288

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BOTULINUM NEUROTOXIN TYPE A FOR THE TREATMENT OF BENIGN PROSTATIC HYPERPLASIA: RANDOMIZED STUDY COMPARING TWO DOSES

Hypothesis / aims of study

Lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) is a very common condition that affects men in adulthood. Medical therapy, including 5α-reductase inhibitor and alpha-adrenergic antagonists, is the most common treatment for BPH. However, improvement of symptoms is often insufficient and side effects can limit its use. Surgical treatment for BPH has high success rates, but its invasiveness and potential side effects may represent significant limitations to the procedures. In this context, there has been much interest in alternative treatments for BPH. Intraprostatic injection of Botulinum toxin A (BoNT-A) has been used in a few series with encouraging results. However, a number of questions remain unanswered including route of administration, sites of injection and dose.

The objective of this study was to assess the efficacy and safety of the transurethral injection of two doses of BoNT-A in the prostate for the treatment of BPH-associated LUTS.

Study design, materials and methods

A prospective study was conducted at a single institution. Over a period of two years, 36 consecutive patients received a single BoNT-A intraprostatic injection. Inclusion criteria were symptomatic BPH with an International prostatic symptom score (IPSS) > 8 and a maximum flow rate (Qmax) < 12 ml/s. All patients had failed medical therapy with at least one alpha-adrenergic antagonist. Exclusion criteria were previous surgery for BPH, urethral stenosis, prostate or bladder cancer, pelvic surgery or radiotherapy, neurological diseases or the presence of complications requiring surgical treatment including urinary retention, bladder stone and bilateral hydronefrosis. Patients were randomized to receive 100 UI or 200 UI of BoNT-A. Follow-up evaluations were performed at 3 and 6 months after BoNT-A injection. The procedure was performed under local anesthesia using a rigid cystoscope. The total BoNT-A dose was diluted in 5 ml of saline. Five intraprostatic injections of 1 ml of the solution were performed including two injections on each lateral lobe and one in the median lobe. Patients were immediately discharged from hospital as soon as they were able to void. The primary outcome measure was the change in the IPSS score after 6 months of treatment. Secondary outcome measures included Qmax, post void residual (PVR), prostate volume (PV) and PSA levels.

Within-group changes from baseline were analyzed and between-groups comparisons were performed using analysis of variance for repeated measurements. A sample size of 17 in each group has 80% power to detect a difference between means of 3.00 (units in the IPSS score) with a significance level (alpha) of 0.05 (two-tailed).

Results

Data from 34 men were available for analysis after the exclusion of two patients who failed to return for the follow-up evaluations. The groups did not differ in terms of any of the baseline characteristics. (Table 1)

Table 1: Baseline characteristics of 34 patients with BPH treated with BoNT-A injection in the prostate

	BoNT-A 100 UI	**BoNT-A 200 UI**	**p-value**
N	17	17	
Age (yr)	66 ± 8.8	67 ± 10.0	0.59
IPSS	22.0 ± 6.4	22. ± 6.9	0.72
Qmax (ml/s)	8.6 ± 3.1	7.0 ± 3.1	0.26
PVR (ml)	131.8 ± 65.0	121.1 ± 73.7	0.88
Prostate Volume (ml)	42.3 ± 18.5	43.1 ± 19.7	0.83
PSA (ng/dl)	3.9 ± 4.1	4.1 ± 2.7	0.86

Keys: IPSS: International Prostatic Symptom Score; Qmax: peak urinary flow rate; PVR: post void residual volume; PSA: prostatic specific antigen.

The effect of the different BoNT-A doses in the various parameters is shown in table 2. Both BoNT-A doses produced significant improvements in IPSS, Qmax and PVR after 3 and 6 months. The effects of the different BoNT-A doses in these parameters were comparable. Prostate volume was affected by 200 U BoNT-A injection after 6 months of treatment. PSA levels were significantly affected in the 100 U group only after 6 months of treatment. In the 200 U group, PSA levels decreased at 3 and 6 months evaluation.

Table 2: Baseline and outcome measures at 3 and 6 months of treatment after BoNT-A injection in the prostate

	BoNT-A 100 U			**BoNT-A 200 U**		
	Baseline	*3rd mo*	*6th mo*	*Baseline*	*3rd mo*	*6th mo*
IPSS	22,0 ± 6,4	8,0 ± 4,4 *	7,5 ± 4,3 *	22,8 ± 6,9	9,5 ± 4,2 *	9,2 ± 3,4 *
Qmax (ml/s)	8,6 ± 3,1	12,8 ± 3,6 *	10,9 ± 2,4 *	7,0 ± 3,1	11,2 ± 4,8 *	11,0 ± 3,2 *
PV (ml)	42,3 ± 18,5	38,9 ± 16,7	38,6 ± 16,6	43,1 ± 19,7	39,8 ± 17,7	37,8 ± 15,5 ***
PVR (ml)	131,8 ± 65,0	39,1 ± 33,5 *	38,5 ± 31,2 *	121,1 ± 73,7	48,1 ± 24,4 *	51,7 ± 24,7 *

PSA (ng/dl)	3,9 ± 4,1	3,2 ± 3,3	3,0 ± 2,5 **	4,1 ± 2,7	3,0 ± 2,1 *	2,7 ± 1,7 *

Keys: IPSS: International Prostatic Symptom Score; Qmax: peak urinary flow rate; PVR: post void residual volume; PSA: prostatic specific antigen.
*p<0.001 **p=0.030 ***p=0.013

Two (5.8%) patients had haematuria requiring bladder irrigation through a Foley catheter immediately after BoNT-A injection. Two other patients were not able to void and required a Foley catheter that was left for five days. Both were able to void after catheter removal. Acute prostatitis occurred in 2 (5.8%) patients, who were treated on an outpatient basis. The injection procedure was well tolerated and no systemic complications such as respiratory depression or hyposthenia were observed.

Interpretation of results

Both doses of BoNT-A produced symptomatic relief of LUTS in men with BPH after three months of treatment and the effect persisted until the six months evaluation. Other series demonstrated similar results to ours. (1, 2) Moreover, significant improvements were also observed in Qmax and PVR. No differences were observed comparing the two doses. Prostate volume was mildly reduced only after six months treatment in the 200 U group. Some series, however, demonstrated reduction of PV after the BoNT-A intraprostatic injection. (1, 3) In our study, although PV reduction was not observed, IPSS, Qmax and PVR improved significantly.

PSA levels reduced only after the six months evaluation in the group treated with 100 UI of the BoNT-A. In the group treated with 200 UI, PSA levels reduced significantly after three and six months of the injection. The reduction magnitude, however, was not different between the groups.

As demonstrated by other series, the procedure is well-tolerated under local anaesthesia. In addition, complications are uncommon and easily treated. (1, 2, 3)

Concluding message

BoNT-A injection in the prostate is a simple and safe therapy for BPH. Both BoNT-A doses produced significant and comparable improvements in LUTS, Qmax and PVR.

References

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