34

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CAN 100 UNITS OF BOTULINUM TOXIN A PRESERVE THE ABILITY OF VOLUNTARY VOIDING AND IMPROVE OVERACTIVE BLADDER SYMPTOMS IN PATIENTS SUFFERING FROM MULTIPLE SCLEROSIS?

Hypothesis / aims of study

Botox™ application into the detrusor with 300 units is a potent therapy of detrusor overactivity in spinal cord injured patients [1]. In idiopathic detrusor overactivity 100 units are used effectively [2]. Still little is known regarding the treatment of multiple sclerosis (MS) patients, who frequently suffer from frequency, urgency and urge incontinence, but often have preserved voluntary voiding [3]. The aim of this study was to evaluate, if the application of only 100 units Botox™ into the detrusor can reduce the frequency and urgency symptoms of MS patients and still preserve their ability to voluntarily urinate.

Study design, materials and methods

Twelve patients (11 female, 1 male) with MS were retrospectively evaluated (mean age: 50.7±10 years). All patients suffered from overactive bladder symptoms like frequency, urgency or urge incontinence. The evaluation of patients and treatment course was performed during three consecutive visits (before, 44.1 ±10.6 days after Botox™ and 113.8±61.4 days after Botox™) using urodynamics at visit 1 and 2 and uroflowmetry at visit 3. Additionally patients had to complete 3-day voiding diaries for all three visits. Every patient received 100 units Botox™ in the detrusor muscle, distributed among 10 localisation using a rigid cystoscope and local anaesthesia. Only one patient received additional 20 units into the urethral sphincter.

Results

All patients showed overactive bladder symptoms in the 3-day voiding diary although some had normal urodynamic results. Uninhibited detrusor contractions and leakage could be observed in 7 patients before and in 3 patients after Botox™ application. Filling volume could be increased in 9 patients significantly from 352.6 to 538.8ml (p=0.008). The other three patients already had a normal bladder capacity of about 600ml and did not show any changes after treatment. In all patients, the maximal detrusor pressure decreased significantly from 38.0 cmH_2O to 16.3 cmH_2O (p = 0.004). The results of the voiding diaries and uroflowmetry are summarised in table 1. Intermitted self-catheterisation was necessary in only 2 patients with a frequency of once to twice daily (on demand). Eleven patients recognized such a good improvement that they would agree to be treated with BTA again.

Table 1

Voiding diary (3-day average)	No. of patients	Visit 1 [mean ±SD]	Visit 2 [mean ±SD]	Visit 3 [mean ±SD]	Significance (α = 0.025)
Micturition/ day	12	11.4 ±3.5 *#	7.1 ±2.1 *	8.5 ±2.6 #	*p = 0.002 #p = 0.004
Micturition/ night	12	2.4 ±1.4*	1.3 ±1.2*	1.9 ±2.0	*p = 0.005
Incontinence	12	3.8 ±5.1	1.9 ±3.2	1.0 ±1.4	
Urgency	12	9.1 ±5.7*#	2.8 ±3.8*	4.4 ±5.2#	*p = 0.013 #p = 0.008
Pad use	12	1.9 ±0.9*#	0.8 ±0.8*	0.7 ±0.9#	*p = 0.02 #p = 0.011
Uroflowmetry					
Voided volume	12	337.4 ±256.5	330.8 ±186.2	221.3 ±132.4	
Qmax	12	27.9 ±21.0	23.1 ±13.2	18.7 ±13.5	
Residual volume	12	98.3 ±77.6*	222.1 ±113.2*	135.2 ±94.8	*p = 0.003

Interpretation of results

Compared to the studies of Kalsi (2007) and Schulte-Baukloh (2006), which investigated the use of 300 units botulinumtoxin type A in MS patients, our results were in a similar range for the 6 weeks follow up, but showed a somewhat lesser treatment effect after 3 months compared to the studies using 300 units.

Although the treatment effect was less after 3 months, none of the 11 content patients rescheduled for a new injection before 5 months after the last Injection and in 2 patients the effect lasted over 1 year now, without taking additional antimuscarinic drugs.
Only 10 injections are necessary and can be performed well tolerated under local anaesthesia in an out patient setting. The therapy with 100 units Botox™ might therefore offer a cost-effective treatment option for patients suffering from MS. Furthermore it seems to be a reasonable alternative to antimuscarinics, which are very often not effective enough and causes side effects like worsened tiredness, visual restrictions and cognitive impairments that are not well tolerated by most of the MS patients due to their pre-existing neurological impairment(s).

In addition to the significant reduction of urgency and frequency, patients may benefit from the preserved ability to voluntary urinate and thus stay more independent without the necessity to perform CISC. However, there is no common agreement on when to start CISC and different criteria on CISC in different studies might influence the according study outcome.

Concluding message

The treatment of overactive bladder in MS patients using 100 units Botox™ into the detrusor muscle seems to be a safe and promising treatment option that significantly reduces the bothersome urgency and frequency but seems to preserve the ability of voluntary micturition without CISC and therefore independency and quality of life.

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