

ATP- AND ADENOSINE- INDUCED RELAXATION OF THE SMOOTH MUSCLE OF THE PIG URETHRA

Aims of Study

Both nitric oxide (NO) and a non-nitroergic non-adrenergic non-cholinergic (NANC) mediator of relaxation have been demonstrated to be released from nerves in the smooth muscle of the pig urethra in response to electrical stimulation, and adenosine 5'-triphosphate (ATP) has been suggested as one possible transmitter mediating this effect (1,2). ATP is believed to cause bladder smooth muscle contraction via P2X receptors, whereas relaxation is mediated via G-protein coupled P2Y receptors. ATP may also induce relaxation via breakdown to adenosine. In the present study, relaxation mechanisms for ATP and adenosine in the pig urethra were investigated together with the possible role of ATP in nerve-evoked urethral relaxations.

Methods

Circular muscle strips from the female pig urethra were mounted in tissue baths, and mechanical activity was recorded. Strips were exposed to electrical field stimulation (EFS) and to increasing concentrations of agonists or antagonists.

Results

Circular smooth muscle strips from the female pig urethra developed a spontaneous contractile tone which was concentration-dependently relaxed by exogenously administered ATP (1-300 μ M). The ATP-induced relaxation was slowly developing and long-lasting. The P2-receptor agonist 2-methylthioATP (2-MeSATP) relaxed the preparations with potency and efficacy apparently similar to that of ATP. The relaxant effect evoked by both agonists at 300 μ M amounted to approximately 50 % of the spontaneously developed tone.

The relaxation evoked by ATP was not significantly affected by treatment with a G-protein activator (guanosine 5'-O-(3-thiotriphosphate; GTP γ S; 1-10 μ M), a G-protein inhibitor (guanosine 5'-O-(2-thio-diphosphate; GDP γ S; 10-100 μ M), suramin (1-100 μ M), or the suggested P2Y receptor antagonist, reactive blue -2 (1-100 μ M).

Adenosine induced a concentration-dependent relaxation of the smooth muscle tone, reaching a maximum of approximately 70 % at 300 μ M. In comparison, the stable adenosine-analogue, 5'(N-Ethylcarboxamido) Adenosine (NECA; 1-300 μ M) only relaxed the preparations by approximately 35 %. The adenosine-induced relaxation was not affected by treatment with the adenosine (P1) receptor antagonist 8-(p-sulphophenyl)theophylline (8-SPT; 1-100 μ M). However, the adenosine reuptake inhibitor NBTI (1 μ M) significantly reduced the relaxation evoked by 300 μ M adenosine.

Adenosine-diphosphate (ADP) relaxed the smooth muscle tone by approximately 40 % (300 μ M), whereas no response to uridine-triphosphate (UTP; 1- 300 μ M) was observed. The effect of α,β -methylene-ATP was negligible (5 % relaxation at 100 μ M).

Electrical field stimulation (EFS; 12 and 30 Hz) caused slowly developing and long-lasting relaxations in the presence of phentolamine (1 μ M), scopolamine (1 μ M) and the nitric oxide synthase inhibitor, L-NOARG (0.3 mM). GTP γ S, GDP γ S, suramin and reactive blue-2 did not affect these relaxations.

Conclusions

The present data suggest that exogenous ATP and adenosine relax the smooth muscle of the pig urethra in a manner similar to that evoked by electrical stimulation of nerves, although no evidence for involvement of a definable P2Y receptor subtype in these relaxations was found.

References

1. Regulation of tone in pig urethral smooth muscle. *J. Urol.*, **150**, 223-228 (1993)
2. Factors involved in the relaxation of female pig urethra evoked by electrical field stimulation. *Br. J. Pharmacol.*, **116**, 1599-1604 (1995).