Journal of Pediatric Surgery 51 (2016) 1496–1500

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

The comparison of dextranomer/hyaluronic acid and polyacrylate-polyalcohol copolymers in endoscopic treatment of vesicoureteral reflux

Suleyman Cuneyt Karakus [a,*], İdil Rana User [a], Beltinge Demircioglu Kılıc [b], Vedat Akçaer [a], Haluk Ceylan [a], Bulent Hayri Ozokutan [a]

[a] University of Gaziantep, Faculty of Medicine, Department of Pediatric Surgery, Gaziantep, Turkey
[b] University of Gaziantep, Faculty of Medicine, Department of Pediatric Nephrology, Gaziantep, Turkey

ARTICLE INFO

Article history:
Received 13 January 2016
Received in revised form 24 February 2016
Accepted 25 February 2016

Key words:
Vesicoureteral reflux
Dextranomer
Polyacrylate-polyalcohol
STING
Double HIT

ABSTRACT

Background: Dextranomer/hyaluronic acid (Dx/Ha;Dexell®) and polyacrylate-polyalcohol copolymer (PPC;Vantris®) are the popular tissue-augmenting substances using for the endoscopic injections of vesicoureteral reflux (VUR). The aim of the study is to evaluate and compare Dx/Ha and PPC in terms of effectiveness, injection techniques and complications with special emphasis on vesicoureteral junction obstruction (VUJO).
Methods: A total of 95 patients who underwent endoscopic VUR treatment between 2009 and 2015 were retrospectively reviewed. The patients were divided into two groups: group 1: Patients underwent endoscopic treatment with PPC (n = 50 patients, 70 renal refluxing units) group 2: Patients underwent endoscopic treatment with Dx/Ha (n = 45 patients, 74 renal refluxing units).
Results: The overall resolution rates based on the number of renal refluxing units studied was 88.6% and 70.3% in group 1 and group 2, respectively. Resolution rates were significantly better in group 1 compared to group 2. VUJO requiring ureteral reimplantation or stent insertion developed in 7 patients in group 1. No VUJO was observed in group 2. VUJO in group 1 was markedly higher than that in group 2.
Conclusions: Endoscopic treatment of VUR with PPC promises better resolution rates but higher VUJO rates compared to Dx/Ha.

Since the description of endoscopic correction for the treatment of vesicoureteral reflux (VUR) by Matouschek in 1981, the minimally invasive treatment of VUR has gained worldwide acceptance with a high success rate [1,2]. Debate over the ideal bulking agent in endoscopic correction has still been going on. Dextranomer/Hyaluronic acid copolymer (Deflux®; Q-Med Scandinavia Inc., Uppsala, Sweden) is the most popular and the only US Food and Drug Administration-approved bulking agent. Positively charged dextranomer/cross-linked hyaluronic acid sodium salt (Dx/Ha; Dexell®; İstem Medikal; Ankara, Turkey) has been used as an alternative to Deflux. Dx/Ha is a non-immunogenic, biodegradable injectable agent with no reported distant migration. The failure rate of up to 22–28.2% and the higher recurrence rates after using Dx/Ha in the endoscopic treatment of VUR prompted the investigation of new tissue-augmenting substances such as polyacrylate-polyalcohol copolymer (PPC; Vantris®, Promedon, Córdoba, Argentina) [3–5]. PPC is a synthetic, biocompatible, non-absorbable bulking agent and consists of polyacrylate-polyalcohol copolymer particles immersed in a carrier that contains 40% glyserol. The high average size of PPC particles (300 μm) prevents distant migration.

The aim of this study is to evaluate and compare Dx/Ha (Dexell®) and PPC (Vantris®) in terms of effectiveness, injection techniques and complications with special emphasis on ureteral obstruction.

1. Material and methods

A total of 95 patients (69 female, 26 male) who underwent endoscopic VUR treatment at Gaziantep University Hospital and Gaziantep Children's Hospital between November 2009 and April 2015 were retrospectively reviewed. The study was approved by the local ethics committee (Conclusion no: 30.11.2015/332).

