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Does intraoperative success predict outcome in the treatment of urethral sphincter insufficiency with bulking agent?

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Summary

Introduction
Sphincter insufficiency is mostly associated with neurogenic and some structural abnormalities in the pediatric population. As a mini-invasive treatment, urethral bulking agents have been used to treat this problem.

Objective
The aim was to evaluate if technical success, defined as intraoperative increase in abdominal leak point pressure (ALPP), predicts the outcome of the treatment of sphincter insufficiency with urethral bulking agent.

Study design
We reviewed all children treated first time with dextranomer/hyaluronic acid (Dx/HA) copolymer (Deflux) for urethral sphincter insufficiency and who intraoperatively had ALPPs measured during 2004–2014. Patient characteristics, change in urinary continence and the duration of the possible response were evaluated in neurogenic and non-neurogenic cases.

Results
The median age of the patients was 7.8 years (range 4.1–14.5) at initial treatment and median volume of Dx/HA instilled was 3.5 mL (IQR 2–5). Twelve patients had neurogenic disease and 15 had non-neurogenic disease. Median ALPPs before and after the injections were 19 cmH_2O (IQR 14–28) and 70 cmH_2O (IQR 48–80), $p < 0.001$. Increases in ALPPs were similar in both patient groups ($p = 0.661$) and in 17 patients with any response and 10 patients with no response ($p = 0.267$). In patients with any response the median duration of the response was only 0.8 years (IQR 0.09–2.0). During a median follow-up of 4.9 years (range 1.7–11.8), 15 patients received one to three repeat injections and eight patients went through sling or bladder neck operation (Summary table). During repeat injections, the preoperative ALPPs had returned to the original levels. Currently, 20% are continent or almost continent with one or more Dx/HA injections. In half of the patients with neurogenic bladder, compliance or volume deteriorated slightly in follow-up. Five out of 15 patients who reached puberty become continent spontaneously after failed bladder neck injection.

Discussion
Intraoperative ALPPs increased significantly in most patients during the procedure. However, only 52% of the patients experienced more than 1 month of success after the procedure, and even in those the effect lasted mostly under a year. With one to four injections one-fifth seem to have had a good long-term result. Although the long-term success rate is limited, bulking agent injection allowed the patients with spontaneous voiding to continue it and the injection did not prevent future treatments.

Conclusion
Intraoperative increased ALPP does not predict a good long-term outcome after Dx/HA injection. At the end, only a fifth of our patients had good result with one or more Dx/HA injections. A change in bladder behavior is possible after treatment.

Summary table Response rates (any response) 1 month after repeat Dx/HA injections for urinary incontinence.

Response rate (*n*)			
Patient group	1st injection	2nd injection	3rd injection
Neurogenic	7/12	5/5	
Male	5/9	4/4	
Female	2/3	1/1	
Non-neurogenic	7/15	6/10	1/6
Male	6/12	6/9	1/6
Female	1/3	0/1	

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Introduction

A cornerstone in the treatment of urinary continence in children relies on a low-pressure bladder with appropriate outlet resistance. Urethral sphincter insufficiency is one of the major determinants of urinary incontinence in children, mainly for neurogenic bladder and some rare structural abnormalities. Because procedures increasing the bladder outlet resistance may increase bladder pressures, they are recommended only when detrusor activity is controlled [1]. In addition to surgical therapies, such as sling operations and bladder neck operations, minimally invasive procedures with bulking agents have become options in the treatment of sphincteric insufficiency [2–4]. Previous reports on urethral bulking in children have presented improvement in continence in about half of patients with neurogenic bladder with various materials [4,5]. However, only limited value has been observed as a secondary operation after failed sling procedures [6].

We have treated children with sphincter insufficiency by dextranomer/hyaluronic acid copolymer (Dx/HA, Deflux) injections since 1995. In 2004 we started to register intraoperative abdominal leak point pressure (ALPP) measurements to improve the results and to validate that outlet resistance increases during the procedure. In this study, we wanted to determine if clinical success is dependent on initial intraoperative result or the in situ permanence of the bulking agent. The increase in ALPP intraoperatively was considered to reflect technical success. In addition, we wanted to evaluate the long-term benefits from the therapy and which patients may benefit from therapy.

