35

Malmberg L[1], Karadzic V[1]
1. *Dept of Urology, Lund University Hospital, Sweden*

EFFECTS OF REPEATED BOTULINUM TOXIN A INJECTION THERAPY IN PATIENTS WITH SYMPTHOMATIC NEUROGENIC DETRUSOR OVERACTIVITY – A 3-YEAR FOLLOW UP.

Hypothesis / aims of study

The majority of patients with symptomatic, neurogenic detrusor overactivity is successfully treated with anticholinergics and/or clean intermittent catheterisation. Studies have shown excellent effects with repeated Botulinum toxin A (BTX-A) injection therapy on neurogenic urinary incontinence in patients who fail maximum conservative treatment. Our observational study evaluates treatment results in patients with neurogenic urinary incontinence and/or frequency/urgency in a clinical setting at a single institution.

Study design, materials and methods

Patients with neurogenic detrusor overactivity who subjectively had severe urinary incontinence and/or frequency/urgency in spite of conservative treatment were eligible for inclusion. Recruitment started in October 2005. This report evaluate the first 3 study years. 36 patients (19 men and 17 women) were screened for treatment with 300 U of BTX-A (Botox®). The drug was administered by intradetrusor injections under local or general anaesthesia. Mean age was 44 years (21 years to 75 years). Causes of neurogenic dysfunction were: Spinal Cord Injury (20 patients), Multiple Sclerosis (11 patients), Cerebrovascular Lesion (4 patients) and Parkinson's disease (1 patient). 1 patient withdrew his consent to participate before treatment. The patients were assessed according to urodynamic parameters, symptoms and quality of life before and six weeks after therapy. All patients were offered repeated treatment at a time decided by themselves. Minimum allowed treatment interval was 3 months.
At the time of analysis 34, 27, 21 and 13 patients have had 1, 2, 3 and 4 treatment episodes, respectively. There were 4 drop-outs after the first treatment, one after the second and one after the third, respectively.

Results

Duration of treatment effect

Median time between first and second treatment was 250 days. The corresponding figures for the second and third treatment intervals were 267 and 262 days, respectively.

Urodynamic studies

BTX-A significantly increased the cystometric capacity and the volume at first involuntary contraction > 10 cmH2O. Reversely, maximum detrusor pressure decreased. Values are median (maximum-minimum)

Cystometric capacity (ml)

Preop, n=36	302 (75-870)
Postop, n=34	480 (300-900)

Maximum detrusor pressure (cmH2O)

Preop, n=36	47 (10-97)
Postop, n=34	26 (0-55)

Volume at first involuntary contraction > 10 cmH2O (ml)

Preop, n=36	210 (35-465)
Postop, n=34	310 (50-870)

Effects on lower urinary tract symptoms

Bladder regimen included: Clean intermittent catheterisation (27 patients), voluntary micturition (5 patients) and indwelling catheter (4 patients). Bladder emptying frequency decreased from 6.1-7.4 preoperatively to 5.2-5.5 postoperatively. The number of wet pads used per week decreased from 17.2 to 6.9 after the first treatment. The number of incontinence-free days per week increased from a mean value of 2.0-3.0 before treatments to a mean value of 4.3-5.6 after the treatments.

Effects on quality of life

The validated, disease-specific questionnaire, I-QoL (highest value = 100), was used to assess quality of life. The patient's quality of life increased significantly after the first treatment, from median value 43 (n=35) to median value 76 (n=34). An increase to the same magnitude was achieved after repeated treatment (second treatment: 39 to 80 (n=26), third treatment: 68 to 80 (n=21) and fourth treatment 56 to 78 (n=13).

Safety

There were no serious adverse events related to the 93 treatments given. Urinary tract infection (UTI) is a common problem in this group of patients. Most infections uncomplicated and only a few causes fever or hospitalisation. Thirteen out of the 36 patients had a history of recurrent UTIs and there were no changes in their individual infection patterns. Two patients with high thoracic spinal cord injuries and a history of autonomous dysreflexia reported weakness in the upper extremities with a duration similar to that of the effect on the bladder. This effect was of the same duration as that in the bladder and lasted longer than the effect reported after treatment of skeletal muscle spasticity. Hypothetically, it may therefore reflect a result of a decreased autonomic overactivity.

Interpretation of results

Repeated intradetrusor injection therapy with BTX-A seems to be a good treatment option in an unselected group of patients with neurogenic detrusor overactivity presenting subjectively severe urinary incontinence and/or frequency/urgency. The duration of the treatment effects seems to be adequate for clinical use. There were no serious adverse events reported in conjunction to BTX-A-

administration, thus the treatment seems to be safe. A marked decrease in symptoms was shown by decreases in pad use, bladder empying frequency and increases in number of incontinence-free days per week. These observations were paralleled by improvements in urodynamic parameters. Most important, BTX-A-treatment caused a significant improvement of the patient-reported quality of life.

Concluding message

Repeated injection treatment with BTX-A in the detrusor seems to be safe and effective in reducing symptoms of neurogenic detrusor overactivity and in increasing quality of life of patients in an ordinary clinical setting. The rate of adverse events appears to be low. Patients with high spinal cord lesions and severe autonomic dysreflexia should be carefully adviced before treatment.

Specify source of funding or grant	**NONE**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**The Regional Ethics Committee of Southern Sweden**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**