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Effect of onabotulinumtoxinA treatment on symptoms and urodynamic findings in pediatric neurogenic bladder

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Abstract *Objective:* To evaluate clinical and urodynamic efficiency of onabotulinumtoxinA (Botox) treatment in pediatric patients with urinary incontinence due to neurogenic overactive bladder.
Patients and methods: Seventeen patients aged from 6 to 17 years (median 11 years) were treated with Botox injections. Clinical response to incontinence, duration of the response, and urodynamic results before and 1–3 months after treatment were evaluated.
Results: Mean incontinence frequency decreased significantly ($p = 0.036$); six of 17 patients had >90% reduction, and a further three patients had a 50–90% reduction in incontinence episodes. Median duration of the response was 15 months (range 3–42 months). Mean bladder volume changed from 380 ± 148 ml to 453 ± 147 ($p = 0.078$), maximal detrusor pressure decreased from 45 ± 31 cmH_2O to 32 ± 21 cmH_2O ($p = 0.030$), and the number of patients with detrusor contractions during filling decreased from 12 to three ($p = 0.005$) after the treatment. The patients with poor bladder compliance had either no response or a short duration of response. At follow-up eight patients had undergone bladder augmentation because of persistent incontinence.
Conclusions: About one third of pediatric patients with neurogenic bladder had a good response to Botox treatment. In many patients, the clinical response was longer than expected. The patients who initially had poor bladder compliance had a poor response to the treatment.

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Introduction

Intradetrusor onabotulinumtoxinA (Botox) injections have become a treatment option mainly for therapy-resistant neurogenic detrusor over-activity (NDO) during the last few years. Botox treatment has been recommended mainly for adults, but it has been used also in children with NDO [1]. Several studies in adult NDO have shown a mean 85% increase in cystometric bladder capacity (CBC), a 44% decrease in maximum detrusor pressure (MDP), and a 69% decrease in incontinence episodes [1]. The duration of the response has ranged mostly between 4 and 10 months [1]. In children, reports on Botox treatment are more infrequent, but a mean 46% increase in CBC, 36% decrease in MDP, and 39% decrease in incontinence episodes have been observed in children [2,3]. Urodynamic values tend to revert towards pre-treatment levels 6–12 months after treatment in children with NDO, and repeat injections are required at 4–18-month intervals [4–6].

Botox treatment has been performed primarily for children with severe NDO with >40 cmH_2O MDP and severe incontinence [2,5,7]. In the present study, we evaluated results in less selected pediatric patients with NDO and urinary incontinence. Some patients had <40 cmH_2O MDP:s and fewer than daily incontinence episodes. In addition to clinical outcome and duration of response, our goal was to evaluate if urodynamic parameters would predict the outcome of the treatment.

Patients and methods

The operative database of the Children's Hospital, University of Helsinki, was reviewed for patients treated with Botox for neurogenic bladder during 2005–2011. Seventeen patients out of 23 were selected for analysis because they were <18 years old and had undergone urodynamic study before and 1–3 months after the treatment. Of the 17 patients included in the study, six had previously undergone a bladder outlet procedure to increase bladder outlet resistance (four patients had Deflux injections and two a collagen sling operation [8]). All patients used clean intermittent catheterization before the Botox treatment, and 15 patients had peroral anticholinergic medication. The patients were instructed to stop oral anticholinergic medication if the patient became continent with Botox treatment and to start oral medication again if incontinence resumed.

Botox was diluted to a concentration of 100 IU/5 ml 0.9% saline and was injected in 0.5-ml boluses with a dose of 12 IU/kg of body weight (maximal dose 300 IU) submucosally to the bladder, sparing the trigone. The number of injections varied from 20 to 30. No catheter was left after the treatment.

In the urodynamic study, abdominal and bladder pressures were measured with 4-Ch feeding tubes. Subtracted detrusor pressure was measured simultaneously using computerized equipment (Dantec Menuet, Denmark). Bladder filling was performed with a separate 6-Ch feeding tube with a slow filling rate of 10–20 ml/min. CBC and MDP values, and the existence of any detrusor contractions during the filling were recorded.

The incontinence score was recorded using a modified version of the scale of Schurch et al. [9] from 0 to 3 (0 = completely dry; 1 = wet less than once a day [not once a day as in original classification]; 2 = wet for less than 50% of the time between daily catheterizations; and 3 = wet for more than 50% of the time between catheterizations) before treatment and at control visit 1–3 months after treatment. In addition, initial success was evaluated according to the recommendations of the ICCS: non-response (NR) 0–49% decrease; partial response (PR) 50–89% decrease; response (R) ≥90%; and full response (FR) 100% decrease in symptoms or less than one symptom occurrence monthly [10]. In addition, long-term follow-up data extending to a median 4.8 (range 1.2–7.4) years after the treatment was collected (duration of response, number of patients having repeat Botox injections and number of patients requiring bladder augmentation).

Pre- and post-treatment urodynamic results were compared with paired *t*-test and incontinence grade pre- and postoperatively with a Wilcoxon sign rank test. The groups with and without previous outlet surgery, as well as with and without any response, were compared by Mann–Whitney test (Statview 5.0.1; SAS Institute, Cary, NC, USA).

Results

The median age of the 17 patients was 11 years (range 6–17 years). Eleven patients had myelomeningocele, two patients had caudal regression, one patient had lipomyelomeningocele, one had diastematomyelia, and one had sustained spinal trauma.

Incontinence grades decreased after Botox treatment from a median of 3 (mean 2.3 ± 0.8) to a median of 1 (mean 1.6 ± 1.3, $p = 0.036$). Four patients received a FR, two patients received an R, three patients achieved a PR, and eight patients got NR. The median duration of any response was 15 months (range 3–42 months). In cystometric studies MDP decreased and CBC tended to increase (Table 1). Before the treatment MDP was observed at the end of filling in 12 patients and at detrusor contraction in the remaining five patients. In addition, the number of patients with detrusor contractions during filling decreased after the treatment (Table 1).

Bladder outlet procedures were previously performed for three patients in the NR group and for one patient in the PR, R, and FR groups. There were no statistical differences in pre-treatment CBC and MDP between six patients with and 11 patients without previous outlet procedures, although the patients with previous outlet procedures had a

Table 1 Cystometric findings in 17 patients with onabotulinumtoxinA treatment.

	Pre-treatment	Post treatment	*p*-Value
CBC (ml)	380 ± 148	453 ± 147	0.078
MDP (cmH_2O)	45 ± 31	32 ± 21	0.030
Detrusor contractions during filling (*n*)	12	3	0.005