

## CAUSES OF FAILED URETHRAL BOTULINUM TOXIN A TREATMENT FOR VOIDING DYSFUNCTION

### Hypothesis / aims of study

Urethral injection of botulinum toxin A (BTX-A) can reduce urethral resistance in patients with voiding dysfunction. However, some patients do not benefit from this treatment. It is essential to identify the causes for these failed procedures.

### Study design, materials and methods

A total of 200 patients receiving urethral BTX-A injections for voiding dysfunction refractory to conventional medication during a ten year period were included. Patients received 50 or 100 units of BTX-A injected into the urethral sphincter. Treatment was considered successful when patients were subjectively satisfied with the outcome and: (1) patients with chronic urinary retention resumed spontaneous voiding, (2) patients with large postvoid residual (PVR) had a reduction in PVR by more than 50%, (3) patients voided with a lower detrusor pressure or lower abdominal pressure to urinate adequately. The therapeutic results and causes of failed treatment were retrospectively analyzed.

### Results

The patients included 112 men and 88 women, aged from 12 to 96 (mean 60 ± 18) years old. The causes of voiding dysfunctions and percentage of patients with successful results are listed in Table. The overall success rate was 88.5% (177 patients), including 47.5% (95 patients) with an excellent result and 41% (82 patients) with an improved result. There were 23 failed urethral injections treatment including 8 in patients with dysfunctional voiding and 8 in detrusor areflexia. The causes of failed treatments were detrusor underactivity with very low abdominal straining pressure in 7, a tight urethral sphincter in 7, bladder neck obstruction in 7 and psychological inhibition of voiding in 2. Transurethral incision of the bladder neck (TUI-BN) was performed in 7 patients who had failed the initial urethral BTX-A injection treatment for detrusor sphincter dyssynergia (DSD, n=3) or detrusor areflexia (n=4). Among these 7 patients, 6 had an excellent result and 1 had an improved result after TUI-BN. All patients could void smoothly either by abdominal tapping or with the aid of abdominal pressure. None of them required repeat urethral BTX-A injection after TUI-BN.

### Interpretation of results

This retrospective study analyzed the causes of failed urethral BTX-A treatment for voiding dysfunction. In this series of 200 patients, the true failure rate was only 11.5%, suggesting urethral BTX-A injection is an effective treatment for voiding dysfunction refractory to medical therapy. Among the various causes of treatment failure, inadequate abdominal pressure to generate enough power to void, bladder neck obstruction, and a high urethral sphincter tone were the most common. Psychological inhibition is a common cause of voiding dysfunction. These patients have strong cortical inhibition of the sphincter center which prevents relaxation in any place or environment where they feel uncomfortable to void. Relaxation of the urethral sphincter by BTX-A injection does not allow these patients to reduce this cortical inhibition adequately. However, if the dose of BTX-A is high enough, these patients can force their bladder outlet to open during abdominal straining, allowing them to void smoothly in a public toilet and thus report an excellent therapeutic result.

### Concluding message

BTX-A urethral injection provides an alternative treatment choice to CISC for patients with voiding dysfunction refractory to medical treatment. However, patients and doctors may have unrealistic expectation from this treatment modality. Patients with bladder neck obstruction might have a better outcome if TUI-BN is performed before urethral BTX-A injection. Patients with a very low abdominal voiding pressure might not benefit from urethral BTX-A injection to treat their detrusor areflexia or underactivity. Patients with a hyperactive urethral sphincter or DSD may need repeat urethral BTX-A injection for a successful outcome. The extent to which patients with psychological inhibition of voiding would benefit from a higher dose of BTX-A aimed at completely relax their bladder outlet. In cases of initial BTX-A treatment failure, careful investigation of the underlying causes of failed treatment by videourodynamic study is mandatory to achieve a satisfactory final outcome by proper selection of adjuvant therapeutic procedures.

Table. Causes and therapeutic results of voiding dysfunction treated with urethral BTX-A injection

| Causes of voiding dysfunction                                   | N= | Excellent     | Improved   | Failed       |
|---|----|---------------|------------|--------------|
| Detrusor sphincter dyssynergia due to SCI or multiple sclerosis | 48 | 19<br>(39.6%) | 26 (54.2%) | 3<br>(6.3%)  |
| Neurogenic or learned dysfunctional voiding                     | 60 | 37<br>(61.7%) | 15 (25%)   | 8<br>(13.3%) |
| Poor relaxation of urethral sphincter                           | 23 | 12<br>(52.2%) | 10 (43.5%) | 1<br>(4.3%)  |
| Idiopathic detrusor underactivity                               | 32 | 15<br>(46.9%) | 16 (50%)   | 1<br>(3.1%)  |
| Detrusor areflexia  | 33 | 11<br>(33.3%) | 14 (42.4%) | 8<br>(24.2%) |

|                                     |     |            |          |               |
|-------------------------------------|-----|------------|----------|---------------|
| Psychological inhibition of voiding | 4   | 1 (25%)    | 1 (25%)  | 2<br>(50%)    |
| Total                               | 200 | 95 (47.5%) | 82 (41%) | 23<br>(11.5%) |

SCI: spinal cord injury

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**CLINICAL TRIAL REGISTRATION:** This clinical trial has not yet been registered in a public clinical trials registry.

**HUMAN SUBJECTS:** This study was approved by the Institution Review Board of Tzu Chi University and Tzu Chi General Hospital and followed the Declaration of Helsinki Informed consent was obtained from the patients.