P19-BASIC SCIENCE (ANATOMY, PHYSIOLOGY, PHARMACOLOGY, BEHAVIOUR): SPINAL CORD

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BOTULINUM TOXIN TYPE A AND NMDA ANTAGONIST: ADDITIVE ANTINOCICEPTIVE EFFECT AT THE SPINAL LEVEL

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Background and aims: Recent studies suggest that botulinum toxin type A (BT-A) might inhibit the release of pain neurotransmitters from central primary afferent terminals, including glutamate. We hypothesized that pre- and postsynaptic NMDA receptors' blockade might enhance BT-A's central antinociceptive effect.
Methods: The effect of BT-A, NMDA antagonist AP5 and their combinations were examined in a total of 48 male Wistar rats using formalin test. Each experimental group contained 6 animals: saline or BT-A (5 U/kg) (intraplantar, subcutaneously into the plantar surface of the right hind paw); saline or BT-A + AP5 (1 µg/ 10 µL intrathecal); saline or BT-A + AP5 (5 µg/ 10 µL intrathecal); saline or BT-A + AP5 (10 µg/ 10 µL intrathecal). BT-A was applied five days, while AP5 10 min before 5% formalin (20 µL) intraplantar injection.
Results: Peripheral BT-A pre-treatment significantly reduced nociceptive behavior during the second phase of formalin test ($p<0.001$). NMDA antagonist reduced pain behavior in both phases in all tested doses ($p<0.001$). Combination of BT-A with AP5 (10 µg) had additive antinociceptive effect ($p<0.05$ compared to AP-5 and $p<0.001$ compared to BT-A) in the second phase. Similar trend was observed in the first phase, although not reaching statistical significance.
Conclusions: Application of high doses of peripheral BT-A is complicated with the development of muscular paralysis. Peripheral BT-A and intrathecal NMDA antagonist, both in effective analgesic doses, have additive antinociceptive effect in combination, thus intrathecal NMDA antagonist might be used to enhance the antinociceptive effect of BT-A.