Materials and methods

We analyzed all 27 patients undergoing first time endoscopic injection by a single urologist (S.T.) with Dx/Ha for urethral sphincter insufficiency during 2004–2014, when ALPPs were measured before and after the injection during the procedure. The study was approved by the institutional ethics committee. The patients were divided to two groups: neurogenic (12 patients) and non-neurogenic (15 patients). Within the neurogenic group, nine patients had myelomeningocele and one each had either lipomeningocele, spinal trauma, or post-infectious paraparesis (9 were males and 3 females). Within the non-neurogenic group, there were five bladder exstrophy patients: nine had epispadias and one had been operated because of ectopic ureter (12 were males and 3 females). The inclusion criteria for injection therapy were symptoms suitable to sphincter insufficiency. In addition, adequate bladder volume for age (>80% of the expected capacity for the age) and low-pressure bladder in the neurogenic group. In the neurogenic group eight patients were on anticholinergic medication and three had undergone ileocystoplasty. Because leak point pressures were close to zero in all patients in the non-neurogenic group and the urodynamic studies were done without an occlusion catheter, we did not apply the criteria for bladder volume in that group. All patients in the neurogenic group were on clean intermittent catheterization (CIC) and all patients in the non-neurogenic group were voiding spontaneously. Prior bladder neck surgery was not done for any patients in the neurogenic group, nor for four out of nine patients in the epispadias group, because of distal epispadias and not for the patient with ectopic ureter. Two out of five patients with bladder exstrophy had had no bladder neck surgery after the primary reconstruction. The remaining three had undergone separate bladder neck reconstruction. Preoperatively, medical history, incontinence charts, urine cultures, urinary ultrasound, and urodynamic investigation were performed.

Patients were under general anesthesia for endoscopic treatment. Injections were performed using pediatric cystoscopes with a working channel and a 0-degree lens, with a flexible needle (Cook Williams Cystoscopic Injection Needle, 3.7 F × 23G, Cook Medical, Bloomington, IN, USA), with a median instilled volume of 3.5 mL (range 0.8–6, IQR 2–5).

Males were injected under the epithelium around the bladder neck in males if it was closing to some degree, and if the bladder neck was very wide along the prostatic urethra or external sphincter. Females were injected mid-urethra. ALPPs were intraoperatively measured before and after injections through a suprapubic catheter and manually compressing a half-full bladder until leakage occurred. A suprapubic catheter was left for 3–5 days to drain the bladder after the injection.

Postoperative results were collected during the control visits, and voiding/catheterization charts were utilized to clarify incontinence. Also, urine cultures and ultrasound were analyzed at these visits. The incontinence score was recorded on a scale from 0 to 3 (0, completely dry; 1, wet less than once a day; 2, wet for less than 50% of the time between daily catheterizations/micturition; and 3, wet for more than 50% of the time between catheterizations/micturition) before treatment and at control visit 1–3 months after treatment [7]. In addition, initial success was evaluated according to the recommendation of the ICCS: Nonresponse (NR) 0–49% decrease, partial response (PR) 50–99%, and complete response (CR) is defined as a 100% decrease in symptoms [8]. The patient was considered to have any response, if the response was CR or PR at least for 2 weeks after the injection. In addition, follow-up data after the first treatment were collected (duration of response, number of patients having repeat injections, and number of patients requiring surgery). In the case of repeat injections the clinical result was re-evaluated.

Statistical analysis was performed using the Fisher exact test for categorical variables and the Mann–Whitney test or Wilcoxon Signed rank test (in the case of repeat measurements) for continuous variables. A p value < 0.05 was taken to be significant.

Results

The median age of the 27 patients was 7.8 years (range 4.1–14.5 years) at initial treatment. The median bladder volume for all patients was 190 mL (IQR 134–338 mL), and a median 97% (IQR 69–138) in relation to the expected bladder volume. Bladder volumes were larger within the neurogenic group, 291 mL (IQR 205–533) versus 133 mL (IQR 97–259), $p = 0.004$). The median maximal detrusor pressure during cystometry was 14 cmH_2O (IQR 8–15.5) in the

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