ROLE OF NOCICEPTIN AND ITS RECEPTOR IN ANIMAL MODEL OF ASTHMA

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Tachykinergic neurotransmission is modulated by an endogenous peptide Nociceptin/orphanin FQ (N/OFQ), via selective activation of N/OFQ peptide (NOP) receptor. The peptide/receptor system is considered a "non- opioid branch of the opioid family" of peptides and receptors, because the N/OFQ–NOP receptor and classical opioid have structural and transductional similarities, but pharmacological and functional differences. Some studies have been showed that N/OFQ-NOP receptor may influence airway physiology by modulating tachykinergic neurotransmission. In this study, we have been evaluated the role of NOP receptor activation in bronchoconstriction induced by capsaicin in isolated and perfused mouse lungs and verified the ability of N/OFQ to protect in a model of allergic asthma in a group of animal sensitised to ovalbumine. We have, also, quantified endogen nociceptin before and after capsaicin, to verify a capsaicin-dependent modulation of N/OFQ**.**

Methods: In wild type and knockout $NOP^{-/-}$ mice we have been studied the responsiveness to Capsaicin, evaluating bronchopulmonary function (total lung resistance R_L and dynamic compliance C_{dyn}). Moreover to confirm a protective action of nociceptin-nop receptor system in a model of allergic asthma, we evaluated the bronchopulmonary function, also, in a group of animal sensitised to ovalbumine.

Results: Capsaicin led to a significant increase in bronchoconstriction in terms of R_L increase in wild type and this effect was higher both in knockout and sensitised mice. In wild type mice this effect was inhibited by pre-treatment with N/OFQ or NOP receptor agonist UFP 112, which mimicks the inhibitory effect of N/OFQ, being 10-fold more potent. Pretreatment with UFP 101, a selective NOP receptor antagonist blocked the effects of both agonists. In knockout mice N/OFQ and UFP 112 was unable to modify the capsaicin-induced bronchoconstriction, while the effects of both NOP agonists on sensitised mice were reduced. Perfusate analysis showed an increase of this endogen substance after administration of capsaicin, in wild type mice, and a decrease of nociceptin in sensitized mice.

Conclusions: These results show that bronchoconstriction induced by capsaicin is inhibited by stimulation of NOP receptor. Moreover, the perfusate data suggest a neuromodulatory effect of nociceptin/orphanin FQ on capsaicin-induced release of tachykinin from capsaicin-sensitive sensory nerve endings.