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Title: TREATMENT OF THE NON-NEUROGENIC STORAGE AND VOIDING DISORDERS WITH THE CHEMICAL DENERVATION CAUSED BY BOTULINUM TOXIN TYPE A- A PILOT STUDY.

Aims of Study:

Functional disorders of the lower urinary tract are thought to be caused by the imbalance between neuronal control and functional relationships within the bladder and urethra. Amongst them the most distressing conditions are bladder overactivity and functional outlet obstruction, occurring in neurologically normal patients. Botulinum toxin type A (BTX) is a neurotoxin acting on presynaptic nerve terminal and causing chemical denervation of an appropriate muscle. BTX is known to produce improvement in both storage and voiding problems (1,2) in patients with spinal cord injury . In neurologically normal patients the BTX action on functional outlet obstruction was studied to the certain extent only (3). To the best of our knowledge BTX action on overactive bladder was not studied in neurologically normal patients.Therefore we decided to evaluate the response to BTX treatment in overactive bladder and functional outlet obstruction in the patients with no underlying neurological cause of their disease.

Methods:

In our studies we included 7 patients (4 females, 3 males, mean age 68.8 years) with idiopathic bladder overactivity and urge incontinence as well as 5 female patients (mean age 44,2 years) with the functional outlet obstruction . None of the patients demonstrated any neurological pathology. In case of bladder overactivity all patients demonstrated prior resistance to anticholinergic drugs or anticholinergic treatment was contraindicated. In case of functional outlet obstruction all patients were treated previously with myorelaxants without any clinical improvement. The pre-treatment evaluation included: history, neurological examination, urodynamic evaluation, voiding diary, urinalysis and urine culture. BTX (Dysport®, Beaufour Ipsen International) was diluted in normal saline to the final titration of 100u/ml . The procedure of BTX injection was performed under short general intravenous anesthesia. **Overactive bladder:** BTX was injected through the cystoscope via 18G Cook endoscopic needle into 10-15 sites of the detrussor muscle, sparing the trigone. 10-20u of BTX was used per injection site up to the total dose of 300u.

Functional outlet obstruction: BTX was injected under the cystoscopic control via 18G Cook endoscopic needle into the sphincteric muscle at 5 and 7 o'clock position in a dose of 20u per injection site. After the treatment, in case of the sphincteric injection the catheter was left in the urinary bladder for 24 hours. The post treatment evaluation included urodynamic evaluation and voiding diary performed one month after the treatment.

Results:

No patient demonstrated urinary tract infection at the time of examination and treatment.

Overactive bladder: all patients voided spontaneously after the procedure. No acute urinary retention occurred. Subjective improvement on the first post treatment day was considerable in terms of frequency, urgency and incontinence. Comparison of mean $\pm$ SD (range) pre- and posttreatment parameters one month after the treatment are shown in table 1.

	Pre BTX	Post BTX
FD (ml)	136,6 ±32,3 (87-180)	189,7 ±80,5 (98-358)
CC (ml)	325,8 ± 89,2 (185-450)	405,4 ± 58,6 (347-473)
Pdet inst (cm H2O)	43,8 ± 18,8 (25-70)	0
D (n)	13,7 ± 2,5 (11-18)	6,4 ± 1,1 (5-8)
N (n)	5 ± 2,4 (3-8)	2 ± 1,2 (0-3)

Table 1: FD-first desire to void, CC–cystometric capacity, Pdet inst–maximum pressure of unstable detrussor , D–number of daytime micturitions, N–nocturia

One month after the treatment no patient demonstrated detrussor instability during urodynamic examination. All patients were continent. All patients voided efficiently without postvoid residual. They reported no dysuria.

Functional outlet obstruction : transitional perineal pain (2 weeks) was observed in 2 patients and resolved spontaneously without treatment. In 2 patients acute urinary retention occurred and was treated with indwelling catheter for 1 and 3 weeks respectively. At 1 month follow-up all patients voided spontaneously Comparison of mean pre- and posttreatment parameters ± SD (range)one month after the treatment are shown in table 2.

	Pre BTX	Post BTX
CC (ml)	334, 7 ± 175,7 (129-600)	340, 8 ± 69,1 (250-430)
Qmax (ml/sec)	7,5 ± 2,6 (1,1-11,5)	14,5 ± 3,8 (9-19,4)
Pdet/Q max (cmH20/ml/sec)	60 ± 38 (35-130)	18,7 ± 9,9 (4-30)
RV (ml)	190 ± 164 (60-480)	28 ± 25 (0-60)

Table 2: CC–cystometric capacity, Qmax–maximum flow rate, Pdet/Qmax–maximum pressure at maximum flow rate, RV–residual volume.

One month after the treatment all patients voided spontaneously and reported a significant subjective improvement of their symptoms.

Conclusions:

Our pilot study demonstrated that BTX might be a treatment of choice in refractory bladder overactivity. The cure rate at one month follow-up is 100% (no instability, no urge incontinence). To the best of our knowledge this is the first study demonstrating the efficacy of BTX in the treatment of idiopathic bladder overactivity in patients without neurological disease. BTX was also found to be effective in the treatment of functional outlet obstruction and improved voiding parameters in these patients.

References:

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