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ROLE OF TACHIKYNINS IN THE BRONCHOCONSTRICTION AND AIRWAY INFLAMMATION INDUCED BY HCL INTRAESOPHAGEAL INSTILLATION IN THE RABBIT

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Background: Gastroesophageal acid reflux is a common disorder associated with exacerbation of asthma (1). In guinea-pigs intraoesophageal HCl instillation induced neurogenic inflammation in airways that was inhibited by the tachykinin NK1 receptor antagonist.
Objective: We investigated in rabbit airways the effects of NK1, NK2 and NK3 tachykinin receptor antagonists (SR 140333, SR 48968 and SR 142801, respectively) on lung function and plasma extravasation induced in trachea and main bronchi by HCl intraoesophageal instillation.
Methods: Anaesthetized New Zealand rabbits were intubated with an endotracheal tube, and with a polyethylene catheter with an attached latex balloon in the midoesophagus for the pulmonary function measurement. Airway microvascular leakage was quantified by extravasation of Evans blue dye (30 mg/kg i.v.), 10 min. after HCl (1N) instillation in the oesophagus, with or without the tachykinin receptor antagonists (1-10 mg/kg, i.v.) pretreatment.
Results: HCl intraoesophageal instillation significantly increased the lung resistance (from 23 ± 2 mg/ml to 37 ± 2.2 mg/ml; n=5, $p<0.01$), that was inhibited by SR 140333 (30 ± 1.6 mg/ml; n=5 $p<0.05$) and SR 48968 (26 ± 2 mg/ml; n=5, $p<0.01$) but not by SR 142801. Moreover, our results showed that HCl intraoesophageal instillation significantly increased plasma extravasation in trachea (HCl: 62.6 ± 4 ng/mg tissue respect to saline 16.6 ± 4 ng/mg tissue; n=5, $p<0.01$) and in main bronchi (52.9 ± 4.3 ng/mg tissue; n=5, $p<0.01$). The trachea effects were significantly inhibited by all the tachykinin receptor antagonists used, while the main bronchi effects were significantly inhibited by the tachykinin NK1 receptor antagonist only.
Conclusions: These findings suggest that bronchoconstriction and protein extravasation in the airway induced by HCl intraoesophageal instillation are mainly dependent by tachykinins release, suggesting that there are neural pathways communicating between the oesophagus and airways.

References

1. Ishikawa T., Sekizawa S.I., Sant'Ambrogio F.B., Sant'Ambrogio G. (1999) J. Appl. Physiol. 86: 1226-1230.