



Factors affecting the success of endoscopic treatment of vesicoureteral reflux and comparison of two dextranomer based bulking agents: Does bulking substance matter?

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Summary

Introduction

Among the interventional treatment modalities for vesicoureteral reflux (VUR), endoscopic subureteric injection seems to be the least invasive method with acceptable outcomes when applied in appropriate patients.

Objective

The aim of the presented study is to investigate the parameters which may affect the outcomes of endoscopic injection and to compare the efficacy of two different bulking agents both composed of dextranomer-hyaluronic acid copolymer.

Study design

The data of patients who underwent endoscopic VUR treatment between 2003 and 2012 were retrospectively reviewed. Patients with history of previous open antireflux surgery, more than one failed endoscopic treatment for reflux, VUR caused by posterior urethral valve, duplex system and overt spinal dysraphism were excluded. Surgical technique was the classical STING method. One of the two dextranomer-hyaluronic acid copolymer agents was used (Deflux in 109 and Dexell in 131 patients). Both agents were composed of similar amounts of hyaluronic acid gel (15 mg in Deflux versus 17 mg in Dexell) but different sized dextranomer microspheres (80–250 μm in Deflux and 80–120 μm in Dexell). During the follow-

up, ultrasonography was performed with 3-month interval, antibiotic prophylaxis was continued until the control voiding cystourethrography (VCUG) was taken. Patient based success was defined as the disappearance of reflux on control VCUG performed 3–6 months after the operation.

Results

Data were available for 240 patients. Mean age and mean postoperative follow-up were 78 ± 41 months and 19 ± 18 months. The overall success rate was 73.2%. Gender, laterality, grade of VUR, presence of voiding dysfunction, renal scar and preoperative breakthrough infection (BTI) were not found to affect the outcome, whereas age younger than 54 months and previous history of failed endoscopic injection were found to negatively affect the outcome both in univariate and multivariate analysis. The postoperative UTI (5 febrile and 43 non-febrile) rate was 20%. Both univariate and multivariate analysis showed that postoperative UTI was more common in patients with persisting reflux, with preoperative breakthrough infections and in girls. Patient characteristics, treatment outcome and postoperative UTI rate were similar regarding the used bulking agent. No ureteral obstruction was experienced within the follow-up period.

Discussion

Our success rate for second injection is about 60%, which is significantly lower than for the patients who

Table Comparison of treatment success regarding several factors (chi-square test).

Male vs female	%66 vs 75.4	$p = 0.174$
Age < 54 m vs > 54 m.	%65.7 vs 78.5	$p = 0.043^{**}$
Unilateral vs bilateral	%77.5 vs 67.6	$p = 0.087$
Grade 1–2 vs 3 vs 4–5	%77.9 vs 73 vs 67.4	$p = 0.455$
Grade 1–2–3 vs 4–5	%74.7 vs 67.4	$p = 0.311$
VD, no vs yes	%80 vs 78.1	$p = 0.774$
Scar, no vs yes	%72 vs 72.4	$p = 0.941$
BTI, no vs yes	%73 vs 74.5	$p = 0.806$
Deflux vs Dexell	%75.2 vs 71.8	$p = 0.545$
Previous failed STING, no vs yes	%75.9 vs 59.5	$p = 0.038^{**}$

BTI = breakthrough infection; VD = voiding dysfunction. * p is lower than 0.05 by chi-square test.

underwent first injection. We could not find any affecting factor for this difference. Contrary to the literature, our success rates were similar in different reflux grades. We can explain this finding that we value the intraoperative orifice configuration more than the grade which can be accepted as a patient selection bias. The lower success rate in children younger than 54 months can be explained by unstabilized bladder dynamics and higher voiding pressures in this age group, who are still in the toilet-training phase. Despite successful endoscopic treatment, UTI might occur. Postoperative UTI was more common in patients with persisting reflux, preoperative BTI and girls. The similar success rates of both bulking agents proved that dextranomer size does not affect the clinical outcome. Limitations of our study can be counted as follows: 1. the data do not include the number of patients in whom conversion to open

surgery was decided intraoperatively because of the unfavorable orifice configuration, 2. our data do not include the injected volume records.

