103

Gousse A[1], Rivera R[1], Tunuguntla H[1], Barboglio P[1]
1. University of Miami Miller School of Medicine

REPEATED INTRADETRUSOR INJECTIONS OF BOTOLINUM TOXIN-A IN NEUROGENIC OVERACTIVE BLADDER: URODYNAMIC, UDI-6 AND QUALITY OF LIFE DATA

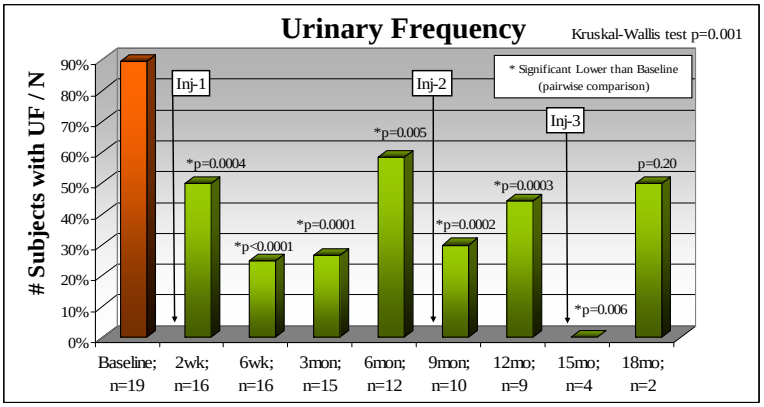
Hypothesis / aims of study:
Intra-detrusor Botulinum neurotoxin type A (BoNTA) injection has emerged as a novel therapeutic option for the treatment of neurogenic overactive bladder (N-OAB).[1,2] We designed an IRB approved prospective trial to evaluate changes in urodynamic findings, symptomatic improvement, and quality of life (QOL) in N-OAB patients (pts) submitted to a scheduled re-injection BoNTA protocol.

Study design, materials and methods:
20 Pts with urinary incontinence associated neurogenic detrusor overactivity requiring clean intermittent self-catheterization (S-CIC) were randomized to receive BoNTA (300 U or 400 U) as 10 U/ml/injection "trigone and dome sparing" (30-40 injections). Prior to injection, the pts were evaluated by: history, physical examination, Urogenital Distress Inventory-6 (UDI6), multichannel videourodynamics (V-UDS), and urine culture. Repeat V-UDS were obtained at 6 weeks, 6, 9, 12, 15 and 18 months. Pts were re-injected using the same randomized dose and technique every 6 months regardless of response. We used T-test or Pearson Chi-square test for analysis and comparison of all time points against baseline. P<0.05 was considered significant. Clinical outcome was assessed by UDI-6 validated questionnaire. We used question (Q) 1 to evaluate urinary frequency (UF) of S-CIC and Q 2 and 3 for urinary urge incontinence (UUI). UDI-6 answers domains 0-1 were taken as negative and domains 2-3 were considered positive. We used Kruskal-Wallis for the statistical analysis. For QOL we used and analogue scale (range 0-10) whereas 10 was considered the worst status and 0 the best.

Results:
Of the 20 pts, there were 16 males and 4 females (Mean age: 40±10); Twenty pts received the 1st injection, ten patients have received a 2nd injection and six a 3rdone. 3 Pts withdrew the study during the first 6 months period after 1st treatment. Two pts stated that they did not gain any improvement and one pt died during a motor vehicle accident.

Table 1. UDS outcome data: Comparison against Baseline

BoNTA Injection #	Period	N = pts	MCC cmH20	Det-max*p* cmH20	UDS-Leak % pts	DO % pts
1st Inj	Baseline	19	364±170	44±27	45%	45%
	6 wk	15	*454±126	35±20	*15%	*15%
	12 wk	15	*459±121	35±19	*13%	*13%
2nd Inj	6 mon	15	*445±131	30±19	30%	30%
	9 mon	10	*483±177	*23±8	38%	13%
3rd Inj	12 mon	8	464±181	*35±22	38%	63%
	15 mon	4	449±193	16±7	25%	0%
	18 mon	2	374±235	18±4	0%	0%
			T-test	T-test	Chi-square	Chi-square
			*p<0.05	*p<0.05	*p<0.05	*p<0.05



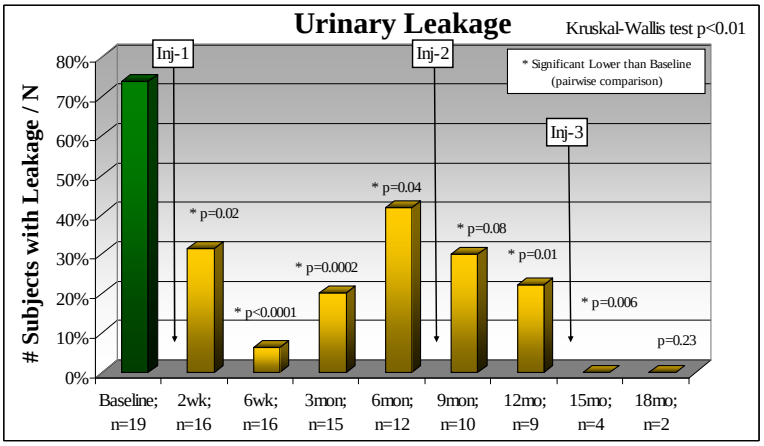


Table 3. Quality of Life (QOL) Outcome data and comparison against Baseline

	Baseline	2wk	6wk	12wk	6mon	9mon	12mon	15mon	18mon
Mean	8.1	6.8	6.3	4.8	5.8	4.1	4.2	2.3	3.5
SD +	2	3	3	3	3	3	4	2	5
N=	19	16	16	15	12	10	9	4	2
T-test Comparison against baseline		*0.092*	*0.039*	*0.001*	*0.014*	*0.004*	*0.014*	*0.008*	*0.411*

Interpretation of results:

BoNTA significantly increased maximum cystometric capacity (MCC) and decreased detrusor maximum pressure (Detmax*p*) when compared to baseline. Pts showed less urodynamic leakage (UDS-Leak) and less detrusor overactivity (DO) after 1st BoNTA treatment (Table 1). UUI episodes and UF of S-CIC significantly decreased after every BoNTA injection according to UDI-6 validated questionnaire (Graphics). QOL significantly increased after each BoNTA injection when compared to baseline (Table 3).

Concluding message:

Intra-detrusor injections of BoNTA 300 U and 400 U repeated every 6 months can provide rapid, well-tolerated, significant improvement on urodynamic and clinical parameters in neurogenic overactive bladder pts already on S-CIC. This is translated into a decrease in urinary incontinence and urinary frequency of S-CIC associated with N-OAB. Quality of life significantly improves when patients are submitted to a repeated schedule of intra-detrusor BoNTA. These data indicate that repeat BoNTA injections 300/400 U may be safe and efficacious in N-OAB patients.

References:

1. Stohrer M, Schurch B *et al. Neurourol Urodyn* **18** (1999), p. 401-2.
2. Scurch B, de Seze M, *et al. J Urol* **174** (2005), p. 196-200.

FUNDING: Allergan provided the study medication and The Veterans Affairs Miami Medical Center contributed with funding
CLINICAL TRIAL REGISTRATION: IRB: 10-1086
HUMAN SUBJECTS: This study was approved by the Institutional Review Board and Veterans Affairs Ethics Committee and followed the Declaration of Helsinki Informed consent was obtained from the patients.