology. 2014;84:689-93.

35. Puri P, Ninan GK, Surana R. Subureteric Teflon injection (STING). Results of a European survey. Eur Urol. 1995;27:71-5.

36. Yucel S, Gupta A, Snodgrass W. Multivariate analysis of factors predicting success with dextranomer/hyaluronic acid injection for vesicoureteral reflux. J Urol. 2007;177:1505-9.

37. Watters ST, Sung J, Skoog SJ. Endoscopic treatment for vesicoureteral reflux: how important is technique? J Pediatr Urol. 2013;9:1192-7.

38. Kalisvaart JF, Scherz HC, Cuda S, Kaye JD, Kirsch AJ. Intermediate to long-term follow-up indicates low risk of recurrence after Double HIT endoscopic treatment for primary vesico-ureteral reflux. J Pediatr Urol. 2012;8:359-65.

39. Akin M, Erginel B, Karadag CA, et al. A comparison of the double hydrodistention implantation technique (HIT) and the HIT with a polyacrylate/polyalcohol copolymer (PPC) for the endoscopic treatment of primary vesicoureteral reflux. Int Urol Nephrol. 2014;46:2057-61.

40. Alizadeh F, Mazdak H, Khorrami MH, Khalighinejad P, Shoureshi P. Postoperative ureteral obstruction after endoscopic treatment of vesicoureteral reflux with polyacrylate polyalcohol copolymer (Vantris(R)). J Pediatr Urol. 2013;9:488-92.