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Botulinum injection is useless on fibrotic neuropathic bladders

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Objective
Studies on the use of intradetrusor botulinum toxin A injection for children with neuropathic bladders are insufficient and the results are controversial. The aim of the present study was to evaluate the effect of intradetrusor botulinum toxin A injection for children with neuropathic bladders that are resistant to anticholinergic treatment, and to reveal any criteria indicating treatment success.

Patients/methods
Hospital records were reviewed of 16 children with neuropathic bladders due to myelomeningocele, and who had botulinum toxin A injections between 2007 and 2010. Botulinum toxin A (10 units/kg) was injected endoscopically into various sites of the detrusor, except the trigone. The success was defined as complete dryness between clean intermittent catheterizations. Urodynamic studies before and after the application were evaluated and parameters, including bladder capacity (measured/expected) and compliance, were also analyzed. Reviewing the results, patients were then classified into two groups: as having fibrotic bladders (non-compliant, acontractile bladders with high pressures) or overactive bladders. Urodynamic findings and therapy success were then compared between the groups.

Results
A total of 19 injections, including repeat injections in three patients, were performed. Results of the 16 initial injections were evaluated. Nine patients had detrusor overactivity, and five out of nine (56%) applications in this group resulted in complete dryness between clean intermittent catheterizations. In bladders with typical detrusor overactivity, there was a significant increase in both the capacity (from 0.53 to 0.74) and compliance (from 4.7 to 8.6 ml/cm H_2O). Looking at the seven patients that displayed fibrotic bladders with very low compliance and no contraction at all, none of them presented with notable clinical improvement from injections. Comparing the urodynamic findings, there was no significant difference in compliance (3.1 ml/cm H_2O before and 3.5 ml/cm H_2O after) and bladder capacity (0.58 before and 0.52 after the treatment) in the fibrotic bladders.

Discussion
Despite its worldwide usage and FDA approval, studies on the effectiveness of botulinumtoxin A on neuropathic bladders in children are controversial. There are now numerous studies attesting to the good results of BoNTA in neuropathic detrusor overactivity; however, only scarce reports comment on the specific features of the disease process among patients and reasons for failure in some. In our study, reviewing the urodynamic findings carefully, it was observed that the patients who did not respond to injections were the ones with no contractions, despite high pressures and low compliance.

Therefore, describing the indications of BoNTA as neuropathic detrusor overactivity and urinary incontinence despite anticholinergic medications may lead to mistreatment of patients in the decompensated phase of a hyper-reflexive detrusor. Pretreatment urodynamic evaluation might be a good indicator, without biopsies, of estimating the degree of fibrosis and the patients who will benefit from the injection.

Conclusion
Botulinum toxin A injection in the neuropathic bladder of myelomeningocele patients was found to be ineffective if the detrusor was fibrotic, of low compliance and had lost contractility. Urodynamic findings should be carefully analyzed in order to select appropriate patients that may benefit from Botulinum injection.

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Introduction

Several studies have presented convincing data showing the benefits of botulinum toxin A (BoNTA) injections in the treatment of neuropathic bladders in adults. In August 2011, FDA (Food and Drug Administration) approved BoNTA for the treatment of urinary incontinence due to detrusor overactivity that was associated with a neurological disease and refractory to oral medication [1]; however, studies in children are still insufficient to recommend its routine clinical use due to a high failure rate [2,3]. On the other hand, there are a number of patients to whom BoNTA would offer a good clinical outcome. The aim of the present study was to evaluate the results of intradetrusor BoNTA injection for children with neuropathic bladders that are resistant to anticholinergic treatment, and to reveal any criteria indicating treatment success.

