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BOTULINUM TOXIN-A FOR PATIENTS WITH IDIOPATHIC DETRUSOR OVERACTIVITY:
EARLY RESULTS FROM A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL.

Hypothesis / aims of study
Results from recent open-labelled studies have shown that intra-detrusor injections of botulinum toxin-A (BTX-A) may be effective in treating patients with idiopathic detrusor overactivity (IDO) refractory to anticholinergics (1, 2). To validate this further, a randomised, double-blind, placebo-controlled trial was instigated at our institution. Statistical analysis showed a total sample size of 32 patients (16 in each group) will have 90% power to detect a significant difference in the primary endpoint variables of this study.

Study design, materials and methods
This study is a single-center, double-blind, placebo-controlled trial of patients with idiopathic detrusor overactivity refractory to anticholinergics. All patients recruited into the trial have symptoms of the overactive bladder and have detrusor overactivity proven on urodynamic studies. Patients are randomised to receive either 200 units of BTX-A or placebo via a flexible cystoscopic technique. Urodynamic and voiding diary parameters were assessed at baseline and at 4 and 12 weeks, post injection. Quality of life (QoL) was assessed using the King's Health Questionnaire (KHQ), Urogenital Distress Inventory (UDI-6) and the Incontinence Impact Questionnaire (IIQ-7). These disease-specific validated questionnaires were all assessed at baseline and at 4 and 12 weeks, post injection. Twenty-five patients have been injected so far and 18 have completed the trial (10 placebo, 8 BTX-A).

Results
In the BTX-A treated group there was a significant reduction in urinary frequency ($p<0.0001$; $p<0.0001$), urgency ($p<0.0001$; $p<0.0001$) and urge incontinence ($p<0.0003$; $p<0.0001$) episodes/24 hour period at 4 and 12 weeks post injection, respectively. Significant increases were also seen in maximum cystometric capacity at 4 weeks ($p<0.005$) and 12 weeks ($p<0.007$) with decreases in maximum detrusor pressure on filling at 4 weeks ($p<0.038$). There was no significant difference in this group with regards to post void residual, although 3 patients have needed to learn intermittent self catheterisation (ISC). QoL in this group was also significantly improved when using the KHQ ($p<0.009$; $p<0.003$), IIQ-7 ($p<0.014$; $p<0.015$) and UDI-6 ($p<0.002$; $p<0.028$) questionnaires at 4 and 12 weeks post-injection, respectively. No statistically significant changes were found in the placebo group in any of the voiding diary, urodynmaic or QoL parameters tested except for urinary urgency which was significantly reduced at 4 ($p<0.026$) and 12 weeks ($p<0.030$) when compared with baseline.

Interpretation of results
BTX-A significantly reduces urinary frequency and urge incontinence episodes when compared to placebo for at least up to 12 weeks. Maximum cystometric capacity is also significantly increased in this group when compared to placebo at 4 and 12 weeks post-injection. Maximum detrusor pressure on filling was significantly reduced in the BTX-A group at 4 weeks when compared with placebo and although this trend continued at 12 weeks this was not statistically significant. Interestingly both BTX-A and placebo statistically reduced urinary urgency at both time points post-injection. This can be attributed to a partial placebo response seen in 3 patients.

Concluding message
BTX-A injections at 200 units appears to improve subjective and clinical parameters compared to placebo in IDO patients at 4 and 12 weeks post injection. Perhaps of more significance from the patients perspective is that BTX-A dramatically improves QoL when

compared with placebo. Careful patient counselling is necessary however, especially about the need to perform ISC.

The protocol for this study has ethical committee approval.

References

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