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EFFICACY AND COMPLICATIONS OF THE INTRADETRUSOR INJECTION OF DYSPORT (BOTULINUM TOXIN A) IN PATIENTS WITH REFRACTORY OAB

Hypothesis / aims of study

Overactive bladder syndrome (OAB) is characterised by a combination of urinary frequency, urgency and urge incontinence. These symptoms are frequently disabling both physically and socially and cause considerable distress as well as cost to both individuals and the health service. Whilst simple management with pelvic floor muscle training and bladder drill, as well as drug therapy with anticholinergic drugs, improves symptoms for the majority of patients there is a minority with refractory symptoms who will require further treatment. Whilst major surgery, in the form of bladder augmentation, is effective it also carries a very high risk of morbidity and longterm complications. The injection of Botulinum Toxin A under cystoscopic guidance has been shown to be effective in the treatment of this condition.(1) There are two Botulinum A products available commercially, BOTOX ® and DYSPORT ®. Most studies to date have used BOTOX ® in doses ranging from 200 to 300IU. BOTOX ® is two to three times more potent than DYSPORT ®. There is as yet very little data on the use of DYSPORT ® in OAB. Our aim was to investigate the response to the intradetrusor injection of DYSPORT ® 500iu in patients with refractory OAB.

Study design, materials and methods

Patients with refractory neurogenic (NDO) or idiopathic detrusor overactivity (IDO) were recruited from two hospitals. All subjects had pre-treatment urodynamics confirming detrusor overactivity and had been through a bladder retraining programme. We only recruited those with refractory OAB and therefore subjects were only included if they had failed anticholinergic therapy for at least 6 months, or if anticholinergic therapy was contraindicated or if they were unable to comply with anticholinergic drugs due to severe side-effects. An additional criterion for inclusion was that the subject would otherwise have been considered for neuromodulation or for augmentation surgery. The procedure was performed in the operating theatre as a day case. DYSPORT® 500iu was diluted in 20ml of Normal Saline and 1ml was injected into the detrusor at 20 sites using a flexible cystoscope, sparing the trigone. Response to treatment was assessed subjectively by recording symptoms of urgency and urge incontinence as well Visual Analogue Scores (VAS 0-10) of the impact of their symptoms on Quality of Life (QOL) at 1 week, 6 weeks, 3 months, 6 months and 9 months following treatment. Objective assessment included Kings Health Questionnaires (KHQ), 24 hour pad tests and voiding diaries pre-treatment and at 6 weeks, 3 months, 6 months and 9 months post –treatment. Saline cystometry was repeated at 3 months post treatment.

Results

23 patients were treated with intradetrusor DYSPORT ® injections, including 20 (87%) females and 3 (13%) males The mean age was 61 (range 37-81). 22 (96%) patients had IDO and 1 (4%) patient had NDO. Subjects had been symptomatic for detrusor overactivity for a mean of 103 months (8.5 years) and been treated with a mean of 3 (range 1-5) anticholinergic drugs prior to treatment. There were no intra-operative or early post-operative complications. Due to the ongoing nature of this study, follow up results were available for 23 patients at 1 week, 19 at 6 weeks and 3 months, 13 at 6 months and 7 at 9 months.There was a significant reduction in mean daily frequency episodes from the first week following treatment which persisted through to the 6 week, 3 month and 9 month follow up visits. This did not reach significance at 6 months possibly due to the sample size. There were significant improvements in a number of quality of life domains on the Kings Health Questionnaire, with a reduction in the severity measures score from 75 pre-treatment to 58 at 6 weeks, remaining significant to 9 months (P=0.035). The urgency domain also showed a significant improvement from a pre-treatment mean of 2.6 to a mean of 1.5 at 9 months (P=0.03).

There was also a siginificant reduction in urge incontinence at 1 week post-treatment with 14 (61%) patients reporting no urge incontinence. At 3 months, 6 (32%) patients were still dry which was statistically significant (P=0.02). Improved Quality of Life Visual Analogue Scores (VAS) were reported with a reduction from a pre-treatment mean VAS 8/10 to 5/10 at 1 week persisting to 5/10 9 months post treatment.

Urodynamic parameters at 3 months were also significantly improved with the mean maximum cystometric capacity increasing from 278ml to 378ml (P=0.003) and the mean volume of first desire to void increasing from 144ml to 270ml (P=0.021).

There was a high incidence of urinary retention in the cohort with 8 out of 19 (42%) patients requiring either clean intermittent self-catheterisation (CISC) or suprapubic catheterisation at 6 week follow-up. 31% of patients were still needing catheterisation at 3 month follow up.

Table One- Subjective and objective data pre- and at 1 week, 6 weeks, 3 months, 6 months and 9 months follow up.

	Before *n=23*	***1week*** *n=23*	***6 week*** *n=19*	***3 month*** *n=19*	***6 month*** *n=13*	***9 month*** *n=7*

Urge Incontinence		22 (95%)	9** (39%)	11* (58%)	13* (68%)	11 11(84%	5 (71%)
Mean QOL VAS (0-10)		8.4	5.3*	5*	5*	7	5
Bladder diary: Mean daily frequency episodes		9.3	7*	6.5*	6.6*	7.5	7.6*
CMG	First Desire Maximum capacity Vol. at first det. contraction	156 278 144			249* 378** 270		
KHQ	Severity measures Urgency Urge incontinence Frequency	75 2.6 2.6 2.6		58* 1.8* 1.6* 1.3**	59* 1.9* 1.8* 2.1	57* 1.5* 1.5 2	21* 1.5* 1.3 1.2*
Need CISC / Suprapubic catheter			4 (17%)	8(42%)	6(31%)	1(7%)	0

*P<0.05 **P<0.005

Interpretation of results

Intradetrusor DYSPORT ® 500iu appears to be an effective treatment for refractory OAB with significant improvements in both objective and subjective measures for up to 9 months post treatment. Concerningly, the incidence of voiding dysfunction was significantly higher than that reported in other studies(2).

Concluding message

Intradetrusor injection of Dysport 500iu is clearly effective in this group of patients. Longer term follow up in a larger group of patients, however, is required to assess if these benefits persist beyond 9 months and to more clearly define the risk of voiding dysfunction.

References

1. BJU Int 2003; 92: 325-326
2. Neurourology and Urodynamics 2005; 24:1

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HUMAN SUBJECTS: This study was approved by the Wandsworth Local Ethics Committee and followed the Declaration of Helsinki Informed consent was obtained from the patients.