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THE USE OF DYSPORT® BOTULINUM A TOXIN FOR DETRUSOR INJECTIONS IN PATIENTS WITH SEVERE NEUROGENIC DETRUSOR OVERACTIVITY

Aims of Study

Single multifocal intramural detrusor injections botulinum A toxin are an effective treatment for refractory neurogenic detrusor overactivity in spinal cord injured patients [1,2]. In human striated muscle the effective toxin equivalence of the two commercially available botulinum A toxin preparations is 1 UI Botox® to 3-5 UI Dysport®. For neurogenic detrusor overactivity 300 UI Botox® is used generally, but a large variety of Dysport® dosages have been reported. In this prospective observational study patients were included who received Dysport® as an initial treatment, or after relapse following Botox®.

Methods

Between 08/1998 and 12/2002, in 26 patients with various underlying causes for neurogenic detrusor overactivity who failed anticholinergic therapy Dysport® was used as primary treatment and in 10 after earlier Botox® injections. Thirteen patients received in total 16 multiple Dysport® treatments. 500 UI were used in 9 cases, 750 UI in 27, and 1000 UI in 16 cases. Clinical and urodynamic assessments were made before and after treatment. The patient data are presented in table 1. Dysport® was originally applied by 20 injections solved in 10 ml NaCl, since March 2002 this was changed to 25 injections solved in 5 ml NaCl.

Table 1. Patient demographic data

	Paraplegic		Tetraplegic	
Male	24		1	
Female	7		4	
Total	**14**		**5**	
Complete lesion	16		0	
Incomplete lesion	15		5	
	Mean	Range	Mean	Range
Duration of lesion	10.3	1-40	4.8	1-15
Age (years)	11.6	6-29	9.2	2-16

Etiology: SCI (27) MMC (3) Vascular (5) MS (1)

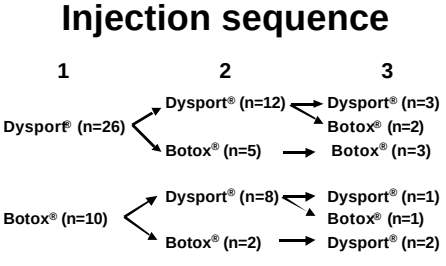
The urodynamic parameters cystometric capacity, overactivity volume (volume at first occurrence of detrusor overactivity), and bladder compliance, the clinical continence volume, clinical functional capacity, and clinical maximum capacity, the anticholinergics dosage, and the patients' subjective satisfaction were recorded before and after treatment.

Statistical comparisons were made by t-tests between the patient groups and by paired t-tests between pre- and post-treatment data. The incidences of incontinence and of anticholinergics use were compared by the χ^2-test. In all cases the two-sided significance level was set at p=0.05.

Results

Thirty-one patients used aseptic intermittent catheterisation for bladder emptying, in 12 as an adjuvant to spontaneous voiding. The other five patients had spontaneous voiding. Seventeen patients were on high dose anticholinergics.

Figure 1. Injections with botulinum A toxin



The succession of the injections is given in fig. 1.

The average follow up duration from the first treatment was 14.1 months (range 1-27 months).

The comparisons between the pre- and the post-treatment data after the first Dysport® treatment are given in table 2. Not all patients had a second observation after this treatment.

A second treatment was given after the effect of the first treatment had faded out. The average

Table 2. Result of treatment 1.		Baseline	Post 1	p	Post 2	p	Statistic
Cystometric capacity (ml)		355	436	**0.0161**	446	**0.0359**	Paired t-test
Overactivity volume (ml)	Not present	5	5	1.0000	5	**0.4397**	$?^2$-test
	Present	254	353	**0.0133**	308	0.2286	Paired t-test
Bladder compliance (ml/cm H_2O)		29.8	42.0	**0.0244**	33.8	0.3029	Paired t-test
Clinical continence volume (ml)		285	462	**0.0001**	359	**0.0304**	Paired t-test
Clinical functional capacity (ml)		323	456	**0.0010**	391	0.2086	Paired t-test
Clinical maximal capacity (ml)		387	563	**0.0010**	468	0.1708	Paired t-test
Anticholinergics use (n=25)*		25	9	**0.0009**	2	0.0789	$?^2$-test
Anticholinergics dose reduction			6		5		
Satisfaction (very) good/minimal/not/failing			17/6/1/2		10/1/2/4		
n=		26	26		17		
			Mean	Range	Mean	Range	
Follow up interval (months)			3.9	2-19	11.1	7-25	

*: One patient used no anticholinergics because of adverse effects and was not included.

interval between the first and the second treatment was 10.1 months (range 2-25 months). There was an apparent dose-dependent increase of the interval with the different Dysport® doses and an overall difference with Botox® used for the primary treatment, but these differences were not significant against the total mean (table 3).

Table 3. Interval between first and second treatment (months).

First treatment	Dysport® 500 UI	Dysport® 750 UI	Dysport® 1000 UI	Dysport® all	Botox®
Interval	9.5	13.2	15.8	12.1	6.7
t-test p	0,0792	0,5022	0,8287	0,3352	0,1604
n=	5	4	8	17	10

The results of the second Dysport® treatment are given in table 4.

Table 4. Result of treatment 2.		Baseline	Post 1	p	Post 2	p	Statistic
Cystometric capacity (ml)		297	394	**0.0181**	353	0.6611	Paired t-test
Overactivity volume (ml)	Not present	5	1	0.1544	0	0.1187	$?^2$-test
	Present	204	337	**0.0425**	296	0.0906	Paired t-test
Bladder compliance (ml/cm H_2O)		21.0	25.6	0.1664	20.4	0.5228	Paired t-test
Clinical continence volume (ml)		245	422	**0.0057**	306	0.1382	Paired t-test
Clinical functional capacity (ml)		301	394	0.0567	309	0.2670	Paired t-test
Clinical maximal capacity (ml)		356	559	**0.0107**	403	0.9766	Paired t-test
Anticholinergics use		16	11	0.4386	4	0.1124	$?^2$-test
Anticholinergics dose reduction			1		0		
Satisfaction (very) good/minimal/not/failing			10/3/2/0		1/2/3/2		
n=		20	16		8		
			Mean	Range	Mean	Range	
Follow up interval (months)			2.3	1-8	12.7	9-14	

Twelve patients underwent a third treatment. The average interval between the second and the third treatment was 9.3 months (range 5-19 months). There is no follow up yet for these patients.

Three patients had transient adverse effects (muscular weakness, obstipation) on Dysport® in the early phase of this study. This was the rationale for changing the amount of carrier liquid. Recently however another patient had observed transient muscular weakness.

Conclusions

750 UI Dysport® diluted in 5ml NaCl and injected at 25 sites is preferred. Its safety, efficacy and the duration is comparable to 300 UI Botox® treatment, with an equivalence ratio of 2.5 to 1. As the effectiveness of first and second line usage of Dysport® is comparable a change of BTX-A brands seems reasonable in case of relapse following Botox®.

References

1. Neurourol Urodyn 1999; 18: 401-402
2. J Urol 2000; 164: 692-697