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BOTULINUM TOXIN A 100 VS 150 UNITS IN IDIOPATHIC OVERACTIVE BLADDER PATIENTS: IS THERE ANY DIFFERENCE?

Hypothesis / aims of study:
This study is an IRB approved, investigator-initiated, randomized, prospective study designed to evaluate the efficacy and safety of scheduled repeated intra-detrusor injections of Botulinum neurotoxin-A (BoNTA) in order to treat patients (pts) with idiopathic overactive bladder (OAB) resistant to antimuscarinic drugs. We aim to compare the clinical response of BoNTA 100 U and 150 U by evaluating urinary urge incontinence (UUI) in patients with OAB wet and urinary frequency (UF) in the entire OAB cohort.

Study design, materials and methods:
A total of 38 OAB pts (22/37 were OAB-wet) of non-neurogenic etiology were randomized to receive BoNTA (100U or 150U) as 10U/ml/injection "trigone and dome sparing" (10 or 15 intra-detrusor injections respectively). We used a 14 Fr flexible cystoscope / 27G-4mm needle. Validated questionnaires, medical history, physical exam, 3 days voiding diaries (3xVD), post-void residual volume, urine analysis and cultures were performed in all pts before treatment (Baseline) and at 2, 6, 12 and 24 weeks after every injection therapy. Multichannel urodynamics were performed prior therapy and 6 weeks after each treatment. UF and UUI episodes per 24 hr were calculated from 3xVD average. The response outcome was calculated using the best improvement status, if any, within a 6 months period using 3xVD. All data obtained was compared to baseline using T-test, and Chi-square (X^2) when assessing improvement's rate. Significance was established by $p<0.05$.

Results:
38 OAB pts enrolled into the trial and received BoNTA intra-detrusor injection; 33 females and 5 males; Mean age was 55 (range: 22-80). Tables 1 and 2 represent the therapeutic outcome when we analyzed UUI episodes and UF in OAB-wet and entire OAB cohort respectively. Tables 3 and 4 illustrate the two groups' outcome with respect to their improvement response rate achieved when compared to baseline.

Table 1. Urge Incontinence episodes (3xVD Mean) in OAB-wet

OAB-wet	Baseline	Response	T-test Comparison
100 U (n=11)	9.2 ± 6	2.8 ± 4	p = 0.006
150 U (n=11)	8.1 ± 5	3.4 ± 6	p = 0.004
T-test Comparison	p = 0.626	p = 0.740	

Table 2. Urinary Frequency (3xVD Mean) in OAB

OAB	Baseline	Response	T-test Comparison
100 U (n=18)	16.6 ± 7	9.9 ± 4	p = 0.002
150 U (n=20)	20.6 ± 12	13 ± 6	p = 0.004
T-test Comparison	p = 0.208	p = 0.059	

Table 3. Urinary Urge Incontinence Improvement (%) Response after BoNTA in OAB-wet

	Good Response		***Moderate Response***		***No Response***	
	≥90% IMP	**70- 89% IMP**	**60-69% IMP**	**50-59% IMP**	**<50% IMP**	**Total**
100 U	3	3	1	1	3	11
150 U	5	1	1	1	3	11
Total	8	4	2	2	6	22

Table 4. Urinary Frequency Improvement (%) Response after BoNTA in OAB

	Good Response	***Moderate Response***		***Mild Resp.***	***No Resp.***	
	75-60% IMP	**50-59% IMP**	**40-49% IMP**	**20-39% IMP**	**<20% IMP**	**Total**
100 U	5	0	3	5	5	18
150 U	2	2	6	2	8	20
Total	7	2	9	7	13	38

Interpretation of results:
There was no statistical difference at baseline between 100 and 150 U OAB-wet groups, in age, urinary frequency and UUI episodes. Both groups showed a significant decrease in UUI (Table1). There was no difference (X^2 $p>0.05$) in UUI between 100 and 150 U when we analyzed the OAB-wet three different groups' improvement response (Good, Moderate and No response). 73% (8/11) of patient's both groups qualified as responders with > 50% improvement in UUI. Although the number of patients showing a "Good" (6/8) and a "Moderate" (2/8) response amongst the responders (8/11) is the same for both dose's groups, pts who received 150 U (5/6) were more likely to become completely dry (>90% IMP) than those with 100 U (3/6) after analyzing (X^2 $p<0.05$) those who achieved a "Good" response (70-100% IMP) (Table 3).

Both groups showed a significant decrease in UF after BoNTA treatment. However, there was no statistical difference between the 100 U and the 150 U groups (p=0.059). There was no difference (X^2 p>0.05) in UF between 100 U and 150 U when we analyzed all OAB patient's different groups of improvement response (Good, Moderate, Mild and No response). Furthermore, there is no difference among the responder groups when we compared 100 and 150 U groups (X^2 p>0.05) (Table 4).

Concluding message:

- It appears that intra-detrusor injections of 100 and 150 U BoNTA accomplished a significant clinical response, decreasing both urge incontinence and urinary frequency in patients with idiopathic overactive bladder refractory to oral antimuscarin medications.
- The therapeutic response in urinary frequency achieved by the 150 U group is not significantly superior than the 100 U group.
- Although BoNTA 150 U failed to show a significant overall difference in urge incontinence episodes when compared to 100 U, patients who received 150 U are more likely to be completely dry (>90% IMP).

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CLINICAL TRIAL REGISTRATION: IRB: 20020122
HUMAN SUBJECTS: This study was approved by the Institutional Review Board and followed the Declaration of Helsinki Informed consent was obtained from the patients.