

## EVALUATION OF THE LONG TERM EFFICACY OF REPEATED DOSES OF INTRADETRUSOR BOTULINUM TOXIN (DYSPORT®) INJECTIONS

### Hypothesis / aims of study

Intradetrusor botulinum toxin injections are effective in the treatment of refractory OAB. At present there is paucity of data on the long term efficacy of repeated courses. Our study evaluated quality of life parameters using the King's Health Questionnaire in a cohort of patients with refractory OAB who required more than one course of Dysport® injections.

### Study design, materials and methods

We prospectively studied the efficacy of repeated doses of intradetrusor injection of Dysport® using the Kings Health Questionnaire (KHQ). Preoperatively, all patients had detrusor overactivity confirmed by urodynamic investigations and underwent bladder retraining. Patients were only included if they had failed more than one anticholinergic agent 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. The procedure was performed in the operating theatre as a day case. Dysport® 500-1000iu was diluted in 20ml of normal saline and 1ml aliquots were injected into the detrusor muscle at 20 sites above the interureteric ridge sparing the trigone and the dome using a grid pattern of 5x4 sites spaced evenly. Response to treatment was assessed at 1 week, 6 weeks, 3 months, 6 months and 9 months postoperatively for each injection procedure. Assessment also included the use of 24 hour pad tests and voiding diaries. Urodynamic assessment was repeated at 3 months

### Results

For the purposes of this study we present outcomes based on the KHQ domain scores. Fifty seven female patients underwent intradetrusor Dysport® injections, over a 3 year period. Of them, 35 women had at least one repeat course of this treatment. The mean and median time interval between the first and the second injection was 9 months. Data for long term follow up (at least 9 months from the second course) were available for 14 patients. The mean age of this cohort was 63 years.

There were no significant perioperative complications apart from voiding difficulty. Improvements in quality of life parameters are demonstrated in table 1 and Fig 1. Those improvements were maintained for 6 to 9 months. The improvements of the quality of life domains were significant for the first and second course but not for the third probably due to the small numbers of women requiring a third injection. The incidence of voiding difficulty defined by symptoms on KHQ domains and / or requirement for catheterisation by any route (IDC, SPC, or CISC) was not increased on subsequent courses.

### Interpretation of results

Repeated courses of Intradetrusor Dysport® appear effective in the treatment of refractory OAB for up to 9 months post treatment. The necessity for repeated courses of intradetrusor botulinum toxin injections appears to be more common in older patients. In our cohort patients requiring repeat courses tend to be older. On review, these patients have reduced PDetMax compared to younger subjects which may predispose them to higher rate of postoperative voiding difficulty. In such patients CISC should be taught preoperatively or consideration given to insertion of an SPC if CISC is not possible because of body habitus or lack of manual dexterity. These represent a difficult group of patients to treat as they have a combination of refractory OAB possibly due to age related detrusor degeneration and associated voiding difficulty.

### Concluding message

Botulinum toxin in this small cohort appears to improve both quality of life and urge frequency symptoms in those with refractory OAB where other conservative treatments have failed. Currently available alternative surgical interventions such as sacro neuromodulation or augmentation cystoplasty are more invasive, costly and associated with higher morbidity. Further consideration should be given to the role of repeat intravesical botulinum toxin injections in women with refractory OAB. Ongoing research is required to determine appropriate patient selection and optimal dosage. However we feel that intravesical botulinum toxin is a valuable effective and minimally invasive option for this difficult group.

Table 1. Mean scores for Various Domains on the King's Health Questionnaire

	Pre/op	1st Course (14 women)				2nd Course (14 women)				3rd Course (9 women)		
		6 wks	3 mo	6 mo	9 mo	6 wks	3 mo	6 mo	9 mo	6 wks	3 mo	6 mo
Urgency	2.54	2.36	2.21	1.62	2	2.16	1.77	1.77	2.4	2	0.8	2.67
Perception of Bladder Condition	74	55	52	56	78	75	51	50	38	57	72	67
Role Limitations	72	59	50	58	72	60	61	50	50	43	56	73
Physical Limitations	69	74	63	58	68	58	61	55	50	71	72	67
Social Limitations	62	62	50	47	66	42	46	34	44	47	48	59
Emotions	64	57	54	52	66	57	63	54	40	63	55	51
Sleep/Energy	68	63	53	63	59	65	68	50	53	62	53	61
Severity Measures	82	66	61	57	60	61	63	57	52	74	73	80