Patients with history of previous open antireflux surgery and anatomical anomalies including posterior urethral valve and ectopic ureter were excluded from the study. The reflux grade in voiding cystouretrography (VCUG) was based on the International Classification System of International Reflux Study Committee. Preoperative differential dimercaptosuccinic acid (DMSA) uptake of refluxing renal units (RRU) were noted.

Surgery was indicated in patients with breakthrough urinary tract infection, progressive renal scarring, nonresolution of VUR and with

* Corresponding author at: Gaziantep University, Faculty of Medicine, Department of Pediatric Surgery, 27310, Gaziantep, Turkey. Tel.: +90 505 7769416; fax: +90 342 3600290.
E-mail address: sckarakus@yahoo.com (S.C. Karakus).

http://dx.doi.org/10.1016/j.jpedsurg.2016.02.092
0022-3468/

parental decision. PPC or Dx/Ha copolymer bulking agents were used. The selection criteria of the agent was dependent on the availability of the material purchased by the hospital based on the repayment conditions of the social security system and public procurement law. Because of the same reason, cost-effective Dexell was preferred to Deflux. Endoscopic treatment was performed under general anesthesia with a pediatric cystoscope (KARL STORZ GmbH & Co KG) and classical subureteric Teflon injection (STING) method or double hydrodistention implantation technique (HIT) were used. All the procedures were performed under the consultancy of first author. There were no complications associated with the endoscopic procedure. Patients were discharged from hospital on the same day. During the follow-up, ultrasonography was performed on the postoperative 10th day in order to exclude early vesicoureteral junction obstruction (VUJO). Patients were then observed by ultrasonography with 3-months interval. All children were evaluated with VCUG and DMSA at the 3rd to 6th postoperative month. Antibiotic prophylaxis was maintained until the resolution of VUR was documented on VCUG. The resolution of VUR on VCUG was considered successful, but downgrade of VUR was accepted as failure.

The patients were divided into two groups:

Group 1: Patients underwent endoscopic treatment with PPC (n = 50 patients, 70 RRUs).

Group 2: Patients underwent endoscopic treatment with Dx/Ha (n = 45 patients, 74 RRUs).

The data collected included age, gender, side of RRU, bilaterality, grade of VUR, differential DMSA uptake, volume of bulking agent, type of injection technique, operation time, follow-up time, success of procedure and complications. The statistical analyses were performed using the SPSS ver. 15.0 (SPSS Inc., Chicago, IL, USA). The data were expressed as the mean ± standard deviation. Mann–Whitney U, chi-square and t tests were used for the statistical analysis. $p < 0.05$ was accepted as statistically significant.

2. Results

Preoperative demographic characteristics of patients are given in Table 1. A total of 50 children (34 female, 16 male) in group 1 and 45 children (35 female, 10 male) in group 2 were evaluated. There was no statistical difference between the groups in terms of sex, mean age of children, side of RRU (right/left ratio), differential DMSA uptake and grade of VUR. The mean volume of bulking agent used per RRU in endoscopic treatment was 0.6 ± 0.36 ml and 0.67 ± 0.35 ml in group 1 and group 2, respectively. The difference was not significantly different (p = 0,237). The mean operation time was 25.46 ± 5.2 min (range, 16–35 min) and 26.16 ± 5.06 min (range, 16–36 min) in group 1 and group 2, respectively (p = 0.405). The mean follow-up time (17.9 ± 5.3 months in group 1 and 19.91 ± 9.72 months in group 2) was not statistically different (p = 0.211). The overall resolution rates based on the number of RRUs after up to three endoscopic treatments were 88.6% (62/70) and 70.3% (52/74) in group 1 and group 2, respectively. Resolution rates were significantly better in group 1 compared to group 2 (p = 0.007). Three of 50 patients in the first group and 2 of 45 patients in the second group presented with febrile urinary tract infection requiring intravenous antibiotic treatment in the postoperative period. This was not statistically significant (p = 0.735).

Table 1
Summary of patient characteristics.

