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FUNCTIONAL RESPONSES OF P2 PURINOCEPTORS IN THE RAT URINARY BLADDER

Hypothesis / aims of study

Adenosine-5´-triphosphate (ATP) is a major contributor to the non-adrenergic, non-cholinergic responses in the rat urinary bladder eliciting a rapid contraction followed by a sustained relaxation. Previous studies have shown that the contractile response depends on the stimulation of the purinoceptor P_{2x}. The relaxatory response has been attributed to the stimulation of the G-protein coupled purinoceptor P_{2Y}. The present study was undertaken to further characterize the functional responses to purinoceptor P_{2Y} stimulation in the rat urinary bladder.

Study design, materials and methods

In the present study 14 rats of the Sprague-Dawley strain were used and detrusor strips from the urinary bladder were excised and mounted in organ baths containing 37^0 C Krebs solution (gassed with 5 % CO_2 in O_2). After equilibration, the detrusor strips were assessed to the P_{2Y} receptor agonist uridine 5´-triphosphate (UTP) in the absence and presence of different purinoceptor antagonists. In order to study relaxatory responses the detrusor strips were pre-contracted with potassium chloride (50 mM).

Results

UTP (1 µM-1 mM) elicited concentration-dependent relaxatory responses of the detrusor strips; 0.83±0.15 $mNmg^{-1}$ at 1 mM (n=6; maximal response). The P_{2Y4} selective antagonist reactive blue 2 (3 µM-0.3 mM) attenuated the relaxatory response to UTP (0.3 mM) from -25±4 % to -7±3 % at 30 µM ($p<0.001$; related to the precontractile level; n=5). The P_{2Y2} selective antagonist suramin (1 µM-0.1 mM) had no effect on the relaxatory response to UTP (0.3 mM). In the presence of the purinoceptor antagonist PPADS (30 µM) the relaxatory response to UTP (0.3 mM; -21±6 %) was changed into a contraction (49±25 %; $p<0.01$; n=5). In separate experiments the contractile response evoked by UTP (0.3 mM) in the presence of PPADS (30 µM) tended to be attenuated by suramin (0.1 mM; from 17±9 % to 4±2 %; n.s.; n=9).

Interpretation of results

The results demonstrate relaxatory P_{2Y4} receptor responses and that a contractile P_{2Y} purinergic response may occur as well.

Concluding message

The study indicates that the purinergic responses in the urinary bladder are mediated by a heterogenous P_2 receptor population.

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