Figure 1. Various domains on the King's Health Questionnaire

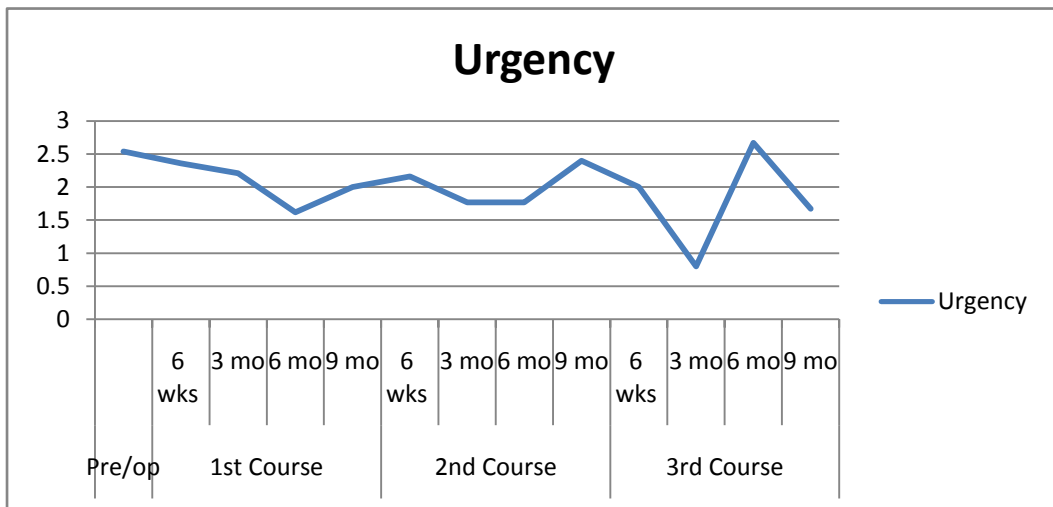
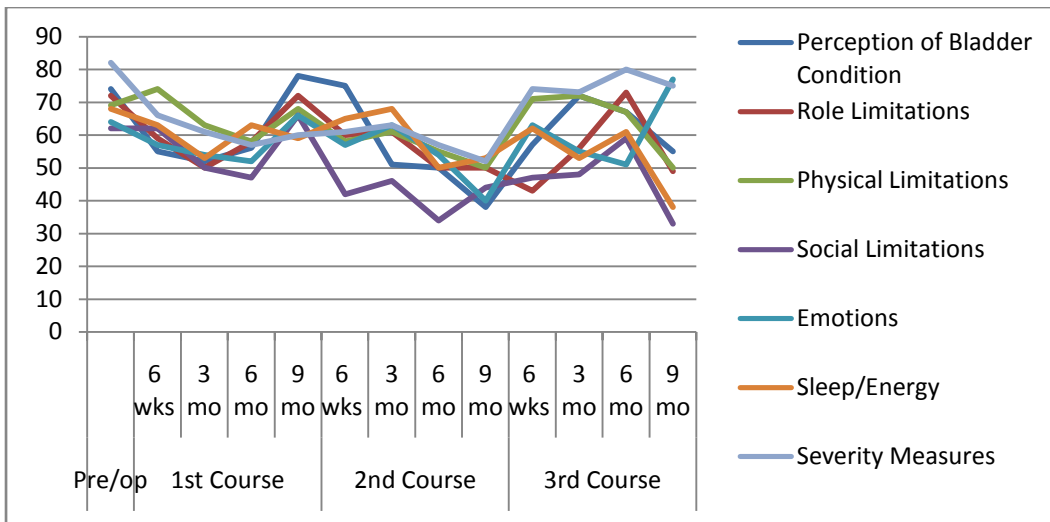


Figure 2. Mean urgency values on the King's Health Questionnaire

<b>Specify source of funding or grant</b>	<b>No funding was required.</b>
<b>Is this a clinical trial?</b>	<b>No</b>
<b>What were the subjects in the study?</b>	<b>HUMAN</b>
<b>Was this study approved by an ethics committee?</b>	<b>Yes</b>
<b>Specify Name of Ethics Committee</b>	<b>Wandsworth ethics committee.</b>
<b>Was the Declaration of Helsinki followed?</b>	<b>Yes</b>
<b>Was informed consent obtained from the patients?</b>	<b>Yes</b>