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Expression, distribution and functional importance of Bradykinin 2 subtype receptor in the rat ureteric smooth muscle

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Introduction: The presence of bradykinin 2 (B_2) receptors has been established in different smooth muscle cells (1), however, the expression, distribution and functional role of B_2 had not been characterized in the rat ureteric smooth muscle. The aim of this study was to explore the functional role, expression and distribution of B_2 receptor along the ureter.

Method: 6-8 weeks Wistar rats of either sex were humanely killed in accordance with UK legislation (Schedule 1 procedure; Animals (Scientific Procedure) Act 1986, UK). The effects of bradykinin on Ca_{2+} signalling and force in the upper, middle, and lower ureter were studied and correlated with the expression and distribution of B_2 receptor along the ureter using immunohistochemistry.

Results: Pre-treatment of the rat ureteric smooth muscle with the selective B_2 receptor blocker, HOE-140 (10μM) had no effect on the contractile responses induced by high-K depolarisation, but fully and selectively blocked the stimulant action of BK (5μM) on the rat ureteric smooth muscles (n=5), $p<0.005$. Immunohistochemical studies revealed the presence and homogenous distribution of B_2 receptors in the urothelium along the whole length of ureter, while a significantly higher B_2 receptor expression in the smooth muscle cells in the proximal part of the ureter. The level of expression of B_2 receptors in the ureteric smooth muscle cells was quantified relative to the urothelium taken for 100% using confocal imaging. It was found that the relative expression of B_2 receptor in the smooth muscle cells of upper, middle and lower parts were 93%±0.6, (n=7), 41%±0.6,(n=9), 51%±0.6, (n=11), respectively, $p<0.005$.

Conclusion: The data obtained provide morphological and functional evidence which indicates that the anatomic distribution of B_2 receptors in the rat ureter corresponded to regions of high sensitivity of ureteric smooth muscle to BK.

Reference:
1. Calixto, J. B. (1995). European Journal of Pharmacology, 281, 279-288.