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CLINICAL, URODYNAMIC AND HISTOLOGIC EFFECTS OF INTRAPROSTATIC INJECTIONS WITH BOTULINUM TOXIN TYPE A FOR LOWER URINARY TRACT SYMPTOMS DUE TO BENIGN PROSTATIC HYPERPLASIA.

Hypothesis / aims of study

Botulinum toxin type A (BTA) causes long lasting muscle relaxation by blockage of acetylcholine release. In prostatic tissue, relaxation of smooth muscle as well as tissue necrosis is found after BTA injection [1-2]. In men with BPH, BTA may improve LUTS by relaxation and decrease in prostate volume. The purpose of this study was to investigate the clinical, urodynamic and histologic effect of BTA injections in the prostate as second line treatment for LUTS suggestive of BPH.

Study design, materials and methods

A prospective pilot study was performed. Inclusion criteria were: males > 55 years, LUTS with IPSS > 7, failure to oral medication, prostate volume 30-50 ml and urodynamic infravesical obstruction > Schäfer grade II. Patients with neuropathic bladder dysfunction, prostate carcinoma, coagulation disorder, postrenal renal insufficiency and myopathic disorder were excluded. Transrectally, ultrasound guided, with antibiotic prophylaxis, 100 IU BTA was injected in each prostatic lobe. Before and 4 weeks after BTA injection six prostate biopsies were taken. Histology was assessed by one pathologist (GJ), using antibodies to PCNA (Proliferating Cell Nuclear Antigen, Ki-67) in order to quantify cell proliferation.
IPSS, AUA-quality of life scores and PSA were measured after 1, 3, 6, 9 and 12 months. Prostate volume was measured before BTA injection and after 1, 6 and 12 months and urodynamic study was done before and after 3, 6 and 12 months.
Students' t-test was used for statistical analysis, considering $p<0.05$ as significant.

Results

Eleven patients with a mean age of 65.0 years (55-77) were included. Results are presented in Table 1.

Table 1

n=11	T 0	T 1	T 3	T 6	T 9	T12
IPSS	24.0±5.7	16.6±6.9*	17.0±8.0 (n=5)	14.3±7.0* (n=7)	10±2.8* (n=2)	11±2.8 (n=2)
QOL	4.6±1.1	3.0±1.8* (n=10)	2.4±0.5* (n=5)	2.6±0.8* (n=5)	3 (n=2)	2±1.4 (n=2)
Prostate volume (ml)	41.0±7.0	40.4±11.6 (n=10)		44.5±15.6 (n=4)		40±10.6 (n=2)
PSA (ng/ml)	2.3± .5	2.8±2.9	2.3±1.4 (n=6)	3.0±1.9 (n=5)	1.5 (n=2)	1.1 ±1.1 1.2 (n=2)
Q-max (ml/s)	7.1±3.5		9.6±3.6* (n=7)	10.1±4.9 (n=7)		7.0±3.3 (n=2)
Post void residual (ml)	242± 80		130±140* (n=7)	105±119* (n= 7)		75±106 (n=2)
Schäfer obstr. grade	3.9±1.0		3.4±1.0 (n=7)	3.5±1.0 (n=5)		4.0 (n=2)

Data are presented as mean ± SD
* = significant difference compared to T0, $p<0.05$

Before and after BTA injection in 9/18, respectively 12/16, sets of biopsies histologic evidence of prostatitis was found. Proliferation before and after treatment did not differ statistically. Five patients underwent TURP because of persisting signs and symptoms of bladder outlet obstruction. Two patients developed clinical prostatitis after BTA injection, treated with oral antibiotics. No retrograde ejaculation was reported and no other complications occurred.

Interpretation of results

Intraprostatic BTA injection improves IPSS, QOL, Qmax and post void residual. No effect on prostate volume, PSA and urodynamic obstruction could be demonstrated. Histologically, cell proliferation did not decrease and prostatitis was a common finding.

Concluding message

Intraprostatic BTA injection is safe and improves LUTS suggestive of BPH but has no effect on prostate volume, PSA and (urodynamic grade of) bladder outlet obstruction.

References

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What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Ethical Committe of the University Medical Center Utrecht, The Netherlands**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**