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BOTULINUM TOXIN A FOR TREATMENT OF NEUROUROLOGICAL PATIENTS: A SAFE POISON

Hypothesis / aims of study

To evaluate effectiveness and adverse effects of Botulinum toxin type A (BoNT-A) for treatment of neurourological patients.
In order to control Neurological Detrusor Overactivity (NDO), oral anticholinergic drugs are widely used. However, these medications are ineffective in some patients or cause systemic side-effects such as dry mouth, blurred vision or constipation. Botulinum toxin type A has gained clinical consensus for treatment of patients unresponsive to oral anticholinergic therapy or affected by severe side-effects. A growing number of observational studies have reported beneficial effects of BoNT-A when injected into urethral sphincter or detrusor muscle, particularly in spinal cord lesion patients (SCLP) affected by Neurogenic Detrusor Overactivity (NDO) or by Detrusor External Sphincter Dyssynergia (DESD).

Study design, materials and methods

We performed a retrospective study on 40 patients (34 men and 6 women, age range 21 to 73 years) referred to our hospital with spinal chord lesion and treated with BoNT-A (American Botulinum NeuroToxin type A) between 2001 and 2009. These subjects were selected from a list of 1200 SCLP who underwent over 2000 videourodynamic studies. Patients were sorted out on the basis of the above-mentioned criteria: poor response to oral antimuscarinic drugs and/or severe systemic side -effects. NDO patients (14 dorsal SCL, 9 cervical SCL, 1 MS) were injected into 20 sites of the detrusor muscle, trigone sparing, with 300 U of BoNTA diluted in 20 ml of sterile saline. DESD patients (14 cervical SCL, 2 dorsal SCL) were injected into the four quadrants of the urethral sphincter with 100 U. of BoNTA diluted in 4 ml of sterile saline. Treatment was preceded by local anaesthesia, performed in aseptic field, using a rigid cystoscope and a 23-g flexible needle. After treatment, a 18 F urethral Foley catheter was left indwelling for 24 hours. Blood pressure and cardiac frequency rate were monitored.

Results

During treatment, all patients had reflex spasms in lower limbs but neither local pain nor autonomic dysreflexia symptoms.
Videourodynamic control after six weeks (14 days to 2 months) indicated that intrasphincteric BoNTA caused a decrease in mean values of maximum detrusor pressure (from 74 cmH2O to 38 cmH20) and a corresponding decrease of post-void residual (from previous 150 ml to 100 ml). No relevant change was observed in maximum bladder capacity (mean from 200 ml to 180 ml). Duration of treatment efficacy was noted between 2 and 7 months. During this period of time, autonomic dysreflexia symptoms occurred less than 1/weeK on average. One patient had fever (39 °) four days after injections and was successfully treated in our hospital with i.v. antibiotics.
Videourodynamic studies of patients who underwent intradetrusor injections of BoNTA after 1 -2 months, indicated increase of mean maximum cystometric capacity (from 225 to 350 ml) and decrease of mean value of maximum detrusor pressure (from 70 cmH2O to 50 cmH2O). Patients self-reports drew attention to a 60 per cent decrease or absence of incontinence. Treatment efficacy lasted from 4 to 9 months. One patient suffered from severe macroematuria seven days after intradetrusor injections of BoNTA, trated such outpatient cystoscopy . In our review, no short or long-term adverse-effects occurred even in subjects who repeated the BoNTA therapy.

Interpretation of results

Two paraplegic patients were treated with intrasphincteric BoNTA after suffering from autonomic dysreflexia caused by DESD with urethral (posterior) diverticula and vesicorenal reflux grade III .This treatment clearly was a “salvage operation”, so oral anticolinergic medication wasn’t discontinued and no incontinence was recorded . Five out of 14 tetraplegic patients treated with intrasphincteric BoNT-A repeated the therapy afterwards. On the contrary, 5 patients of the same group opted for endoscopic sphincterotomy in order to avoid further administrations of BoNT-A. Nevertheless, intrasphincteric injections of Botulinum toxin type-A allowed these subjects to consider how they could better manage their Neurogenic Voiding Dysfunction.
One out of the 6 SCL women who received intradetrusor BoNT-A chose to undergo augmentation cystoplasty 12 months later . One of the 18 men twice treated with intradetrusor BoNT-A, a young person with cervical SCL, opted for intrasphincteric injection and subsequent sphincterotomy. A third SCL patient who wasn’t really satisfied with BoNT-A detrusor therapy , chose to face a nerve-sparing cystectomy with neo-urethra and ileal neo-bladder.

Concluding message

BoNTA intrasphincteric injections are a safe therapy for SCLP, but treatment efficacy can be very short (2 months), so that about 30 per cent of patients choose a more durable option (sphincterotomy). Botulinum toxin type-A intradetrusor injections are safe as well. Nonetheless a relevant variability of efficacy and duration has to be expected, along with further administrations of BoNTA. As a result, a significant percentage of patients eventually prefer long-term therapies.

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Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**No**
This study did not require eithics committee approval because	**it is a retrospective one.**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**