

DETRUSORIAL INJECTIONS OF BOTULINUM TOXIN IN MULTIPLE SCLEROSIS: LONG-TERM EXPERIENCE OF A SINGLE CENTRE

Hypothesis / aims of study

Detrusorial injections of botulinum toxin (ITox) are used in the treatment of neurogenic detrusorial overactivity (D+) which resists conventional treatment, especially in spinal cord injuries. We report our long-lasting experience in a small sample of patients with multiple sclerosis (MS).

Study design, materials and methods

From January 2000 to December 2011 treatment with ITox was administered to 23 subjects with MS (4 males, 19 females; mean age 44 years, minimum 30, maximum 72). Average duration of the disease prior to beginning treatment was 13.8 years; 11 patients had the exacerbation-remittent form, 7 the primary-progressive form and 5 the secondary-progressive form. The mean score on the Expanded Disability Status Scale (EDSS) was 4.3 (minimum 2, maximum 8.5). The D+, which was resistant to anticholinergic drugs, provoked urge-urinary incontinence in 18 cases and storage symptoms in 5; 6 women had only spontaneous micturitions whereas 17 patients used clean intermittent catheterisation (CIC), 8 for the removal of post-void residual (PVR) and 9 for inability to void (complete CIC). Voiding diaries were kept for all patients for 3-4 days pre- and post-ITox. A videourodynamic examination (UD) was performed for all subjects; it confirmed D+ at a mean value of 58 cm H₂O (minimum 20, maximum 80). One woman presented concomitant urethral sphincteric deficit and another active bilateral vesico-ureteral reflux (VUR).

Urgency and quality of life (QoL) were evaluated using a visual analogical scale (1 = no urgency at all → 5 = serious urgency; 1 = QoL very poor → 5 = QoL excellent).

English botulinum toxin (Botox) was mainly used at a dosage of 300 IU in 11 cases and of 100 IU in 8 cases in which the patients desired to maintain spontaneous micturitions; american botulinum toxin (Dysport) was used at the dosage of 750 UI in 4 cases.

Results

Patients were evaluated at 10-20 days from treatment and subsequently as needed. The follow-up period ranges from 4 to 145 months, with an average of 62 and a median of 69. At the last follow-up examination, the mean EDSS had passed from 4.8 to 6.7.

Complications were observed in 2 women (3 operations of ITox), both treated with high dosages of Dysport: 7-10 days after ITox they complained serious asthenia, dysphonia and dysphagia with the need of admission to hospital in 1 case. These side-effects lasted about 40 days decreasing gradually.

As regard the bladder symptoms in all cases urgency and the number of pads used per day decreased and the QoL improved. Urgency fell from a mean value of 4.5 to 1.2, QoL increased from 1.5 to 4 and the number of pads per day decreased from 3.1 to 0.7. In 15 cases it was possible to suspend the anticholinergic drugs.

Patients were divided into three groups:

- the 9 patients using complete CIC reduced the number of CIC from an average of 6.8 to 4.5 per day and the average bladder capacity increased by 100% (from 230 to 475 ml).

- partial CIC (for the removal of PVR): 1) 5 out of 8 subjects, with PVR pre-treatment superior to the volume voided, became unable to void and passed to complete CIC with an average increase in bladder capacity of 30%. 2) In 3 out of 8 cases, with PVR pre-ITox inferior to the volume voided, partial CIC was continued with an average reduction of the number of CIC from 2.6 to 1.6 per day and PVR stable at <150 ml; the number of micturitions per day decreased by 50% (from 16 to 8), with an average increase of 30% in the volume voided.

- spontaneous micturitions: 4 out of 6 women maintained the ability to void without PVR. The number of micturitions decreased on average from 15 to 8.2 with an average increase in bladder capacity of 100% (from 108 to 207 ml). At the UD in these cases there was D+ at high pressures (>70 cm H₂O) and in 1 woman the dosage of botulinum toxin used was 300 IU. Two out of 6 women lost the ability to void and passed to complete CIC.

The effect of ITox lasted on average 8.8 months (minimum 4, maximum 14), and 13 patients repeated the treatment (average 4 times, minimum 1, maximum 13) with efficacy.

UD was carried out at follow-up in selected cases and VUR disappeared in the sole patient having it.

All patients are still being monitored by our neuro-urological team and in 5 of them the evolution of the MS required the insertion of indwelling catheters after a mean of 3.2 treatments. Moreover 3 young women in selfCIC with a low bladder capacity (about 100 ml) stopped the treatment after a mean of 2 ITox.

Interpretation of results

ITox is a mini-invasive treatment which could improve dramatically the QoL of patients with MS having D+. By suppressing D+, botulinum toxin abolishes or drastically reduces urinary incontinence and consequently the number of pads used and the degree of the devastating urgency. Our experience, while numerically limited, reveals some specific facts: 1) ITox transform incomplete urinary retention into complete retention whenever pre-treatment PVR is superior to the volume voided; 2) in women capable of voiding without PVR and with high pressure D+, ITox can resolve the storage symptoms without compromising spontaneous voiding; 3) low bladder capacity is a relative contraindication to ITox in patients in CIC, because the mean doubling of bladder capacity is still a poor result for their QoL 4) in patients who wish to maintain spontaneous micturitions it is better to use reduced dosages of botulinum toxin that produce minor duration of the therapeutic effect and thus of any possible

urinary retention; 5) high dosages of American botulinum toxin should be avoided in SM patients for the risk of serious complications.

Some assumptions are difficult to verify because MS presents polymorphous neurological symptoms that vary over time in such a way as to frequently impede reliable urological examinations.

Concluding message

ITox is an efficacious treatment of D+ in patients with MS. Before treating a patient the urologist should be able to foresee the possible results of this treatment, considering the gender, the voiding modalities and the urodynamic data. We observed serious complications in 2 patients with high dosages of american toxin.

References

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Disclosures

Funding: None **Clinical Trial:** No **Subjects:** HUMAN **Ethics not Req'd:** It didn't **Helsinki:** Yes **Informed Consent:** Yes