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ENGLISH BOTULINUM TOXIN-A IN THE TREATMENT OF NEUROGENIC DETRUSOR OVERACTIVITY

Aims of Study

Botulinum Toxin type A (BTX-A) has utilized in urologic field to treat spinal cord injured patients (SCI) who suffer from detrusor-external sphincter dyssynergia (DESD). In 1990 was published the only double-bind, placebo-controlled study of BTX-A injection into the external urethral sphincter in 5 male patients with SCI and DESD. In 1999, some Authors reported their good preliminary results using BTX-A injections in 30 sites into the detrusor and trigone-sparing. BTX-A is an inhibitor of acetylcholine release at the presynaptic neuromuscular junction, BTX-A inhibits calcium mediated release of acetylcholine vesicles at neuromuscular junction, which results in reduced muscle contractility. BTX-A has catalytic zinc finger motif that may block activity of SNAP-25, protein important in synaptic vesicle fusion. Normally, calcium influx at neuromuscular junction drives fusion and release of neurotransmitter vesicles, process in which SNAP-25 usually participates. Re-sprouting fibers are expected after 2-3 months of injections and they disappear after BTX-A block of synapsis finish. In literature we have data mainly on 300 U.I. of American BTX-A (Botox™), but few data about English BTX-A (Dysport™) with different dosages 500, 750, 1000 are reported without a clear profile of efficacy and safety. A recent experience on 87 patients using either 300 U.I. of Botox™ or 500 to 750 U.I. Dysport™ that demontrated the efficacy of the treatment without any adverse effect, but without analysis of any difference using Botox™ or Dysport™. Other Authors observed hypostenia in patients treated with high-dose intravesical BTX-A injections (300 U.I. Botox™ or 1000 U.I. Dysport™). The only study published about the results of the repeat injections is based on the use of either toxins. We report our data of a restrospective study about results and adverse effect using Dysport™ with different dosages after first injection and multiple re-injections excluding patients treated with Botox™ or either toxins.

Methods

Between September 1999 and March 2003 we treated with intravesical BTX-A injection 178 patients. We selected an homogeneous population of 93 SCI patients with neurogenic detrusor overactivity (NDO) treated with intravesical English BTX-A only. They were 63 males and 30 females, mean age was 37.5 years (range 20-71). Neurological lesion degree according to the ASIA scale are reported in table 1. Lesion level were as follows: 17 (18.2%) cervical, 65 (69.8%) dorsal, and 11 (11.8%) lumbar. All patients have a NDO refractory to anticholinergic therapy and use intermittent catheterizzation (IC). We administered oxybutynin 5 mg tablet 3 times/day, gradually reducing the dosage until total suspension in the third week post-injection. We injected, with a 17 Ch cystoscope and a 23 G needle-tipped catheter (5 Fr), in 20-30 sites into detrusor muscle, trigone-sparing, 20 minutes after intravesical instillation of 40 ml of lidocaine 2%. The dosages were 500, 750, 1000 U.I. diluited in 10-20 ml of saline solution. Bladder diary was cecked pre-treatment and during follow up. Videourodynamic and ultrasound evaluation were performed before and after each treatment. Re-injections were planned at recurrence of urinary incontinence previous urodynamic assessment.

N. Pts. (%)	ASIA
74 (79.5)	A
10 (10.7)	B
4 (4.3)	C
4 (4.3)	D
1 (1,0)	E

Table 1: Patients' stratification according to ASIA scale.

Results

In all patients, we recorded an average improvement of bladder capacity of 210.5 ml (range 180-420) at least for a period of 4 months but four cases needed re-injection from 1 to 3 months after the last BTX-A treatment. Urodynamic evaluation showed a significant decrease

in mean maximum detrusor pressure from 60 to 20 cmH_2O. A total of 165 treatments were performed: number of treatments for each patient from 1 to 5, mean dosage, and mean duration time are reported in table 2. In one patient, not listed in table, we perform 7 treatments. In this caseload series 5 (5.3%) patients referred hypostenia with reduced supralesional muscle force. Hypostenia disappeared from 2 to 4 weeks after injection and it depends on two main associate variables: high dosage BTX-A (1000 U.I. Dysport™) used in SCI patients with cervical complete lesion.

N. Treatment	**N. Pts. (%)**	**Mean Dosage U.I. (range)**	**Mean Duration months (range)**
I°	93	779,5 (500-1000)	-
II°	44 (47,3)	748,8 (200-1000)	12 (3-40)
III°	15 (34,0)	600,0 (500-1000)	13 (1-29)
IV°	8 (53,3)	593,7 (500-750)	14 (5-27)
V°	3 (37,5)	583,3 (500-750)	16 (5-26)

Table 2.

Conclusions

Our study confirmed the efficacy of the Dysport™ for patients with NDO using IC. We obtained a significative increased bladder capacity with detrusor pressure reduction. An important side effect is hypostenia that was no severe and it had a temporary duration not more than 1 month. The same problem may occur in patients with occulte myastenia. For this reason we tried a lower dose and this series showed to be effective avoiding side effects. Clinical, urodynamic, and duration data show no significative differences between high (1000 U.I.) and lower dosage. Patients reported subjective improvement of continence and improved quality of life. Re-injection data using Dysport™ did not reveal resistant to the toxin and duration time showed a trend to be longer from the first to the last treatments. All the patients were able to suspend or reduce anticholinergic drugs. Our study confirm the efficacy of BTX-A for the treatment of NDO as reported in literature, but demonstrated particularly, the efficacy and tolerability of English BTX-A after first and repeated detrusor injection too.

References

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