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THE NATURAL HISTORY OF URINARY URGENCY FOLLOWING INTRADETRUSOR INJECTIONS OF BOTULINUM NEUROTOXIN A – A COMPARISON BETWEEN PATIENTS WITH NEUROGENIC (NDO) AND IDIOPATHIC (IDO) DETRUSOR OVERACTIVITY (DO).

Hypothesis / aims of study
The pathological sensation of urgency is now recognised as the core symptom of the overactive bladder (OAB) syndrome, with a marked negative impact on patient's quality of life (QoL). DO-associated urgency has been shown to be successfully suppressed at least in the short term by intradetrusor BoNT/A injections in a comparable fashion in NDO or IDO patients. The decrease in urgency corroborated the impressive improvements in patients' QoL.
To date, no study has investigated the immediate effect of intradetrusor BoNT/A on urinary urgency and pinpointed the time at which it diminishes after treatment. We examined the effect of intradetrusor BoNT/A on urgency and associated LUTS by studying the daily changes from baseline during the week succeeding treatment of patients with NDO or IDO.

Study design, materials and methods
Twenty-five patients, 16 with NDO (mean age 44.1 years) and 9 with IDO (mean age 45.6 years), treated with 300U BOTOX® (NDO) or 200U BOTOX® (IDO) were asked to complete a 4-day voiding diary before and at 4 and 16 weeks post treatment, as well as a 7-day voiding diary starting the day immediately after the injections. Patients participated in a study approved by the local Ethics Committee. Data on urgency, urgency incontinence ("leak"), and 24-hour frequency were analysed for intra-group daily changes during the 1st week and for further changes at 4 and 16 weeks. Statistical analysis was performed using the parametric t-tests (significance at $p<0.05$).

Results
No differences were noted at baseline between the 2 groups in either urgency (p=0.46), 24-hour frequency (p=0.26), or incontinence (p=0.12)
Intra-group changes for the 3 efficacy variables (expressed as mean ± standard error) are presented in the following Tables.

Table 1. Changes in LUTS in the NDO group

	Urgency	**Urgency p value (Pre v ...)**	**Frequency**	**Frequency p value (Pre v …)**	**Leak**	**Leak p value (Pre v …)**
Pre	8.1 ± 0.8		11.4 ± 0.7		3.3 ± 0.9	
Day 1	7.3 ± 0.8	0.11	10.6 ± 1.7	0.46	1.9 ± 0.8	0.24
Day 2	4.9 ± 0.7	**0.0005***	9.6 ± 0.9	**0.01***	1.3 ± 0.5	0.17
Day 3	3.9 ± 0.8	**<0.0001***	9.1 ± 0.9	**0.001***	0.7 ± 0.3	**0.02***
Day 4	4.8 ± 1.1	**0.005***	9.2 ± 1.0	**0.02***	0.4 ± 0.2	**0.005***
Day 5	3.6 ± 0.8	**<0.0001***	8.0 ± 0.8	**<0.0001***	0.6 ± 0.3	**0.01***
Day 6	4.4 ± 0.9	**0.002***	8.4 ± 1.0	**0.001***	0.7 ± 0.3	**0.02***
Day 7	3.7 ± 1.0	**0.002***	7.5 ± 1.1	**0.002***	0.4 ± 0.2	**0.008***
4 weeks	2.6 ± 0.7	**<0.0001***	6.5 ± 0.9	**<0.0001**	0.3 ± 0.2	**0.005***
16 weeks	2.1 ± 0.9	**<0.0001***	7.2 ± 0.8	**0.002**	0.4 ± 0.2	0.09

***p<0.05**

NDO: Significant improvements in both urgency and 24-hour frequency were seen as of Day 2 (48-72 hours) post-injection and incontinence as of Day 3 (72-96 hours)

Table 2. Changes in LUTS in the IDO group

	Urgency	**Urgency p value (Pre v ...)**	**Frequency**	**Frequency p value (Pre v …)**	**Leak**	**Leak p value (Pre v …)**
Pre	9.3 ± 1.7		12.9 ± 1.3		6.3 ± 1.9	
Day 1	9.7 ± 2.7	0.77	13.4 ± 1.9	0.59	5.2 ± 2.1	0.39
Day 2	6.8 ± 2.4	0.09	13.3 ± 1.9	0.69	4.4 ± 1.9	0.12
Day 3	10.0 ± 3.8	0.99	14.8 ± 3.1	0.51	4.9 ± 2.1	0.09
Day 4	3.8 ± 0.9	**0.0002***	9.6 ± 1.3	**0.02***	4.1 ± 1.7	**0.04***
Day 5	2.7 ± 1.1	**0.006***	9.5 ± 2.0	0.18	3.3 ± 2.6	0.72
Day 6	4.3 ± 0.8	**0.33**	11.2 ± 2.0	0.79	3.2 ± 2.8	0.62
Day 7	2.4 ± 1.1	**0.03***	8.8 ± 1.2	0.21	1.8 ± 1.4	0.07
4 weeks	1.9 ± 0.8	**0.002***	7.5 ± 0.8	**0.004***	2.4 ± 1.3	**0.04***
16 weeks	6.3 ± 3.3	**0.04***	10.8 ± 2.5	0.07	0.8 ± 0.6	0.14

IDO: No significant changes in urgency were seen till Day 4 post-treatment (96-120 hours). Similarly, a decrease in 24-hour frequency and incontinence appeared to start at day 4, despite absence of consistent statistical significance. A significant reduction in all 3 variables was established at 4 weeks, only a reduction in urgency was sustained at 16 weeks, but small patient numbers with available data (n=5) may have affected significance.

Interpretation of results

Previous studies have shown a comparable decrease in urgency, 24-hour frequency, and incontinence at 4 and 16 weeks post intradetrusor BoNT/A between NDO and IDO patients. The immediate response in all 3 variables appears to be most rapid in the NDO population and followed a systematic pattern. By contrast the changes in the IDO group were more erratic and took longer to reach significance, with urgency showing the most consistent trend. This difference may either be because IDO patients formed a less homogeneous group or because they had been treated with a lower dose of toxin.

Concluding message

Intradetrusor BoNT/A significantly improves symptoms of the OAB syndrome within the 1st week of treatment. The somewhat delayed IDO response may be dose dependant.

Urgency is the most consistently affected symptom in both the NDO and IDO populations, with the earliest noticeable change being observed within 48-72 hours post treatment.

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