infravesical obstruction in mice were similar to those previously found in rats. This model may be useful for investigations of genetically modified mice.

References
(1) J. Urol., 141: 1245, 1989
(2) J. Urol., 148: 183, 1992
(3) J. Urol., 157: 1109, 1997
(4) J. Urol., 161: 1015, 1999
(5) J. Urol., 137: 1291, 1987

67

Author(s): S Elneil, JN Skepper, EJ Kidd, JG Willamson, and DR Ferguson

Institution, city, country:
University of Cambridge, Cambridge, United Kingdom

Title (type in CAPITAL LETTERS, leave one blank line before the text):

THE DISTRIBUTION OF $P2X_1$ AND $P2X_3$ RECEPTORS IN THE RAT AND HUMAN URINARY BLADDER

Aims of the Study Adenosine 5'-triphosphate (ATP) is well recognized as a neurotransmitter in smooth muscle preparations [1,2,3]. There is evidence to show that ATP both causes bladder contractions [1,2,4] and may have a sensory role in processing physiological information in the urinary bladder [5]. These effects are likely to be mediated by P2X receptors [2,4], namely $P2X_1$ and $P2X_3$, respectively. This study set out to investigate their distribution using subtype-specific antibodies to localise these receptors in the rat and human urinary bladder.

Methods Sections of rat and human urinary bladder, the latter obtained from male donor subjects, were incubated with antibodies to $P2X_1$ and $P2X_3$ receptors. Antibodies to the sensory neuropeptide, calcitonin gene-related peptide (CGRP) were used to identify sensory neurones in the rat [6] and human urinary bladder. Colocalisation studies with the CGRP and $P2X_3$ receptor antibodies were also performed.

Results $P2X_1$ receptor immunoreactivity was found on detrusor muscle fibres of both species. $P2X_3$ receptor immunoreactivity was mainly found in the urothelium and labelling was also seen in the suburothelial layers of the rat and human urinary bladder. The sensory innervation of the urinary bladder of both species was shown using the antibodies to CGRP. No clear evidence for colocalisation of CGRP and $P2X_3$ immunoreactivity was seen in the urinary bladder of either species.

Conclusion This study has confirmed the presence of $P2X_1$ receptors on the detrusor muscle of the rat [7] and human urinary bladder. Interestingly, $P2X_3$ receptors were found on urothelial cells, the first demonstration of a non-neuronal localisation for $P2X_3$ receptors. No clear evidence was found for the presence of $P2X_3$ receptors on CGRP-containing nerves and therefore $P2X_3$ receptors may not mediate the sensory response to ATP in the urinary bladder.

References:

1 Burnstock G, Dumsday B, Smythe A. Atropine resistant excitation of the urinary bladder: the possibility of transmission via nerves releasing a purine nucleotide. *Br J Pharmacol* 1972: 44: 451-461

2 Fujii K. Evidence for adenosine triphosphate as an excitatory transmitter in the guinea-pig, rabbit and pig urinary bladder. *J Physiol* 1988: 404: 39-52

3 Burnstock G. Purinergic neurotransmission. *Semin Neurosci* 1996: 8: 171-257

4 McMurray G, Dass N, Brading AF. Purinoceptor subtypes mediating contraction and relaxation of marmoset urinary bladder smooth muscle. *Br J Pharmacol* 1998: 123: 1579-1586

5 Ferguson DR, Kennedy I, Burton TJ. ATP is released from rabbit urinary bladder epithelial cells by hydrostatic pressure changes - a possible sensory mechanism? *J Physiol* 1997: 505: 503-511

6 Gabella G, Davis C. Distribution of afferent axons in the bladder of rats. *J Neurocytol* 1998: 27: 141-155

7 Vulchanova L, Arvidsson U, Reidl M, Wang J, Buell G, Suprenant A, North RA, Elde R. Differential distribution of two ATP-gated ion channels (P_{2X} receptors) determined by immunocytochemistry. *Proc Natl Acad Sci* 1996: 93: 8063-8067

68

H. Takeda, *K. Kaidoh, Y. Yamazaki, S. Akahane, H. Miyata, M. Akahane, Y. Ajisawa, *Y. Igawa, *O. Nishizawa & **K. -E. Andersson

Central Research Laboratories, Kissei Pharmaceutical Co., Ltd., Hotaka, *Department of Urology, Shinshu University School of Medicine, Matsumoto, Japan and **Department of Clinical Pharmacology, Lund University Hospital, Lund, Sweden

EFFECTS OF SELECTIVE β2- AND β3-ADRENOCEPTOR AGONISTS ON PROSTAGLANDIN-E2-INDUCED BLADDER HYPERACTIVITY AND CARDIOVASCULAR SYSTEM IN CONSCIOUS RATS

AIMS OF STUDY

There is much evidence supporting that activation of the sympathetic nerves causes a relaxation of the detrusor via activating of β-adrenoceptors. Recently, we have reported that the subtypes of β-adrenoceptors that contribute to the relaxation of the detrusor are β2- and β3-adrenoceptors in rats *in vitro* (1). In the present study, we studied the effects of β2- and β3-adrenoceptor agonists on micturition in conscious rats with bladder hyperactivity induced by intravesical instillation of prostaglandin E2 (PGE2). Separately, we also investigated the possible effects of β2- and β3-adrenoceptor agonists on the cardiovascular system in conscious rats.

METHODS

Female Sprague-Dawley rats weighing 170-235 g were anesthetized with sodium pentobarbital. A catheter was implanted into the bladder through the dome and a separate catheter was implanted into the right jugular vein. Cystometric investigations were performed without any anesthesia two or three days after the operation. To induce a bladder hyperactivity, saline containing PGE2 (60 μM) was instilled into the bladder continuously during cystometric investigations. Then, the effects of intravenous (i.v.) administration of CL316243, a selective β3-adrenoceptor agonist, or procaterol, a selective β2-adrenoceptor agonist on cystometric parameters were investigated. In separate animals, a catheter was implanted into the left carotid artery for investigation of the effects on the blood pressure and heart rates, and a separate catheter into the right jugular vein for drug administration. Two days after the operation, the effects of i.v. administration of CL316243 and procaterol on blood pressure and heart rates were examined.

RESULTS

Intravesical instillation of PGE2 induced bladder hyperactivity and decreased bladder capacity, as reported previously (2). CL316243 (0.1-100 μg/kg i.v.) increased bladder capacity in a dose-dependent manner (Fig. 1A) and suppressed the PGE2-induced bladder hyperactivity at 100 μg/kg.