Patients/methods

Hospital records were reviewed of 16 children with neuropathic bladders due to myelomeningocele and who had botulinum toxin A injections between 2007 and 2010. Before the injections were given, all patients were wet, despite oral anticholinergic medication and clean intermittent catheterization (CIC). A total of 19 injections, including repeat injections in three patients, were performed. The clinical outcomes of these initial applications are shown in the present study. Onabotulinum toxin A (Botox, Allergan Pharmaceuticals, Irvine, CA, USA) was used and diluted to a concentration of 100 IU/5 ml with 0.9% NaCl. Under general anesthesia, the injections were performed endoscopically with a rigid cystoscope in 25—40 sites with 0.5 ml boluses, starting from the center and moving the cystoscope radially to both sides along the bladder wall sparing the trigone. A dose of 10 IU/kg was injected, with a maximal dose of 360 IU [4].

Clean intermittent catheterization was continued, starting 4 h following the application [4]. All patients under antibiotic prophylaxis for CIC and their antibiotics were resumed. Patients were evaluated in terms of continence between CIC in the first, third, sixth month and within six-month periods thereafter. A urodynamic study was routinely performed at the third month of therapy and then at the time of clinical worsening. Pre and post-treatment urodynamic parameters, as capacity and compliance, were evaluated. For a comparative analysis, bladder capacity was evaluated as "measured capacity/expected capacity for age". Expected bladder capacity was calculated using the formula [30 + (age in years × 30)] [5]. Treatment success was defined as complete dryness between CIC. Reviewing the results, patients were classified into two groups: having fibrotic bladders or having overactive bladders. Noncompliant, acontractile bladders with high pressures were regarded as fibrotic bladders. Urodynamic findings and therapy success were then compared between the groups. Statistical analysis was performed using paired *t*-test and significance was accepted for $P \leq 0.05$.

Results

Urodynamic findings and the clinical responses of the 16 initial injections were evaluated. Two patients had high lumbar, three patients had low lumbar, six patients had lumbosacral and five patients had sacral spinal lesions. No relation between level of the lesion and responsiveness to BoNTA was observed. The median age of the patients was nine (range 2—14).

Evaluating the urodynamic parameters, nine patients were regarded as having overactive detrusors, due to better compliance and typical contractions (Fig. 1a). The other seven patients had a very low compliance and no contractions during the urodynamic study and were therefore regarded as having fibrotic bladders (Fig. 2a). Five of the nine (55.5%) applications in the overactive group resulted in complete dryness between CIC at the first, third and sixth-month evaluation. In these patients with overt overactive features, there was a clear increase in both the capacity (0.53 before and 0.74 after, $P = 0.006$) and compliance (4.7 ml/cm H_2O before and 8.6 ml/cm H_2O after, $P = 0.01$) at the third-month urodynamic study (Table 1, Fig. 1b).

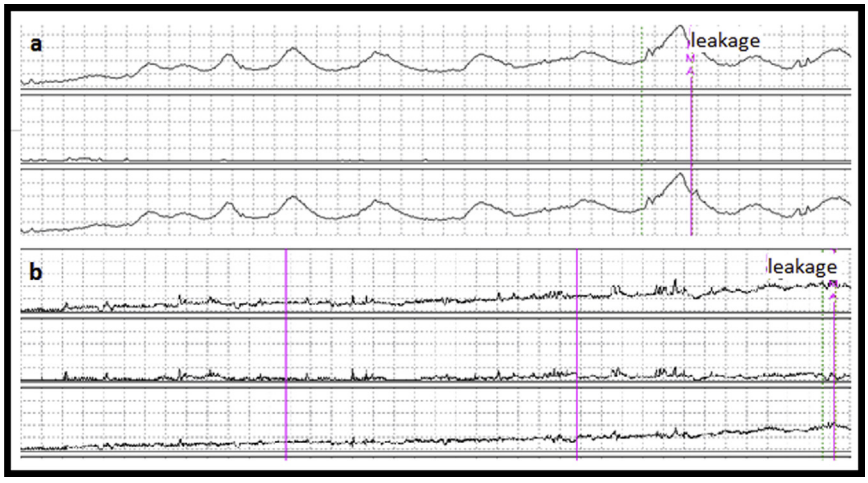

Figure 1 Representative urodynamic study of a patient in the overactive bladder group (a) before (b) after the injection.