

NOVEL ACTION OF BOTULINUM TOXIN ON THE STROMAL AND EPITHELIAL COMPONENTS OF THE PROSTATE GLAND

Hypothesis / aims of study

Intraprostatic injection of botulinum toxin type A (BTX-A) has demonstrated clinical improvement in men with bladder outlet obstruction [1]. The objective of this study was to investigate the mechanisms of action of BTX-A on the prostate.

Study design, materials and methods

Adult male S.D. rats were injected with varying doses of BTX-A into the prostates, and the prostates were harvested after either 1 or 2 weeks. The effects of BTX-A on prostate histology, and proliferative and apoptotic indices were determined by using H&E staining, proliferative cell nuclear antigen staining and TUNEL staining, respectively. The change of α_{1A} adrenergic receptor and androgen receptor were evaluated by western blotting.

Results

One week after BTX-A injection a generalized atrophy of the prostate was observed. There were significantly increased in apoptotic cells (12 fold, 16 fold, and 22 fold increase for 5U, 10U, and 20U respectively) and decreased in proliferative cells (38%, 77%, and 80% reduction for 5U, 10U, and 20U respectively) and α_{1A} adrenergic receptor (13%, 80%, and 81% reduction for 5U, 10U, and 20U respectively). There was no significant change in androgen receptors. The effects were decreased two weeks after BTX-A treatment.

Table 1 Effects of saline, 5 U, 10 U, and 20 U Botulinum toxin A (BTX-A) on ventral prostate weight, PCNA staining, and TUNEL staining at 1 and 2 week.

	Prostate weight/body weight/100g	PCNA (500 cells, 4 high power field)	TUNEL (500 cells, 4 high power field)
A. Saline 1week (N=6)	0.166±0.010	214.8±5.9	3.7±0.8
B. 5 U 1 week (N=6)	0.125±0.012	132.8±5.8	45.0±4.2
C. 10 U 1 week (N=6)	0.115±0.009	50.0±2.2	57.7±3.3
D. 20 U 1 week (N=6)	0.075±0.009	44.0±4.4	82.7±4.3
E. Saline 2 week (N=6)	0.167±0.009	244.8±21.2	3.0±0.6
F. 5 U 2 week (N=6)	0.146±0.007	231.7±20.2	2.8±0.5
G. 10 U 2 week (N=6)	0.139±0.008	193.5±15.7	4.0±0.6
H. 20 U 2 week (N=6)	0.119±0.007	163.2±13.2	4.8±0.5

Data presented as means ± S. E.

P value	A vs B	A vs C	A vs D	B vs C	B vs D	C vs D	E vs F	E vs G	E vs H	F vs G	F vs H	G vs H
Weight	0.192	0.046	0.000	0.999	0.060	0.236	0.912	0.688	0.076	1.000	0.708	0.922
PCNA	0.018	0.000	0.000	0.016	0.007	1.000	0.999	0.391	0.019	0.746	0.085	0.906
TUNEL	0.000	0.000	0.000	0.097	0.000	0.000	1.000	1.000	1.000	1.000	1.000	1.000

Scheffe post-test

Interpretation of results

BTX-A injection into the prostate alters the cellular dynamics by inducing apoptosis, inhibiting proliferation and downregulating α_{1A} adrenergic receptors [2].

Concluding message

BTX-A may be the potential drug to have dual actions on the static component and dynamic component of BPH.

References

1. Relief by botulinum toxin of voiding dysfunction due to benign prostatic hyperplasia: results of a randomized, placebo-controlled study. Urology, 62: 259-265, 2003.

Formatted: Bullets and Numbering

2. Botox induced prostatic involution. Prostate, 37: 44-50, 1998.

Formatted: Bullets and Numbering

FUNDING:

NIH

and

NSC-Taiwan