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Minireview

Tachykinins and tachykinin receptors: effects in the genitourinary tract

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Abstract

Tachykinins (TKs) are a family of peptides involved in the central and peripheral regulation of urogenital functions through the stimulation of TK NK_1, NK_2 and NK_3 receptors. At the urinary system level, TKs locally stimulate smooth muscle tone, ureteric peristalsis and bladder contractions, initiate neurogenic inflammation and trigger local and spinal reflexes aimed to maintain organ functions in emergency conditions. At the genital level, TKs are involved in smooth muscle contraction, in inflammation and in the modulation of steroid secretion by the testes and ovaries. TKs produce vasodilatation of maternal and fetal placental vascular beds and appear to be involved in reproductive function, stress-induced abortion, and pre-eclampsia. The current data suggest that the genitourinary tract is a primary site of action of the tachykininergic system.

Keywords: Tachykinins; Tachykinin receptors; Urinary tract; Genital tract

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Introduction

Tachykinins (TKs) are a family of peptides sharing a common C-terminal sequence (FXGLM-NH2) which enable them to act as full agonists of specific G-protein coupled receptors termed tachykinin NK_1, NK_2 and NK_3. Substance P (SP), neurokinin A (NKA) and neurokinin B (NKB) are prototypic of endogenous NK_1, NK_2 and NK_3 receptor agonists, respectively; however the selectivity of endogenous TKs at these receptors is limited, so that the pharmacological characterization of TK receptors expressed on a given tissue requires the use of selective agonists or antagonists.

In the genitourinary tract, the major recognized sources of TKs are the primary afferent neurons expressing transient receptor potential vanilloid-1 receptors (TRPV1), which have the unique property of releasing transmitters both in the periphery (efferent function) and the spinal cord (afferent function) upon stimulation (Jancso et al., 1977; Lembeck and Holzer, 1979; see Lecci and Maggi, 2001, 2003, for reviews). These neurons typically express the alternative spliced beta-form of mRNA of the *TAC1* gene which codes for both SP and NKA. However, as will be detailed later, alternative non-neuronal sources such as neuroendocrine cells, uterus, placenta, and oocytes could become important in particular physiological conditions (Chiwakata et al., 1991; Pennefather et al., 1993, 2004; Page et al., 2000; Patak et al., 2003a; Pintado et al., 2003). Furthermore, expression of TKs in other neurons (capsaicin-resistant) could also potentially occur in pathophysiological conditions (e.g., inflammation); this has been demonstrated in airways (Lecci and Maggi, 2003) but as yet not in the genitourinary tract.

The importance of TKs expressed in sensory neurons in the regulation of lower urinary tract function is supported by experimental data on the co-localization of these peptides with TRPV1 receptors in various spinal cord segments. For instance, recently it has been shown that the co-