Variables	Group 1	Group 2	p
No. of patients/RRUs	50/70	45/74	
Male/Female	16/34	10/35	0.286
Mean age (years), (range)	6.02 ± 3.34 (3mo–15y)	5.47 ± 3.36 (9mo–15y)	0.428
Unilateral/Bilateral	30/20	16/29	0.017
Side of RRU (right/left)	32/38	33/41	0.893
Grade of VUR (RRUs) (%)			0.165
I	4	1	
II	3	8	
III	26	35	
IV	24	21	
V	13	9	
Differential DMSA uptake,% (range)*	44.87 ± 21.79 (7–100)	47.12 ± 19.24 (5–93)	0.512

RRU: renal refluxing unit, VUR: vesicoureteral reflux, DMSA: dimercaptosuccinic acid.
* Differential DMSA uptake of RRUs was reported > 50% because of the renal scarring of the contralateral RRU in some of the bilateral VUR.

VUJO requiring ureteral reimplantation or stent insertion developed in 7 patients in group 1. No VUJO was observed in group 2. VUJO in group 1 was markedly higher than that in group 2 (p = 0.005). Sex, side of RRU, grade of VUR and mean volume of bulking agent used per RRU were not statistically significant in the development of VUJO in group 1 (p = 0.666, p = 0.522, p = 0.191 and p = 0.730, respectively). The mean age of the patients with and without VUJO following endoscopic treatment was 3.79 ± 1.95 years (range, 18 months–6 years) and 6.39 ± 3.39 years (range, 3 months–15 years), respectively and this difference was statistically significant (p = 0.036). In group 1, VUJO was observed in 6 of 34 RRUs treated with double HIT and in only 1 of 36 RRUs treated with STING method. VUJO was significantly higher in double HIT compared to STING method in group 1 (p = 0.030).

Characteristics of patients with VUJO are given in Table 2. The mean duration time between endoscopic treatment and the incurrence of VUJO was 8.86 ± 5.18 months (range, 4–18 months). Five of the patients manifest with hydroureteonephrosis in the follow-up ultrasonographies performing 3-months interval and 2 of them presented with anuria, requiring percutaneous nephrostomy in one and double J stent insertion in another. Five of the patients with VUJO resolved by stent insertion, whereas 2 of them underwent open ureteroneocystostomy. In both patients, extensive extravesical and intravesical dissection was performed in order to free the ureters from bladder wall owing to the inflammatory response to PPC. Distal 3 cm of both ureters was significantly narrowed. Modified Paquin technique was performed following the excision of narrowed ureteral segments in both patients. The histopathologic analysis of the narrowed ureteral segments showed chronic inflammation in the submucosal layer and significantly narrowed ureteral lumen in one patient (Fig. 1), and subepithelial chronic inflammation with thin and irregular muscular layer in another patient (Fig. 2). One patient whose differential DMSA function was 38% preoperatively, was lost to follow-up for 6 months. She showed total loss of function on the ipsilateral kidney because of VJUO. Unfortunately, differential function increased to 12% following open ureteroneocystostomy.

3. Discussion

Since the introduction of subureteric injections using polytetrafluoroethylene paste (PTFE; Teflon, DuPont Co., Wilmington, DE) by Puri and O′Donnell, this simple, minimally invasive and outpatient procedure with resolution rates up to 90% has become the firstline therapy in the surgical management of children with all grades of VUR [2]. After the popularization of STING clinically, different bulking agents utilized for endoscopic correction of VUR have been described. Despite of the data showing the long-term efficacy of PTFE as a bulking agent, the possibility of PTFE particle migration eliminated the use of this material in the treatment of VUR [6]. The low long-term success rates of collagen, polydimetylsiloxane and calcium hydroxyapatite prompted the investigation of a new promising substance [7–9]. Dx/Ha is the only tissue-augmenting agent approved by Food and Drug Administration in the endoscopic treatment of VUR. Deflux® is a biocompatible and biodegradable implant which consists of dextranomer microspheres in a carrier gel of stabilized hyaluronic acid. The dextranomer microspheres range in size between 80 and 250 μm with an average size of about 130 μm. Dexell® is another non-allergic, non-immunogenic and biodegradable Dx/Ha copolymer that consists of cross-linked dextranomer particles with a size of 80–120 μm size. These particles have positively