Hemokinin-1 acts at the tachykinin NK_1 receptor in the oestrogen-treated mouse uterus

M. Gozali[1], E. Patak[1], J.N. Pennefather[2], [1]Dept of Anaesthesia, Royal Women's Hospital, Carlton, VIC, Australia, [2]Dept of Pharmaceutical Biology and Pharmacology, Monash University, Parkville, VIC, Australia

We have previously established that the mammalian tachykinins (TKs) substance P (SP), neurokinin A (NKA) and neurokinin B (NKB) induce uterine contractions in the oestrogen-primed mouse uterus by acting at an NK_1 receptor[1]. Recently a new TK termed hemokinin-1 (HK-1) has been discovered[2] which exhibits remarkable selectivity for the NK_1 receptor[3]. In the periphery HK-1 appears to be expressed in non-neuronal cells in contrast to the largely neuronal expression of the other mammalian TKs. Our aim was to investigate the effects of HK-1 and the SP analogue, septide, in mediating uterine contractility in the oestrogen-primed mouse uterus. Myometrium was obtained from oestrogen-treated (20 μg/kg s.c.) BalbC mice which had been humanely killed. Preparations were set up in organ baths to record force produced by the longitudinal muscle layer. Discrete log concentration-response curves (LCRCs) were constructed to SP, NKA, HK-1 and septide (0.1nM - 1μM) in the absence (n=9-10) and presence (n=5) of the NK_1 receptor-selective antagonist SR 140333 (10nM). In the presence of phosphoramidon (10μM) and captopril (10μM) all four agonists produced concentration-related responses with the LCRC to SP lying to the left of those for the other agonists. SP and HK-1 produced significantly lower maximum responses than NKA and septide (one-way ANOVA, $P<0.05$). The NK_1 receptor antagonist SR 140333 (10nM) reduced responses to all four agonists. These results are consistent with a role for TKs acting at the NK_1 receptor in regulating uterine function in the oestrogen-primed mouse. However we propose that HK-1 and SP may act differently at the NK_1 receptor than do NKA and septide.

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3. Zhang Y et al (2000) Nat. Immunol., 1, 392-397.