

PHARMACOLOGICAL CHARACTERIZATION OF PIG DETRUSOR CONTRACTILE RESPONSES RESISTANT TO CHOLINERGIC BLOCKADE.

Hypothesis / aims of study

Excitatory innervation of the bladder is mainly mediated by 2 neurotransmitters: Acetylcholine via muscarinic receptors and ATP through P2X1 receptors. This assertion, however, has been recently challenged. The aim of this study is to characterize the neurotransmitters mediating contractile response to electrical field stimulation (EFS) in a porcine model after blocking cholinergic and purinergic pathways

Study design, materials and methods

Detrusor strips from adult pigs were studied in vitro in organ baths. Intrinsic detrusor innervation was stimulated by EFS trains (26V, 0-30 Hz) and the amplitude of the contractile response was measured. The cholinergic contribution to EFS contractions was characterized by atropine 1 μ M and the non-cholinergic component by tetrodotoxin (TTX), the purinergic antagonists NF 279 (10 μ M), suramin (100 μ M), apamin (1 μ M) and MRS 2500 (1 μ M), desensitization with alfa-beta-methylene-ATP, the NK1 antagonist SR 140333 (10 μ M) and the NK2 antagonist GR94800 (1 μ M),

Results

EFS induced a frequency-dependent contraction with a maximum response at 20Hz. Atropine reduced the amplitude of EFS contraction by $-56\pm 2.97\%$ ($p<0.05$) and the residual contraction was fully blocked by TTX. Neither NF 279 nor suramin nor apamin nor MRS 2500 affected non-cholinergic EFS contractions. Following the desensitization of the purinergic receptors with $\alpha\beta$ -meATP, we found a significant decrease in the EFS contractile response of $-34\pm 8.06\%$ at 20Hz ($p<0,05$). The addition of the NK2 antagonist did not affect the contractility, which was significantly reduced by the NK1 antagonist ($-58\pm 4.02\%$ at 30Hz).

Interpretation of results

Acetylcholine is the main neurotransmitter involved in the contraction of the porcine detrusor following EFS. The addition of TTX almost abolished any EFS contraction, suggesting that this response is mediated through the electrical stimulation of intrinsic detrusor excitatory motor neurons. The absence of effect of the different purinergic antagonists suggests us that the purinergic-mediated detrusor EFS contraction is not to be mediated by P2X123 nor P2Y1 receptors, although the inhibitory effect of desensitization with $\alpha\beta$ -meATP indicates that purines play a role in the detrusor contraction. The decrease of contraction after incubation with NK1 antagonist suggest that tachykinins could play a role in this cholinergic and purinergic resistant contraction through NK1 receptors.

Concluding message

Acetylcholine and ATP or a related purine are neurotransmitters involved in pig detrusor contraction. The purinergic-mediated detrusor EFS contraction seems not to be mediated by P2X123 nor P2Y1. There is a residual contractile response which is resistant to cholinergic- and purinergic-receptor blockade. Tachykinins are involved in this residual contraction through NK1 receptors.

Disclosures

Funding: None. **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Pig. **Ethics Committee:** Ethical Review Board of the Hospital de Mataró, Barcelona