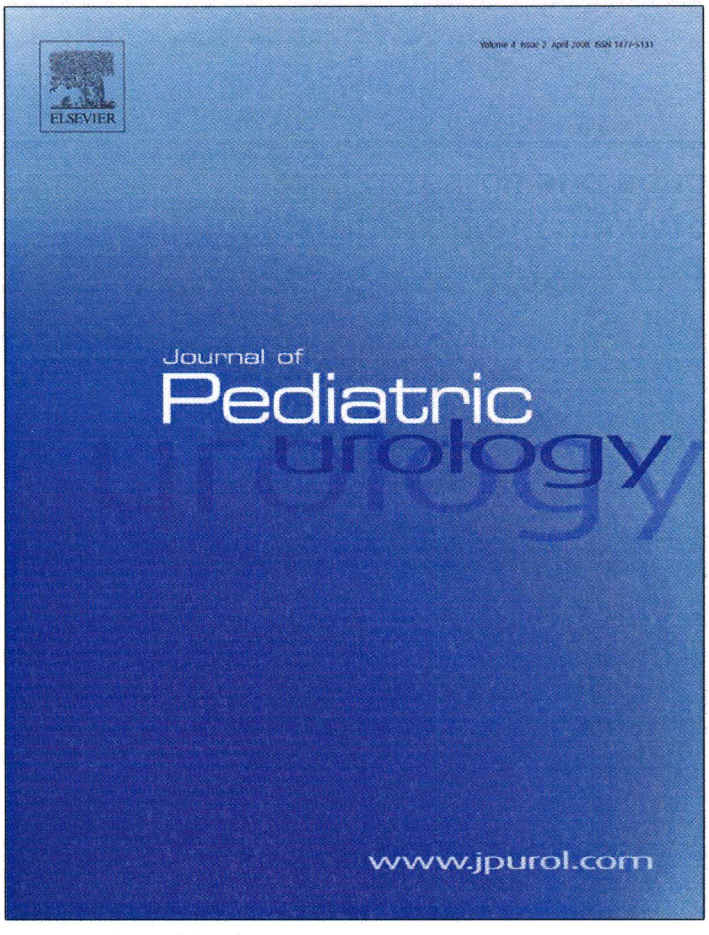

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Total endoscopic management (TEM approach) of children with non-compliant neuropathic bladder: A preliminary report

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Abstract *Purpose:* We prospectively evaluated the efficacy and durability of a combination of intradetrusor botulinum-A toxin (BTX-A) and endoscopic treatment of vesicoureteric reflux (VUR) to manage children with myelomeningocele (MMC) and non-compliant refluxing bladders who were not responding to standard conservative therapy. We also evaluated whether this combined therapy can lower intravesical pressure, increase bladder capacity, gain social continence and protect the upper tract from recurrent urinary tract infection.
Material and methods: A total of 10 patients with a mean age of 5.9 ± 3.6 years (range 2–12 years) with MMC (eight females and two males) were prospectively involved in the study. All patients were fully compliant to clean intermittent catheterization, and all were non-responders (failed to gain continence and/or poor compliance) to the maximum tolerable dose of anticholinergics and catheterization. All patients were subjected to cystoscopic intradetrusor injection of 12 U/kg (maximum 300 U) of BTX-A in an infection-free bladder. They all had VUR (16 refluxing ureters, six patients with bilateral VUR) and did not show resolution in the pretreatment voiding cystourethrogram; accordingly, submucosal injection of Deflux® was performed either with the second BTX-A treatment (initial four patients) or with the first BTX-A treatment (the other six patients). The grade of reflux was G III, IV and V in three, seven and six ureters, respectively.
Results: The maximum bladder capacity increased significantly from 79 ± 49 to 155 ± 57 ml ($p < 0.022$), and the maximum detrusor pressure decreased significantly from 55 ± 16 to 37 ± 11 cm H_2O ($p < 0.001$). Fifteen out of 16 (93.75%) refluxing ureters were completely resolved (one of them on second attempt), and one (6.25%) (GV reflux) remained unchanged despite of two attempts. Of six incontinent patients, five reached complete dryness between catheterizations and one showed partial improvement.

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Conclusions: A combination of BTX-A and endoscopic correction of VUR is a simple and effective way to overcome the increased risk of high intravesical pressure and recurrent UTI. This treatment decreases the incidence of renal damage in children on whom conservative management fails to help, in a minimally invasive way.

Introduction

VUR is a common problem encountered in children with neuropathic bladder (NB) secondary to neural tube defects, affecting 15–50% of these patients [1]. The current standard treatment is to start them on clean intermittent catheterization (CIC) combined with anticholinergic medications, which can lead to spontaneous resolution in 43–58% [2] of cases. Granata et al. [3] elaborated on the use of either endoscopic correction of VUR or cross-trigonal ureteric reimplantation combined with CIC to treat VUR associated with NB; those with poor compliance or small bladder capacity for their age were excluded from this line of treatment and needed reconstructive bladder surgery.

In the last decade, there has been increasing evidence that botulinum-A (BTX-A) toxin is a highly effective second-line treatment for patients with an NB that is not responding to standard conservative treatment. This therapy was pioneered in adults by Schurch et al. [4], with an excellent result reproduced in the pediatric population [5–7]. When we used BTX-A as a solo treatment for refractory NB, our initial experience was also encouraging, with a similar excellent response [8].

