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EFFECT OF A TRANSIENT RECEPTOR POTENTIAL VANILLOID RECEPTOR 1 ANTAGONIST ON BLADDER OVERACTIVITY INDUCED BY CAPSAICIN OR MENTHOL

Hypothesis / aims of study

Vanilloid receptors, transient receptor potential vanilloid receptor 1 (TRPV1), have been identified in afferent nerves and urothelial cells in the urinary bladder. Activation of these receptors induces bladder overactivity. In this study, we examined the effect of a novel TRPV1 antagonist (9515223-4, Neurogen corporation) on the response of the bladder to the administration of capsaicin or menthol.

Study design, materials and methods

In urethane anesthetiezed (1.2 gm/kg, s.c.) female SD rats. A jugular vein was cannulated to inject drug. Detrusor overactivity was induced by intravesical infusion of capsaicin (50 µM) or menthol (3 mM). Cystometrogram (CMG) were performed by infusing saline into the bladder (0.04 mL/min) via a tube inserted through the urethra and were done before and after irritation, or graded doses of the TRPV1 antagonist (300 nM-30µM intravesically, or 0.3-3 mg/kg intravenously).

Results

TRPV1 antagonist (0.3-3 mg/kg, i.v.) partially reversed the effect of capsaicin. Compared to the inter-contractile interval (ICI) in normal control (18.7 ±1.97 min), the ICI were 25.8%, 55.2%, 59.3%, and 45.3% after administration of capsaicin, TRPV1 antagonist 0.3, 1 and 3 mg/kg, respectively (n = 5). TRPV1 antagonist (300 nM-30µM intravesically) also partially blocked the capsaicin effect, the ICI decreased to 12.6%, 17.7%, 22.2%, and 38.2% after treatment with capsaicin, TRPV1 antagonist 300nM, 3 and 30µM, respectively, as compared to normal control (16.1 ± 2.43 min) (n = 9). Low dose (30 nM) of intravesical TRPV1 antagonist was not effective in blocking the capsaicin effect. Intravesical TRPV1 antagonist could not block the effect of menthol, the ICI were 74.7%, 68.6%, 63.4%, and 64.8% of normal control (14.1 ± 3.19 min) after menthol, TRPV1 antagonist 300nM, 3 and 30µM, respectively (n = 7). TRPV1 antagonist did not alter the amplitude or duration of large-amplitude bladder contraction.

Interpretation of results

TRPV1 antagonist (0.3-3 mg/kg, i.v. or 300 nM-30µM intravesically) partially blocked the effect of capsaicin. Intravesical TRPV1 antagonist could not block the effect of menthol. TRPV1 antagonist did not alter the amplitude or duration of large-amplitude bladder contraction.

Concluding message

Capsaicin administrated intravesically may work at two different sites: 1) in the urothelium on the lumen side which accessible to intravesically administrated antagonist. 2) in the bladder wall, presumably on afferent nerves, a site accessible to intravenously administrated antagonist. TRPV1 antagonist may selectively block the effect of capsaicin without influencing the effect of menthol.

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