Inhibitory effect of botulinum neurotoxin on mustard oil-induced inflammation

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Abstract

In normal human body and animal tissues, the contact with mustard oil may selectively stimulate peripheral sensory C-fibers, leading to a significant inflammation reaction; such evoked inflammation is less significant for tissues lacking sensory nerves (especially C-fibers). This indicates that the C-fiber is a vital factor for inflammatory reaction. Substance P, stored at the distal vesicles of C-fibers, has a strong effect of vasodilatation. Upon the excitation of C-fibers, substance P is released and diffuses into surrounding tissues, resulting in a so-called neurogenic inflammation. Botulinum neurotoxin (BOTOX) could prevent the release of acetylcholine from the distal vesicles at the motor nerve fibers to lead to muscular paralysis. Many experiments have showed： that the control mechanism for the adherence and adhesion between cellular vesicles and cell membrane, as well as the release of chemical substances into surrounding environment are extreme similar among almost all eukaryotic organisms, from yeasts of a lower level unicellular organism to advanced primates. Therefore, substance P and acetylcholine may be released via a same mechanism. We confidently assumed that BOTOX also could prevent the release of substance P from the distal end of C-fiber and then to prevent the neurogenic inflammation. This study was aimed to probe into the following issues: (1) the inhibitory effect of a pre-injection of BOTOX on the inflammation, including plasma extravasation and tissue swelling at the hind paw of climacteric rats induced by a mustard oil injection, (2) the duration for such inhibitory effect, (3) the comparison between the inhibitory effect of BOTOX, lidocaine (a topical anesthetic), and L-733060 (an antagonist for substance P Neurokinin-1 receptor) on the mustard oil-evoked inflammation, and furthermore the action mechanism of BOTOX to inhibit the inflammation based on the specific sites of action of these various agents. Normal saline, lidocaine, or BOTOX was separately pre-injected to the hind paw of male Sprague-Dawley rat (250-350 g) while L-733060, an inhibitor of NK-1 receptor of substance P, was administrated intravenously. At 10 or 15 minutes after the injection of normal saline, lidocaine or L-733060, or 1 to 10 days after the pre-injection of BOTOX, mustard oil was injected to the same site to induce an inflammation. The volume of the hind paw was measured by displacement of

water and the difference between the volume before and after the injection of mustard oil was calculated and referred to be the swelling level. At 10 minutes before the injection of mustard oil, an Evans Blue solution was administrated by a jugular vein injection to climacteric rat. After scarifying the rat, the hind paw was removed for measurement of the Evans Blue excretion was measured by a spectrophotometer to define the inflammation-induced plasma extravasation. Results as below： (1) serious swelling and plasma extravasation was evoked by an injection of mustard oil to a hind paw with a pre-injection of normal saline, (2) a pre-injection of BOTOX of 5 U, Lidocaine, or L-733060, all could effectively reduce the inflammation, (3) a BOTOX pre-injection of 5 U commenced to act at 7 days after the injection with a duration for at least 10 days. This study has revealed that BOTOX has an inhibitory effect on neurogenic inflammation!