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SHORT-TERM OUTCOMES OF A RANDOMIZED, DOUBLE-BLIND PLACEBO CONTROLLED TRIAL OF BOTULINUM A TOXIN FOR THE MANAGEMENT OF SEVERE IDIOPATHIC DETRUSOR OVERACTIVITY INCONTINENCE.

Hypothesis / aims of study

To determine the effectiveness of 200u and 300u of Botulinum-A toxin (Botox) compared to placebo when administered cystoscopically to subjects with severe idiopathic detrusor overactivity (IDO)

Study design, materials and methods

IRB approval was obtained at both institutions. Subjects were recruited for two separate trials using virtually identical methods. The data has been combined for this preliminary report. Inclusion criteria included ≥ 3 leakage episodes related to IDO per day on a three day bladder diary, a 24 pad weight ≥100 gms and failed oral anticholinergic medications. Exclusion criteria included a cough leak point pressure <100cm H2O, a postvoid residual volume (PVR)>100ccs, urinary tract infection (UTI) or a neurologic etiology for the urge incontinence. Subjects were randomized to placebo, 200u or 300u of Botox. Under cystoscopic guidance, the detrusor was injected at 8-10 sites above the trigone with the study solution. Evaluations were performed at baseline, 3 and 6 weeks after injection. Evaluations included urinalysis with culture, 3-day bladder diary, 24-hr pad weight and IIQ-7 and UDI-6 questionnaires. In addition, at the baseline and 6-week visits, cystometrograms, pressure flow studies, and PVR were performed. Change from baseline values was determined for each variable.

Results

Data for 38 subjects was available. Eighteen were recruited from one institution and 20 from the second institution. Data for the 2 Botox groups were combined. Because this is an interval analysis, p values were set to 0.01. There were no differences in mean baseline measurements between the 2 groups (Table 1). Incontinence was greatly reduced in Botox group over placebo. The values shown are the relative changes from baseline values in each subject for each group. There were no differences between the group in nocturnal voids or daily voiding frequency. Six subjects receiving Botox experienced PVR > 200cc and two subjects required intermittent clean catheterization for bladder emptying. Six subjects experienced UTIs, 5 (17%) in the Botox group and 1 (10%) in the placebo group (NS).

Table 1	Baseline Placebo	Baseline Botox	p	Placebo 3 weeks Δ from baseline	Botox 3 weeks Δ from baseline	p	placebo 6 weeks Δ from baseline	Botox 6 weeks Δ from baseline	p
Incontinence episodes/day	7.61	8.1	NS	1.03	0.40	<.0001	1.00	0.36	<.0001
24 pad weight (gms)	387.9	798.18	NS	0.97	0.34	0.001	0.80	0.26	0.0049
# pads/day	5.24	5.17	NS	1.18	0.47	1E-04	1.02	0.42	0.0004
IIQ-7 score	43.8	60.15	NS	1.85	0.60	0.068	1.78	0.48	0.0357
UDI-6 score	43.6	51.18	NS	1.05	0.67	0.026	0.94	0.62	0.0804
Max cystometric capacity (cc)	258.4	261.5	NS	N/A	N/A	N/A	0.98	1.47	0.0515

Interpretation of results

Compared to placebo Botox can significantly reduce daily episodes of incontinence, daily pad usage and volume of urine lost in the short-term. Cystometric capacity and quality of life appear to be improved as well. There is a risk or urinary retention requiring self catheterization.

Concluding message

Botox can significantly reduce urge urinary incontinence due to IDO. There is a risk of urinary retention requiring self catheterization. These studies are ongoing.

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HUMAN SUBJECTS: **This study was approved by the university of Rochester Research Subjects review Board and followed the Declaration of Helsinki Informed consent was obtained from the patients.**