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CAN CYSTOGRAPHY PREDICT THE RESULTS OF BOTULINUM TOXIN-A INJECTION FOR THE TREATMENT OF SPINAL CORD INJURY PATIENTS WITH REFRACTORY NEUROGENIC DETRUSOR OVERACTIVITY?

Hypothesis / aims of study
To assess whether the bladder shape shown by cystography can predict which patients with neurogenic detrusor overactivity refractory to anticholinergic drugs respond better when treated with toxin botulinum A injection into detrusor.

Study design, materials and methods
Thirty nine patients with spinal cord injuries were evaluated prospectively. All patients emptied their bladder by clear intermittent catheterization, presented urinary incontinence despite using high doses of two different anticholinergics or association of oxybutinin oral and intravesical and underwent detrusor injection of botulinum toxin A (300 U). Pre-treatment assessment included urodynamic, ultrasonography of the kidneys and urinary tract and cystography. Follow-up consisted of urodynamic and outpatient consultation one month after and the clinical outcome was evaluated through outpatient consultations and telephone contact. The treatment was considered effective if a patient sustained 4 months without incontinence whether or not this occurred while using anticholinergic agents. Using cystography, the outcome was evaluated in relation to the bladder shape, bladder capacity, and diverticula presence. Bladder shape was characterized as either round, “pyriform” or “pine tree” shaped. Cystometric capacity was categorized as either very reduced (≤ 200 ml), decreased (from 200 to 399 ml) or normal (≥ 400 ml). The number of diverticula was either large, small, or absent. The present study is motivated by the observation that bladders evaluated by cystography and cystoscopy during the injection procedure revealed different characteristics that could influence the treatment outcome. In terms of shape, two major types have been identified: 1.) A normally-shaped bladder without any diverticula and 2.) An abnormally shaped bladder that is “pyriform” or “pine-tree” shaped and/or has a large number of diverticula.

Results
Twenty-seven patients (69%) were completely continent after the procedure, including four patients who had clinical responses lasting less than four months and whose response was considered ineffective. At the four week follow-up, urodynamic evaluation revealed increases in reflex volume and cystometric capacity and decreased amplitude of detrusor overactivity. There was no statistical difference in urodynamic parameters: maximum cystometric capacity ($p = 0.920$), detrusor overactivity ($p = 0.989$), reflex volume ($p = 0.932$) between the group who showed improvement and those who remained incontinent. However the baseline compliance was higher in patients with good response compared to those who had an unsatisfactory response ($p = 0.032$).
An absence of diverticula in cystography occurred in 83% of patients with effective results. Additionally, the presence of a large number of diverticula was found in 80% of patients with unsatisfactory outcomes, and together these results demonstrate a significant association between number of diverticula and quality of results ($p < 0.001$). Rounded bladder forms presented good results in 95% of cases while “pyriform” and “pine tree” shape bladders only in 20% ($p<0,001$). The statistical association between bladder capacity and quality of response, was borderline, according to Fisher's exact test ($p = 0.056$).

Interpretation of results
In our study, we observed continence during a period of more than 4 months in 59% of patients who had undergone BTX-A treatment. In studies with similar patient populations, the percentage of continence after toxin injection has ranged from 42 to 87%. Karsenty *et al.* reported that anticholinergic agents could be discontinued in 28 to 58%of patients following BTX-A therapy and the requirement could be substantially reduced in the remaining patients (1). We found that only 8% had suspended use for a period, and 41% had decreased the dose. We observed that some of these patients did not reduce the medication by insecurity after achieving good results. Thus, these numbers may contain a bias.Other authors have reported limiting factors of the effectiveness of BTX-A injections into the detrusor, such as high doses of anticholinergics before the procedure, the optimal dose of BTX-A, different pharmaceutical formulations and injection technique (2). These factors may explain differences in the results of different studies. Although our patient population was similar to previous studies, the results were different. Despite all patients presenting NDO refractory to anticholinergic agents and having similar urodynamic parameters before the procedure, outcomes varied between satisfactory and unsatisfactory results. Here, cystography was not used as a screening test for the procedure.
Although it has been reported that ultrastructural changes occur in the detrusor muscle from NDO (3), we think that the morphology of the bladder (shape and the presence of diverticula) may influence the results of BTX-A injection into the detrusor of patients with refractory NDO. These abnormal bladder shapes are probably the result of smooth muscle hypertrophy and changes in the connective tissue matrix that do not respond well to any conservative treatment.
We believe that a limitation of our study, like others on this topic, is the small number of patients. Despite this limitation, we found a statistically significant association between the bladder characteristics analyzed by cystography and the quality of response to the procedure.
Although the present study has a small number of patients, it suggests that patients who present with bladders with multiple - diverticula, “pyriform” and/or a “pine-tree” shape would be best treated by surgery, such as augmentation cystoplasty. In contrast, rounded bladders and/or bladders without diverticula are more likely to show good outcomes after BTX-A injections.

Concluding message

Cystography may be a predictive factor of response to botulinum toxin type A in the treatment of refractory neurogenic detrusor overactivity.

A rounded bladder with no diverticula was more likely to show improvement after the procedure. In contrast, patients with “pyriform” and “pine-tree-shaped” bladders and/or a large number of diverticula were more likely to show unsatisfactory outcomes.

References

1. Karsenty G, Denys P, Amarenco G, De SM, Game X, Haab F et al. Botulinum toxin A (Botox) intradetrusor injections in adults with neurogenic detrusor overactivity/neurogenic overactive bladder: a systematic literature review. Eur Urol 2008: 53(2):275-287.
2. Smaldone MC, Ristau BT, Leng WW. Botulinum toxin therapy for neurogenic detrusor overactivity. Urol Clin North Am 2010: 37(4):567-580.
3. Haferkamp A, Dorsam J, Resnick NM, Yalla SV, Elbadawi A. Structural basis of neurogenic bladder dysfunction. III. Intrinsic detrusor innervation. J Urol 2003: 169(2):555-562.

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