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INTRAVESICAL BOTULINUM NEUROTOXIN TYPE A (BTX-A) INJECTION FOR PATIENTS WITH REFRACTORY DETRUSOR OVERACTIVITY: EFFICACY, SAFETY AND PATIENT SATISFACTION

Hypothesis / aims of study

The aim of this study was to assess the subjective and objective therapeutic outcomes after intravesical injection of Botulinium A toxin (BXA) for neuropathic and idiopathic detrusor overactivity (DO). We also assessed patient satisfaction after BTX-A therapy knowing that BTX therapy will be on a regular basis.

Study design, materials and methods

This is an open-label prospective study that included patients of either sex with OAB symptoms for more than 6 months and urodynamic diagnosis of DO whether the etiology was neurogenic (NDO) or idiopathic (IDO). Patients all had failed oral pharmacotherapy (due to poor efficacy or tolerability) and clean self intermittent catheterization (CSIC). A requisite for inclusion in the study was the demonstration of DO with standard cystometry.

Women who were pregnant or breast feeding, as were patients on anticoagulant therapy, patients with neuromuscular transmission disorders, or those taking drugs that might interfere with neuromuscular transmission (eg aminoglucosides). Exclusion criteria were pregnancy and Myasthenia gravis, breast-feeding, and patients on anticoagulant therapy.

Following enrolment, and signing the informed consent, patients were interviewed to ascertain their symptoms of frequency (nocturnal and diurnal), nocturnal enuresis, urgency and urge incontinence episodes. The frequency of micturitions, urge incontinence episodes were assessed. Patients were required to complete the UDI-6 questionnaire[9], focused neurological evaluation, urinalysis and culture, multi-channel urodynamic study, post-void residual urine volume, and abdominal ultrasound evaluation. In addition, all patients underwent an MRI examination to exclude spinal cord pathologies. Multichannel urodynamic testing was done in a standardized way following the recommendation of the ICS.[10]. The urodynamic parameters assessed included bladder volume when the 1st unstable detrusor contraction occurred (Vol@1st UDC), maximal amplitude of the unstable detrusor contraction, maximum cystometric capacity (MCC), Detrusor Leak Point Pressure (DLPP), detrusor pressure at maximum flow rate (Pdet@Qmax), maximum flow rate (Qmax), voided volume, and post void residual. Follow-up visits were 2 weeks and at 3 and 6 months after injection therapy. If the postvoid residual volume exceeded 150 mL, CISC was recommended for evacuation of the bladder at least four times daily.

Evaluation of treatment satisfaction

The details, risks, efficacy and efficacy of augmentation cystoplasty and BTX-A injection were explained to patients. Patients were also informed that BTX-A will be on regular basis once the symptoms recurred (average every 6 – 9 months). Patients were asked which procedure they do prefer for their condition.

Injection Technique and Dosage

Patients with NDO were injected with a total dose of 300 U Botox and those with IDO were given 200 U of Botox (Allergan, Irvine, Calif).

Satisfaction with treatment

Satisfaction was assessed using a part of the Surgical Satisfaction Questionnaire (SSQ) (we used the Global satisfaction subscales of the SSQ i.e. questions 6,7 and 8). The original SSQ is an 8-item questionnaire, with responses recorded on a 5-point Liker type scale with responses from 0 ="Very Unsatisfied" to 4 = "Very Satisfied." The higher the score is, the greater the degree of satisfaction. Items 1 and 2 are used to calculate the Pain subscale; items 3, 4, and 5 are used for the Return to baseline subscale: and items 6, 7, and 8 are used for the Global satisfaction subscale. Each subscale is calculated in the same manner as the overall SSQ score. The SSQ is not designed to be condition specific and has not yet been validated.

Statistical Method

Non-parametric statistical tests were used (the Wilcoxon signed rank test to compare related samples and Mann-Whitney tests to compare unrelated samples. We used the two-sample paired t-tests when the relevant variables were normally distributed. Normality was verified with Shapiro-Wilk tests. Significance tests were two-sided and a P value of <0.05 was considered significant. Statistical analysis was performed using SPSS 16 (SPSS, Inc., Chicago, IL).

Results

A total of 31 patients (22 women and 9 men) with a mean age of 27.9 (range 18 to 72) years were treated with BTX-A. The etiology of DO included idiopathic (IDO) in 10 subjects (8 women and 2 men) with a mean age of 21.8 years, and neurogenic (NDO) in 21 subjects, (14 women and 7 males) with mean age of 29.9 years. The etiology of NDO included spina bifida in 9, spinal cord injury in 8, transverse myelitis in 1, old cerebrovascular lesion (hemorrhage) in 1 and Parkinsonism in 2 subjects. No significant differences (independent t test) were noted at baseline between the two groups as regards age, daytime frequency, nocturia, or incontinence episodes. The amplitude of the UDC, Pdet@Qmax and the DLPP were significantly higher in the IDO than in the NDO. No differences were noted between the 2 groups in the other urodynamic parameters. Thirteen patients with NDO and 2 patients with IDO were on CIC before therapy.

Idiopathic Detrusor Overactivity

All patients with IDO had UI before injection. Six weeks after injection, 30% were completely dry (p=0.01). At 6 months, although no patient was completely dry, there was a significant reduction in severity of UI when compared to preoperative status.

In addition, there were significant improvement in the mean number of UI episodes, diurnal and nocturnal frequency (table 1). The mean amplitude of the IDC, DLPP, and Qmax decreased significantly decreased 6 weeks after injection. The therapeutic benefits had declined gradually with symptom measures returning to baseline values by 6 months.

One case (12.5%) with IDO – with no significant PVR prior to injection – developed a PVR > 100 mL and was managed by CSIC that lasts for 6 weeks post-injection.

Neurogenic Detrusor Overactivity

All patients with NDO had UI before injection. Six weeks after injection, 33.3% were completely dry (p=0.04). At 6 months no patient was completely dry.

Significant improvements in the mean number of UI daytime frequency, and nocturia were seen as of 6 weeks post-treatment. There was no statistically significant difference between the 2 groups as regard the degree of improvement in the mean number of UI episodes, daytime frequency and nocturia. These improvements were also not sustained 6 months post-treatment (table 1) though they were still statistically less than the baseline.

4 cases (50%) with no significant PVR prior to injection – developed a PVR > 150 mL and were managed by CSIC that lasts for 6 weeks post-injection. Urinary tract infection developed in 2 patients.

Treatment Satisfaction

61.3% (n=19) of patients injected with BTX stated they were satisfied by this therapy, 45.2% (n=14) would be reinjected again with BTX, while 54.8% (n=17) stated they would recommend BTX for others. On the other hand, 38.7% were not satisfied by BTX therapy, 54.8% (n=17) of patients would not recommend BTX therapy for others and would not recommend it for others. Reasons for this negative attitude towards BTX were lack of the desired clinical response and the inability of patients to accept the concept of injecting BTX on regular basis every 6 – 9 months.

Interpretation of results

BTX injection is associated with improved subjective and objective parameters. Patient satisfaction is variable based on the knowledge that BTX should be injected on a regular basis.

Concluding message

BTX-A injections into the detrusor had a significant and comparable beneficial effects in refractory neurogenic and idiopathic DO as early of 6 weeks post-treatment. However, these therapeutic benefits had declined gradually with symptom measures returning to baseline values by 6 months. Voiding dysfunction is not uncommon after BTX therapy. About 40% of patients injected with BTX may not be satisfied due to regular injection every 6-9 months.

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Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**