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INTRAPROSTATIC BOTULINUM TOXIN A ADMINISTRATION PRODUCES ANALGESIC AND ANTIINFLAMMATORY EFFECTS AGAINST CAPSAICIN INDUCED PROSTATITIS MODEL IN RATS

Hypothesis / aims of study
Chronic nonbacterial prostatitis is a commonly encountered clinical entity characterized by prostate pain in the absence of identifiable infection. Botulinum toxin type A (BoNT-A) has been claimed to inhibit nociceptic responses. Using a capsaicin-induced prostatitis model in rats, we evaluated the analgesic and anti-inflammatory properties of BoNT-A in the prostate.

Study design, materials and methods
Adult male S.D. rats (350-400gm weight) were injected with BoNT-A (5-20U) (Allergan, Irvine, CA) into the prostates followed by capsaicin (10 mM, 0.1 cc) injection to induce prostatitis after either 1 or 2 weeks. The nociceptive effects of capsaicin on the prostate were evaluated for 30 min by using a behavior approach and then the prostate was removed for histology by using H&E staining and for the change of cox-2 protein concentration by using western blotting.

Results
Capsaicin (10 mM, 0.1 cc) induced increase of painful behavior (eye movement, from 1.7±0.2 to 4.2±0.3, vehicle vs capsaicin; locomotion, from 1.8±0.3 to 4.5±0.2, vehicle vs capsaicin, $p<0.001$; eyes movement: scoring 1 for normal opening, scoring 5 for complete closing; locomotion: scoring 1 for normal motion, scoring 5 for complete limpness of hindlimbs or motionless), which effects were significantly decreased by BoNT-A in a dose dependent fashion (eye movement , 3.0±0.4, 2.2±0.3, and 1.7±0.3 for 5U, 10U, and 20U respectively; locomotion, 3.2±0.4, 2.8±0.2, 2.7±0.2 for 5U, 10U, and 20U respectively).) Capsaicin induced increase of polymorphonuclear cells accumulation (PMN, from 29.2±2.5 to 672.0±81.5, vehicle vs capsaicin, $p<0.001$) and cox2 protein expression (30.3±3.6 fold increase vs vehicle, $p<0.001$), which effects were significantly decreased in BoNT-A 1 week pretreatment (PMN 434.0±93.2, 207.3±54.8, and 43.7±3.9 for 5U, 10U, and 20U respectively; COX-2 expression 17.8±1.7 fold, 9.2±3.4 fold, and 3.2±0.6 fold for 5U, 10U, and 20U respectively). The effects were decreased at two weeks pretreatment with BoNT-A.

Fig. 1 Western blot for detecting COX-2 expression. Protein amount of COX-2 was increased by capsaicin injection, which effect was decreased in BoNT-A treated animals in a dose dependent fashion.

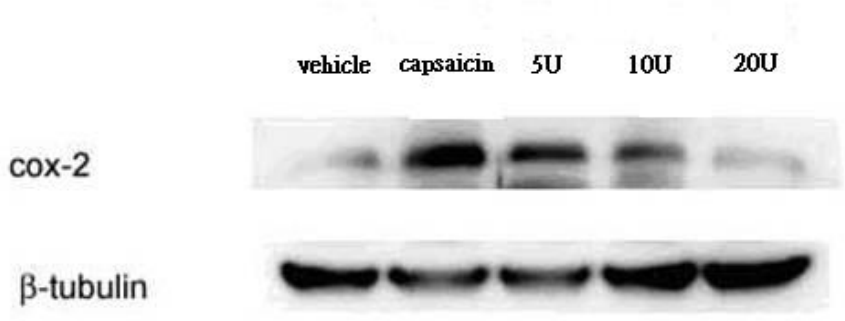

Table 1. Effects of capsaicin (10 mM) and therapeutic effects of 5 U, 10 U, and 20 U BoNT-A on eye movement, locomotion, cell number of polymorphonuclear cells (PMN), and COX-2 expression one week before capsaicin injection.

	Eye	Locomotion	PMN number	COX-2
Vehicle	**1.7±0.2**	**1.8±0.3**	**29.2±2.5**	**1.0±0.0**
Capsaicin (Cap,)	**4.2±0.3**	**4.5±0.2**	**672.0±81.5**	**30.3±3.6**
5 U BoNT-A+Cap	**3.0±0.4**	**3.2±0.4**	**434.0±93.2**	**17.8±1.7**
10 U BoNT-A+CaP	**2.2±0.3**	**2.8±0.2**	**207.3±54.8**	**9.2±3.4**

20 U BoNT-A+CaP	**1.7±0.3**	**2.7±0.2**	**43.7±3.9**	**3.2±0.6**

Data presented as means ± S. E.
N=6, for each group

Interpretation of results

BoNT-A can decrease polymorphonuclear cell accumulation, downregulate COX-2 expression and reduce prostate pain responses induced by capsaicin. BoNT-A injection into the prostate produced analgesic and anti-inflammatory effects on capsaicin induced prostatitis model in rats.

Concluding message

Intraprostatic BoNT-A injection could inhibit the capsaicin induced inflammatory change of prostate and reduce prostate pain. BoNT-A may be the potential drug to treat nonbacterial prostatitis in human.

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