Here, we review our experience managing patients with NB secondary to myelomeningocele (MMC) and who have a VUR that has failed to respond to conservative treatment; we used an endoscopic combined management for their non-compliant bladder and VUR. To our knowledge, this is the first report of such a combined approach for the endoscopic management of NB and VUR.

Material and methods

In 2003, we started using BTX-A in children with NB secondary to MMC who were not responding to our standard conservative treatment (CIC combined with anticholinergic medication). Out of this group, 10 patients (eight females and two males, with a mean age 5.9 ± 3.6 years, range 2–12 years) had VUR with 16 refluxing ureters (four unilateral and six bilateral VUR). The grade of reflux was G III, IV and V in three, seven and six ureters, respectively.

Both the endoscopic intravesical injection of BTX-A and the endoscopic correction of VUR were performed in the first four patients at the second BTX-A therapy session, and the last six patients received their endoscopic treatment of VUR during the first session of BTX-A treatment. We repeated the BTX-A injection after 6 months in all patients.

All 10 patients had 12 U/kg BTX-A diluted in 20–30 ml of normal saline (maximum dose 300 U) injected intravesically using a 3.7-F injection needle that was introduced through a 10-F cystoscope with an offset lens. The injections (0.5–1 ml/injection) were spread along the midline and lateral walls of the bladder, sparing the trigone and the bladder dome. The endoscopic treatment was done using the hydrodistension implantation technique 'HIT', where the aim was to have an 'HO' ureteric orifice at the end of the treatment [9]. When both treatments were combined, we used the same endoscopic session with two different needles, with an average time of 15–20 min. An indwelling catheter was kept overnight, and CIC was resumed the next day.

Urodynamic studies were performed 1 month and 6 months post-injection, and the mean change in bladder volume and maximum detrusor pressure was assessed. The success of the endoscopic correction of VUR was assessed by VCUG 2 months post-treatment with Deflux.

Results

The maximum bladder capacity increased significantly from 79 ± 49 to 155 ± 57 ml ($p < 0.22$) after 1 month and 149 ± 51 ml ($p < 0.013$) after 6 months, and the maximum detrusor pressure decreased significantly from 55 ± 16 to 37 ± 11 cm H_2O ($p < 0.001$) after 1 month and 38 ± 10 cm H_2O ($p < 0.023$) after 6 months. Bladder compliance improved significantly from 1.4 to 4.3 ml/cm H_2O ($p < 0.003$) after 1 month and 4.1 ml/cm H_2O ($p < 0.003$) after 6 months.

Out of six incontinent patients, five (83%) experienced complete dryness between CICs up to 6 months post-treatment, and one showed partial improvement. The VUR resolution rate is given in Table 1.

One of the initial four patients who received BTX-A therapy only during their first treatment showed initial reflux resolution. After a repeat VCUG confirmed relapse in this patient after hospitalization for acute pyelonephritis during the follow-up period, we changed our policy accordingly, and combined management from the first therapy session in the last six patients. In this subgroup the bladder gave the same response in both treatment sessions, and all

Table 1 VUR resolution outcomes

Grade	No. of ureters	Resolution (%)
III	3	3 (100)
IV	7	7 (100)
V	6[a]	5 (83.3)
Total	16	15 (93.25)

[a] Two ureters injected twice in one patient.

six showed a significant improvement in intravesical pressure after both treatment sessions.

No side effects of any of the procedures were reported from this combined approach. None of the patients had symptomatic UTI related neither to the procedures nor after Deflux treatment, except the one patient mentioned above who suffered a relapse after initial reflux resolution. We did not record any deterioration in the intravesical pressure or volume after treatment in any of the patients during the study period.

Discussion

To include patients with NB and VUR in an anti-reflux procedure, the standard criteria are to have at least 60% of the expected bladder capacity and for bladder compliance to be normal or only moderately compromised [3] before subjecting them to either cross-trigonal ureteric reimplantation or endoscopic VUR correction. All our patients had a small non-compliant bladder. Treating this group of patients with BTX-A therapy improved capacity and compliance significantly (100% increase in capacity, 35% decrease in pressure) and, during the same session as this minimally invasive technique, we were able to manage their VUR with a 93.75% success rate.

Initially, we tested whether BTX-A alone was sufficient to resolve VUR by lowering the intravesical pressure. Due to the observed negative results, our current policy, which we began to follow with the last six patients, is to combine BTX-A therapy and VUR endoscopic management from the first cystoscopy session.

Although there was a significant improvement in bladder compliance even after 6 months, the difference between compliance at 1 month and 6 months showed that the bladders would lose this improvement with time. Accordingly, we standardized the BTX-A treatment to be given every 6 months.

The use of BTX-A in children is still in its preliminary phase, and most reports show encouraging results [5–8]. If we combined this new method of management with a well-established endoscopic treatment for VUR (total endoscopic management approach), a proportion of our patients might not need major reconstructive surgery, with its well-known long-term morbidity [10]. To our knowledge, this is the first report to describe the combined use of an intradetrusor injection of BTX-A and endoscopic treatment of VUR with Deflux® in patients with NB and VUR with encouraging results and no co-morbidity.

Conclusions

In this group of patients, we were endoscopically able to improve bladder compliance, increase bladder capacity, enhance continence and protect the upper urinary tract from recurrent upper UTI by using a combined endoscopic treatment with intradetrusor injection of BTX-A to manage the NB and endoscopically correct VUR using Deflux. Although our results are promising, further long-term randomized studies in a larger group are warranted to explore this new method of treatment.

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