Author(s) B.A O'Reilly[1], G.Knight[2], R.Popert[1], J.M Rymer[1], G.Burnstock[2], S.B McMahon[3]

Institution, city, country [1-]Department of Gynaecology and Urology, Guy's & St. Thomas' Hospital, [2-] Autonomic Neuroscience Institute, Royal Free Hospital, [3-]Division of Neurophysiology, King's College, London, UK.

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THE DISTRIBUTION AND FUNCTION OF P2X RECEPTORS IN DETRUSOR INSTABILITY

Aims of study

It is clear from previous work that ATP is released as a contractile co-transmitter with acetylcholine from parasympathetic nerves supplying the mammalian bladder, but the functional significance of P2X receptors in human bladder innervation has not been adequately investigated.

Methods

Female patients with Detrusor Instability were recruited for cystoscopy and bladder biopsy with ethical approval. Control tissue was obtained from patients with stable bladders. One sample was cryostat sectioned for immunohistochemical analysis with purified IgG derivative of antisera to P2X 1-7 receptors using an ABC technique with nickel-DAB enhancement. Two other samples were analysed in an organ bath for functional studies of the detrusor muscle including firstly nerve-mediated contraction studies looking at the effects of the P2X receptor antagonists on these responses and secondly the response of the muscle strips to purinergic and cholinergic agonists.

Results

P2X1 receptors were located on the smooth muscle membrane and P2X3 receptor was sensory neurone specific. Response to nerve stimulation of the bladder strips from DI patients was significantly desensitised by the P2X1 specific agonist αβ-meATP compared to muscle strips from control bladder. Nerve-mediated contractions were blocked by the P2X antagonist PPADS to a greater extent in the DI bladder.

Conclusion

ATP acting as a neurotransmitter causes smooth muscle contraction in human bladder mainly through the P2X1 receptor. The detrusor tissue from DI patients derives a greater purinergic contribution to its contraction than control tissue. This could imply a novel target for the pharmacological manipulation of the unstable bladder.