

Infections/Inflammation of the GU Tract: Interstitial Cystitis
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**BOTULINUM TOXIN TYPE A INHIBITS SUBSTANCE P RELEASE IN
INFLAMMATORY RAT BLADDER MODEL**

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Introduction and Objective: An increasing body of evidence suggests that neurogenic inflammation originating from afferent bladder neurons may play a role in urinary tract disorders such as interstitial cystitis. We sought to determine the effect of botulinum toxin type A (BTX-A) on the release of the nociceptive neurotransmitter, substance P (SP), in a bladder model of chronic inflammation. We hypothesized that BTX-A administration would suppress SP release. **Methods:** Adult male Sprague-Dawley rats underwent intraperitoneal injection of cyclophosphamide (CYP) (75 mg/kg) every third day for ten days. Control animals received a corresponding volume of saline. Whole organ bladder specimens were obtained from all animals on day ten and mounted on polystyrene rods. Bladders were incubated (15 min per incubation) in two tissue baths (1.0 ml) containing physiologic salt solution (PSS) to allow for equilibration. The bladders were then transferred to another bath (PSS, 1.0 ml) and incubated for 15 min. These samples were collected and used as a measure of basal SP release. To measure the effect of BTX-A on release of SP, bladders were incubated (6 hrs) in an organ bath containing BTX-A (50 μ M) or vehicle following equilibration. SP release was determined by radioimmunoassay. **Results:** Basal release of SP was 245 ± 45 pg/g in control group. Basal SP release in the CYP-treated group increased to 430 ± 155 pg/g, representing a 76% increase over control ($p < 0.05$). Bladder histology following CYP application revealed atrophic epithelium, cytologic atypia, and hemorrhagic lamina propria. BTX-A application reduced SP release to 293 ± 155 pg/g, representing a 32% reduction in basal release of SP as compared to the inflammatory model. Basal SP release in CYP group pre-treated with BTX-A demonstrated no statistical difference from control animals ($p = 0.21$). **Conclusions:** Application of BTX-A inhibits release of SP from nerve terminals in an inflammatory rat bladder model. This finding suggests a potential clinical benefit of BTX-A application in the treatment of neurogenic inflammation that may underlie bladder disorders such as interstitial cystitis.

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