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A DOUBLE-BLIND, PLACEBO CONTROLLED STUDY INVESTIGATING EFFICACY OF BOTULINUM TOXIN TYPE A (DYSPORT®) IN MS RELATED OVERACTIVE BLADDER SYNDROME (OAB): QUALITY OF LIFE (QOL) DATA.

Hypothesis / aims of study: The use of botulinum toxin type A (Dysport®) in the treatment of OAB is increasing. However, with few placebo controlled studies performed assessing the role of Dysport the majority of current evidence supporting its efficacy depends on non-randomised and anecdotal data. Our aim was to undertake a pilot placebo controlled study assessing the impact on the quality of life (QoL) of botulinum toxin type A (Dysport®) in MS related overactive bladder syndrome (OAB).

Study design, materials and methods: 20 patients with a formal diagnosis of MS for at least one year, made by a Consultant Neurologist, were included and randomised into the study. Each also had OAB syndrome diagnosed by a Consultant Urologist and had at least one episode of leakage per day. All had urodynamically proven detrusor overactivity and had found anti-cholinergics either ineffective or their side effects intolerable. Patients with symptoms of stress related incontinence were excluded from the study. With the investigators and recruits "double-blinded", 10 patients were injected with 500units Dysport® diluted in 5ml 0.9% saline, and 10 patients with 5mls placebo. Injections were performed via flexible cystoscopy. SF-36, Hospital Anxiety and Depression Scale (HADS) and the Kings Health Questionnaires were completed prior to injections (baseline), 12 weeks and at 36weeks. Patients were asked if they had seen an overall improvement in symptoms, those who had not were withdrawn from the study at 12 weeks as it was deemed unethical to subject these people to further urodynamics and to go without treatment for a further 6 months.

Results: 13 patients noticed improvements and stayed in the trial. 7 withdrew at the 12 week stage; none of which had been given active treatment. For analysis the change in median values from baseline to the 12 week stage were compared between the placebo and active arms using the Mann-Whitney test. As only 3 subjects receiving placebo were present at the 36 week stage a paired t-test was performed between the active group at baseline and 36 week point. Changes in score for each domain within the three questionnaires are illustrated in table 1.

A significant improvement was seen in incontinence impact, role limitations, physical limitations, physical relationships, sleep/energy and severity measures at the 12 week stage; comparing active to placebo. Comparing baseline values to those at 36 weeks, in the active arm alone, these measures were also found to be significant at this stage. In addition, compared to baseline, those patients in the active arm also perceived that their general mental health, health perceptions and overall health compared to the previous year had improved.

Interpretation of results: In MS patients suffering from associated OAB wet botulinum toxin type A (Dysport ®) is effective in improving patients overall quality of life. In the short term it gives the perceived improvement in the impact of incontinence and those features affected directly as a result of leakage, such as overall energy, role and physical limitations. In the longer term, patients feel an improvement in their overall mental and general health.

Concluding message: In MS patients suffering from associated OAB wet botulinum toxin type A (Dysport ®) is effective in improving patients overall quality of life and, more importantly, it also gives them a perceived improvement in symptoms.

			Median difference 12wks - baseline	Mann – Whitney Test p value	Mean difference 36wks - baseline	95% CI for difference	Paired t – test p value
SF 36	Physical functioning	Placebo	5.55		-	-	
		Active	2.80	0.85	-2.20	(-26.8, 22.4)	0.843
	Role limitations	Placebo	0.00		-	-	
		Active	0.00	0.94	12.50	(-13.1, 38.1)	0.299
	Bodily pain	Placebo	-6.25		-	-	
		Active	0.00	0.20	3.00	(-7.89, 13.89)	0.549
	Social function	Placebo	0.00		-	-	
		Active	0.00	0.71	15.00	(-1.76, 13.89)	0.074
	General mental health	Placebo	-4.00		-	-	
		Active	12.00	0.15	11.60	(3.02, 20.18)	0.014‡
	Emotion problems	Placebo	0.00		-	-	
		Active	0.00	0.41	6.70	(-20.4, 33.7)	0.590
	Vitality, energy or fatigue	Placebo	10.00		-	-	
		Active	-2.50	0.20	5.00	(-5.66, 15.66)	0.316
	General	Placebo	0.00		-	-	

	health perceptions	Active	2.50	0.45	11.00	(0.36, 21.64)	0.044‡
	Health comp to last year	Placebo	0.00		-	-	
		Active	0.00	0.31	25.00	(1.2, 48.8)	0.042‡
HADS	Anxiety	Placebo	0.50		-	-	
		Active	-3.00	0.10	-2.70	(-5.44, 0.04)	0.053
	Depression	Placebo	0.00		-	-	
		Active	-1.50	0.52	-1.90	(-3.991, 0.191)	0.070
Kings Health	General health perceptions	Placebo	0.00		-	-	
		Active	0.00	0.97	0.00	(-16.86, 16.86)	1.00
	Incontinence impact	Placebo	0.00		-	-	
		Active	-50.05	0.004*	-43.35	(-62.99, -23.71)	0.001‡
	Role limitations	Placebo	-8.35		-	-	
		Active	-41.70	0.017*	-43.35	(-65.25, -21.45)	0.002‡
	Physical limitations	Placebo	-16.60		-	-	
		Active	-50.05	0.001*	-45.02	(-61.92, -28.12)	>0.001‡
	Social limitations	Placebo	-16.65		-	-	
		Active	-27.80	0.13	-36.68	(-58.23, -15.13)	0.004‡
	Personal relationships	Placebo	0.00		-	-	
		Active	0.00	0.01*	-20.00	(-42.34, 2.34)	0.073
	Emotion	Placebo	0.00		-	-	
		Active	-33.30	0.08	-30.01	(-51.88, -8.14)	0.013‡
	Sleep/ energy	Placebo	0.00		-	-	
		Active	-33.30	0.023*	-28.33	(-45.24, -11.42)	0.004‡
	Severity measures	Placebo	-4.15		-	-	
		Active	-58.35	0.003*	-49.81	(-71.32, -28.30)	0.001‡
	Symptom score	Placebo	-1.50		-	-	
		Active	-9.50	0.076	-7.50	(-11.78, -3.22)	0.003‡

Table 1: table illustrating changes in scores for each of the questionnaires SF-36, Hospital Anxiety and Depression Score and Kings Health Questionnaire. Each questionnaire has been broken down into their respective domains. Median difference in quality of life scores 12 weeks following injection and at baseline have been compared between the active and placebo arms; Mann – Whitney Test, a significant difference between the groups has been highlighted (*), $p < 0.05$. Mean difference in the active arm at 36 weeks post injection and baseline are also compared; paired t – test, significant differences have been highlighted (‡), $p < 0.05$).

Specify source of funding or grant	**Unrestricted grant from Ipsen, Slough, UK.**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**Yes**
Specify Name of Public Registry, Registration Number	**MHRA, UK.**
Is this a Randomised Controlled Trial (RCT)?	**Yes**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Lothian Ethics Committee, Scotland.**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**