Conclusion

Endoscopic treatment of VUR has satisfying outcomes in properly selected cases. Younger age (<54 months) and previous history of failed injection history were found to be related to unfavorable results. Postoperative UTI occurs more frequently in patients with persisting reflux, preoperative breakthrough infection history and girls. The choice of one of the dextranomer-based substances does not affect the surgical outcome and postoperative UTI development.

Introduction

Vesicoureteral reflux (VUR) is one of the most important causes of pediatric nephropathy in many countries including ours [1,2]. Understanding the physiopathology and course of the disease has led to conservative management of most patients. However, there remains a group of patients with recurrent febrile urinary tract infections (UTI) under antibiotic prophylaxis, whose chance of spontaneous resolution is unlikely and whose kidneys are scarred, who require interventional treatment modalities [3,4]. The interventional modalities include open, endoscopic and laparoscopic approaches. Among these, endoscopic subureteric injection seems to be the least invasive method with acceptable outcomes when applied in appropriate patients [5,6].

The aim of the present study is to investigate the parameters which may affect the outcomes of endoscopic injection, and to compare the efficacy of two different bulking agents both composed of dextranomer-hyaluronic acid copolymer.

Materials and methods

We reviewed the data of patients who underwent endoscopic injection between 2003 and 2012 for treatment of VUR. Patients with history of previous open antireflux surgery, more than one failed endoscopic treatment for reflux, secondary VUR caused by posterior urethral valve, duplex system and overt spinal dysraphism were excluded. Data were available for 240 patients, and these were recorded to a standard sheet. Preoperative patient characteristics are given in Table 1. Reflux was classified as low (grade 1–2), moderate (grade 3) and high (grade 4–5). Voiding dysfunction was defined as the presence of lower urinary

tract symptoms (presence of urge, incontinence, weak stream, hesitancy, frequency and urinary tract infections, but without overt uropathy or neuropathy) in children older than 5 years evaluated by symptom score [7] or urodynamic study. Behavioral modification and/or medical treatment were given appropriately before any intervention.

Surgery was indicated in patients with recurrent febrile urinary tract infections under antibiotic prophylaxis, whose chance of spontaneous resolution is unlikely, whose kidneys are scarred and with parental decision. Surgical technique was the classical STING method performed by or under supervision of one of the pediatric urologists (S.T and H.S.D) [8]. One of the two dextranomer-hyaluronic acid copolymer agents (Deflux in 109 and Dexell in 131 patients) was used. Both agents used in this series were highly viscous and were composed of similar amounts of hyaluronic acid gel (15 mg in Deflux versus 17 mg in Dexell) but different sized dextranomer microspheres (80–250 μm in Deflux and 80–120 μm in Dexell). The selection of the agent was dependent on the availability of the material in the hospital, in accordance with the reimbursement conditions of the social security system. As ours is a referral center, most of our patients live in other geographic areas of the country. Therefore, after the procedure patients were hospitalized for an average of 1 day (0–2). During the follow-up, ultrasonography was performed with 3-month interval, antibiotic prophylaxis was continued until the control voiding cystourethrography (VCUG) was taken. Patient-based success was defined as disappearance of reflux on control VCUG, which was performed 3–6 months after the operation.

Effects of several parameters were examined on outcome. The SPSS 15.0 software program was used to perform statistical analysis. Mann–Whitney, chi-square and *t* tests were used where appropriate and logistic regression analysis was used for multivariate analysis. A *p* value < 0.05 was used for determination of statistical significance. Multicollinearity status between the parameters found to be significant in multivariate analysis was investigated by collinearity statistics. A calculated variance inflation factor (VIF) value of more than 5 indicated a multicollinearity problem.

Ethical approval was not required for this study.

Results

Mean age of the patient and mean postoperative follow-up was 78 ± 41 months and 19 ± 18 months. The overall

Table 1 Patient characteristics.

Sex (m/f), <i>n</i>	53/187
Unilateral/bilateral, <i>n</i>	138/102
Reflux grade (1–2/3/4–5), <i>n</i>	68/126/146
Breakthrough infection, %	47
Scar, %	44
Voiding dysfunction, %	49
Previous STING history, %	15.7
Deflux/Dexell, <i>n</i>	109/131

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