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Watanabe T[1], Masago T[1], Miyagawa I[1]
1. *Dept. of Urology, Tottori University*

DOSE BOTULINUM TOXIN-A INDUCE APOPTOSIS IN RAT DETRUSOR MUSCLE?

Hypothesis / aims of study

In recent years there has been an increasing use of botulinum toxin-A (BTX-A) for treatment of detrusor overactivity [1]. In contrast, intraprostatic injection of BTX-A has been demonstrated to cause apoptosis in the prostate in humans and in animals [2]. However, the apoptotic action of BTX-A on the detrusor muscle, which could possibly induce atrophy of the bladder, is as of yet unknown. The aim of this study was to examine BTX-A-induced apoptosis in the detrusor muscle in male rats.

Study design, materials and methods

In adult male Sprague-Dawley rats, the bladder wall and prostate were injected with BTX-A (10U). The tissues were harvested after 2 weeks, with the effects of BTX-A on the proliferative and apoptotic index then determined by using proliferative cell nuclear antigen (PCNA) and TUNEL staining, respectively. In addition, real-time polymerase chain reaction was used to measure the mRNA expressions of the apoptosis-related gene, bcl-2, and BAX in the detrusor muscle.

Results

There were no significant changes in the weight of the prostate, while significant increase of the bladder weight was seen in the BTX-A group (Table 1, 2). Although there were significant increases in both the apoptotic and proliferative cells in the prostate and vesical mucosa, respectively, there were no significant changes noted in the detrusor muscle (Figure 1, 2). In addition, the hyperplastic urothelium and the fibrotic lamina proplia were seen in the BTX-A group. As shown in Table 1 and 2, there were no significant changes in the BTX-A group as compared to the control for the mRNA expressions of bcl-2/β-actin and BAX/β-actin in either the detrusor muscle or the prostate.

Table 1. The effects of BTX-A on bladder

	Bladder weight/ 100g body weight	bcl-2/β-actin	BAX /β-actin
Control (n=8)	0.035 ± 0.002	25.7 ± 7.8	2.3 ± 1.0
BTX-A (n=8)	0.079 ± 0.016*	33.9 ± 10.3	4.4 ± 1.5

Each value represents the mean ± SEM. *: $p < 0.05$ compared with Control.

Table 2. The effects of BTX-A on prostate

	Prostate weight/ 100g body weight	bcl-2/β-actin	BAX /β-actin
Control (n=8)	0.096 ± 0.009	1.6 ± 2.5	3.4 ± 1.2
BTX-A (n=8)	0.090 ± 0.007	3.9 ± 1.6	3.8 ± 2.5

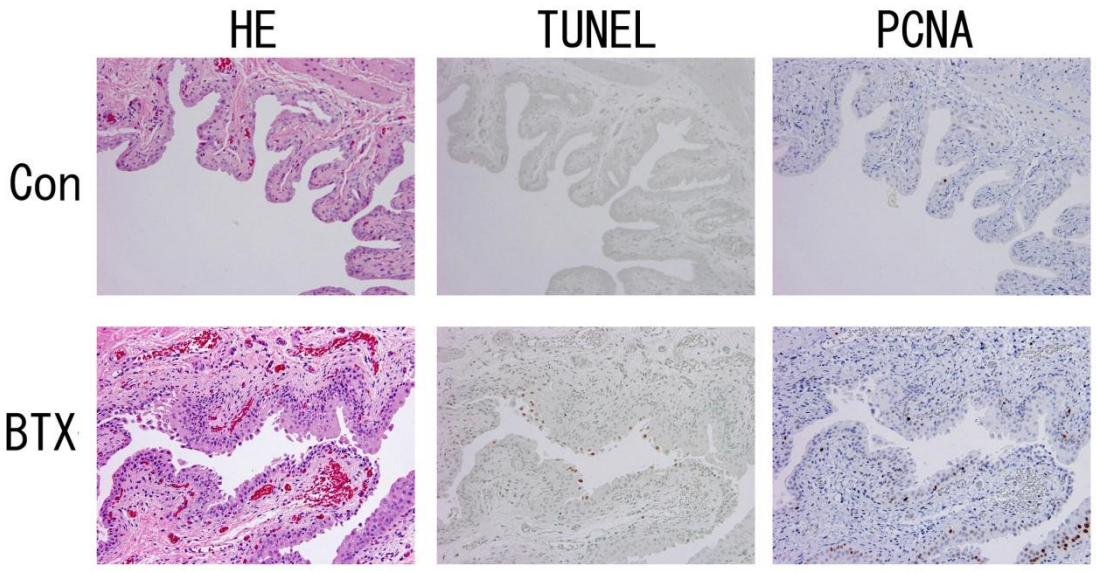

Fig. 1. Photomicrographs of bladder sections. Con: Control, BTX: BTX-A.

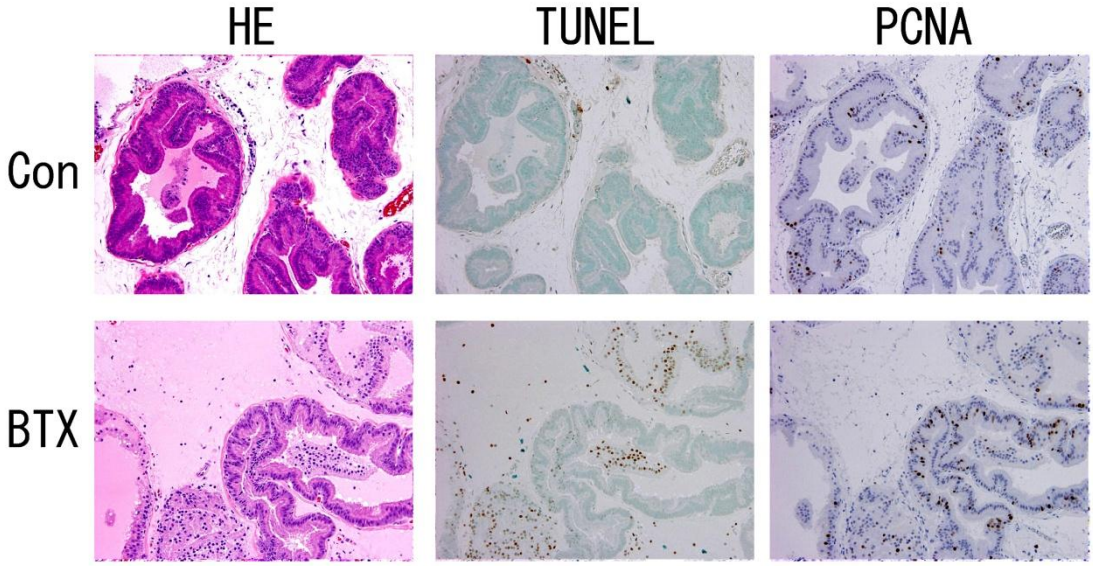

Fig. 2. Photomicrographs of prostate sections. Con: Control, BTX: BTX-A.

Interpretation of results

Although BTX-A injection induces apoptosis in the prostate and vesical mucosa, in the current study there were no significant changes noted in the detrusor muscle cellular dynamics. In addition, we speculated that the increase of the bladder weight seen in this study was caused by the overdistention due to residual urine volume.

Concluding message

These findings suggest that BTX-A injection into the detrusor muscle for overactive bladder may not induce atrophy of the bladder.

References

1. Eur Urol (2006) **50**; 684-710.
2. J Urol (2006) **175**; 1158-1163.

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Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**The University of Tottori institutional Animal Care and Use Committee**