102

Gousse A[1], Cohen B[1], Rodriguez D[1], Barboglio P[1]
1. University of Miami Miller School of Medicine

BOTULINUM TOXIN A: INTRADETRUSOR RE-INJECTIONS IN IDIOPATHIC OVERACTIVE BLADDER EVERY 6 MONTHS – 3 YEARS FOLLOW UP

Hypothesis / aims of study:
In this prospective, IRB approved, randomized, ongoing study we evaluated the efficacy and safety of scheduled repeated intradetrusor injections of botulinum neurotoxin-A (BoNTA) in order to treat patients (pts) with idiopathic overactive bladder (OAB) resistant to antimuscarinic drugs. The aim of this study was to assess the therapeutic response of every injection period, analyzing the dominant symptom: urinary urge incontinence (UUI) in OAB-wet and urinary frequency (UF) in OAB-dry (without UUI) through an every 6 months re-injection protocol (3 year follow-up).

Study design, materials and methods:
38 OAB pts, 33 females and 5 males with non-neurogenic etiology were randomized to receive BoNTA (100U or 150U) as 10U/ml/injection "trigone and dome sparing" (10 or 15 intradetrusor injections respectively). We used a 14 Fr flexible cystoscope / 27G-4mm needle. Patients were re-injected using the same dose every 6 months. 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. ANOVA (one-way) was used for the multi-analysis and significance was established with $p<0.05$. Bonferroni test was implemented for the pairwise comparison at all time points against baseline and significance was established with $p<0.002$.
The response outcome was calculated during each 6 months period of every BoNTA injection. In order to evaluate this, we considered as favorable response: More than 50% improvement (IMP >50%) in UUI episodes in OAB-wet pts and more than 40% in UF in those OAB-dry pts (Tables 1 and 2)

Results:
A total of 22 OAB-wet and 16 OAB-dry pts with a mean age of 55 years old (range: 22-80) enrolled the protocol. Grapchics 1 and 2 illustrate the average of UF and UUI episodes at all time points. Tables 1 and 2 describe the number of BoNTA injections that each group of OAB pts has accomplished and the response rate achieved with respect on their dominant symptom.

Interpretation of results:
Both groups showed a significant distribution, UUI episodes in OAB-wet pts ($p<0.0002$) and UF in those OAB-dry ($p=0.001$). Graphics illustrated a sloping trend, whereas drops were localized between 6 and 12 wk and peaks at every 24 wk injection period. Each BoNTA treatment demonstrated to be significantly lower than baseline during all periods when UUI and UF where analyzed in OAB-wet and dry respectively. The only exception was at BoNTA 6^{th} injection. However this was due to the small number of pts reaching this time of interval injection. When we analyzed each patient response based on their dominant symptom (Table 1-2) we noted a persistent favorable response after the 3^{rd}BoNTA injection and subsequent injections, superior to 40% and 50% in the OAB-dry and wet groups respectively, when compared to baseline.

Concluding message:
- BoNTA provides a rapid, well-tolerated clinical and significant improvement on the dominant symptom in idiopathic OAB patients wet and dry.
- This significant decrease in urinary frequency and urge incontinence can be sustained if OAB-dry and wet pts respectively, are subjected to a scheduled re-injection BoNTA therapy
- Not all the patients responded to the therapy.
- No age or sex difference was identified.

Patients with OAB-wet who achieve a clinical improvement in urge incontinence superior than 50% from baseline after the first injection, never became refractory after following therapy.
To our knowledge, this is the first trial showing repeated BoNTA injections outcome data in idiopathic OAB with 3 years follow-up.

FUNDING: Allergan provided the study medication and some funding.
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.

Table 1. UF Response in OAB-dry

# - Inj	N=	IMP <40%	IMP >40%
1st-Inj	16	5 (31%)	11 (69%)
2nd-Inj	9	2 (22%)	7 (78%)
3rd-Inj	4	0	4 (100%)
4th-Inj	4	0	4 (100%)
5th-Inj	4	0	4 (100%)
6th-Inj	1	0	1 (100%)

Table 2. UUI Response in OAB-wet

# - Inj	N=	IMP <50%	IMP >50%
1st-Inj	22	6 (27%)	16 (73%)
2nd-Inj	14	4 (36%)	9 (64%)
3rd-Inj	8	2 (25%)	6 (75%)
4th-Inj	6	0	6 (100%)
5th-Inj	4	0	4 (100%)
6th-Inj	2	0	2 (100%)