

DOSE-FINDING PROSPECTIVE RANDOMIZED STUDY TO EVALUATE THE EFFICACY AND SAFETY OF BOTULINUM-A TOXIN FOR REFRACTORY IDIOPATHIC OVERACTIVE BLADDER.

Hypothesis / aims of study

Botulinum Toxin-A (BTA) is a promising emerging therapy for Idiopathic Overactive Bladder (I-OAB) refractory to antimuscarinic therapy. However, the optimal BTA dosage to be used remains to be established. Several investigators have reported satisfactory outcome using 200 to 300 Units. We report the results of a dose-finding prospective randomized study comparing 100 Units vs 150 Units using validated instruments to evaluate the efficacy and safety of "Low-Dose" BTA in the management of I-OAB.

Study design, materials and methods

Twenty patients (14 female, 70%; 6 male (30%); 26 to 75 years of age (mean, 52.6 ±13.4) with I-OAB refractory to oxybutynin and tolterodine were prospectively evaluated and subsequently randomized to either 100 Units (N=10) or 150 Units BTA (N=10). Evaluation included: History and physical, Urogenital Distress Inventory-6 (UDI-6), Global-visual analog scale QOL-improvement (0-100%), 24-hour voiding diary with attention to tidal voided volume (t-VV), urine analysis and culture, post-void residual (PVR), and multichannel urodynamics. BTA is injected (10 Units/ml) transurethrally in the posterior bladder wall sparing the trigone using a Storz rigid cystoscope with a working element through which a 22 G injection needle is inserted. Under IV sedation, study patients were re-injected every 6 months.

Student's t test measured: 1) Age and gender vs pre and post BTA variables (tidal voided volume, 24 hr-urinary frequency, improvement in Global-QOL, UDI-6, PVR) 2) *Paired student's t-test* assessed for differences in same variables before and after BTA. *Rank-order correlations (Spearman rho)* were computed between paired variables to investigate various possible correlations. Associations between the number of BTA injection sessions at 6 month interval at both dosage (100 vs 150 Units) and the aforementioned variables were calculated.

Results

Follow-up included 6 to 24 months (mean 14 months). There was no association between BTA injection outcome measures and age group: <50 vs ≥50, gender, and dosage (100 Units vs 150 Units). Tidal volume voided, 24-hr frequency, and Global-QOL significantly improved following BTA at both dosages. Significant correlation (*Spearman rho*) was noted between 1) percent improvement global QOL and pre-Botox QOL, ($\rho = -0.60$, $p = 0.006$), percent global QOL improvement and post BTA t-VV ($\rho = 0.51$, $p = 0.023$), & pre and post BTA QOL ($\rho = 0.50$, $p = 0.025$). Increased t-VV (ml) was observed with increasing number of BTA sessions: 258.8 ± 176.1 versus 538.2 ± 294.4 ml for single vs >2 sessions ($t = 2.67$, $p = 0.016$). No BTA toxicity or hematuria was noted. One female patient developed bacterial cystitis in the 150 Units group. She had a transient rise in PVR up to 200 ml.

Variable	100 Units Botox	150 Units Botox	p value
Tidal voided volume, ml (pre-Botox)	79.5 ± 31.5	73.5 ± 15.4	0.606*
Tidal voided volume, ml (post-Botox)	223.5 ± 253.7	217.6 ± 278.7	0.459*
Urinary frequency /24hrs (pre-Botox)	14.9 ± 5.5	19.4 ± 15.1	0.456*
Urinary frequency/24hrs (post-Botox)	8.6 ± 3.7	7.4 ± 3.1	0.432*
UDI-6 (pre-Botox)	14.5 ± 2.7	13.2 ± 4.4	0.408*
UDI-6 (post-Botox)	5.6 ± 5.2	5.3 ± 3.7	0.853*
PVR (preBotox), ml	43.4 ± 23.2	51.7 ± 44.5	0.635*
PVR (postBotox), ml	51.7 ± 44.1	81.0 ± 27.5	0.527*
Patient-perceived percent global symptom improvement	59.5 ± 14.2	53.0 ± 28.3	1.000**

*Paired t-test (2-tailed,) Maximum UDI-6 =18

**Chi-square test

Interpretation of results:

In Idiopathic OAB patients Intravesical Botulinum toxin A injections are effective at both dosage 100 and 150 Units. Tidal voided volume is increased and correlates with improvements in Global QOL and reduction in urinary frequency at both dosage. Repeat injection sessions improve voided volume more than the first BTA session. PVR is not statistically increased at both dosage used

Concluding message

Lower dosage Botox-100 Units may be as effective as the higher dosages which have been previously used.