

## **REPEAT DETRUSOR INJECTIONS OF BOTULINUM A TOXIN IN PATIENTS WITH NEUROGENIC LOWER URINARY TRACT DYSFUNCTION DO NOT CAUSE INCREASED DRUG TOLERANCE.**

### **Aims of Study**

Detrusor injections with botulinum A toxin into the detrusor offer an effective and relatively non-invasive treatment for patients with refractory neurogenic detrusor overactivity [1]. The therapeutic effect lasts for about 9 months, after which the patients may elect a repeat injection.

This study examines the results of repeat injections in order to discover a possible increase of drug tolerance.

### **Methods**

One hundred and ten patients with various underlying causes for their neurogenic detrusor overactivity were treated with botulinum A toxin because of failing anticholinergic therapy (refractory incontinence or unbearable adverse events). Forty-seven patients received more than one injection (47 with two injections, 13 with three, 4 with four, and one patient had 5 injections). The underlying causes were: traumatic spinal cord injury in 37, myelomeningocele in 6, other spinal cord pathology in 4.

Two preparations were used for the injections: Botox<sup>®</sup> or Dysport<sup>®</sup>. As these preparations have different therapeutic efficacy, the doses were different. For Botox<sup>®</sup> a dose of 200 IU was used in the early phase of the study, before it turned out that 300 IU is the best dose for this treatment in adults. For Dysport<sup>®</sup> a similar path led from 500 IU via 1000 IU to 750 IU as the dose that is used normally now.

Botox<sup>®</sup> was used in 35 first injections, Dysport<sup>®</sup> in 12. In the follow-up injections, this distribution was: #2: Botox<sup>®</sup> 34, Dysport<sup>®</sup> 13; #3: Botox<sup>®</sup> 12, Dysport<sup>®</sup> 1; #4: Botox<sup>®</sup> 2, Dysport<sup>®</sup> 2; #5: Botox<sup>®</sup> 1.

The outcome parameters were the interval between the treatments, the clinical parameters dosage of anticholinergic drugs, type of incontinence, functional and maximum bladder capacity, subjective satisfaction; and the urodynamic parameters reflex volume, detrusor compliance, (maximum) cystometric capacity, maximum voiding pressure, post void residual.

The parameters were compared between the treatments using the appropriate statistical tests. The significance level was set at  $p=0.05$ .

### **Results**

The interval between the first and the second treatment was 11 months, between the second and the third 8 months, and between the third and the fourth 11 months again. For the one patient with 5 treatments, the last treatment was given 9 months after the fourth. The interval between the second and the third treatment differed significantly from the preceding and the subsequent intervals.

From the first to the second treatment, the interval was significantly different between Botox<sup>®</sup> (12 months), Dysport<sup>®</sup> (8 months).

All clinical parameters showed significant improvement as compared to the pre-treatment conditions after the first injection. These improvements subsided in the course of time, and improved significantly again after the second injection. The number of patients in the subsequent injections is too small to allow sensible statistical comparisons, but improvements were noticed again. The patients value Botox<sup>®</sup> injections better than Dysport<sup>®</sup> injections.

Five patients showed no benefit despite multiple injection sessions.

With the exception of the reflex volume, no statistical significant differences were found between the pre- and post-treatment urodynamic parameters. Neurogenic detrusor overactivity was present in 35 patients pre-treatment, in 17 after the first, and in 5 after the second injection.

A paired comparison between the 17 patients who had neurogenic detrusor overactivity both before and after the treatment demonstrated a significant increase of the reflex volume (mean 248 ml) after the first treatment as compared to the pre-treatment volumes (mean 198 ml). The small number of patients available for this

analysis after the following treatments are too small to prove significant differences between the relatively little volume differences.

### **Conclusions**

A second botulinum A toxin treatment appears to last somewhat shorter than the first treatment, but later treatments seem to have an efficacy interval that compares to that after the first treatment. Whether this difference might be based on psychological grounds, both on the patients' and on the caregiver's side remains to be discussed.

The apparent better efficacy of Botox<sup>®</sup> compared to Dysport<sup>®</sup> might be caused by inadequate dosage of Dysport<sup>®</sup> in the first treatments with this compound. Those patients who had been treated with lower doses of Botox<sup>®</sup> in the early phase of this study also had less benefit.

The patient benefit from this treatment appears to be explained mainly by the effective suppression of the neurogenic detrusor overactivity.

The data from this study do not indicate an increased drug tolerance after multiple treatments.

### **Reference**

1. (Authors) Botulinum A toxin for treating detrusor hyperreflexia in spinal cord injured patients: A new alternative to anticholinergic drugs? Preliminary results. J Urol 2000; 164: 692-697.