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Neurokinin receptor antagonism in asthma

The basic mechanisms which lead to wheezing in asthma are undoubtedly complex and new avenues of treatment continue to be explored. Recent work from Japan (Masakazu Ichinose and colleagues, *Lancet* 1992; 340: 1248-51) concentrates on the possibility that one factor in airway inflammation may be an axon reflex which results in the antidromic release of neuropeptides from vagal nerve endings. Among these neuropeptides are the tachykinins, substance P and neurokinin A. A cyclopeptide (FK-224) derived from the fermentation product of *Streptomyces violaceusniger* has been shown to act as a tachykinin receptor antagonist. Inhaled bradykinin is a potent bronchoconstrictor in people with asthma¹ but not in others and it is postulated that the bronchoconstriction may be mediated, at least in part, by bradykinin-induced release of tachykinin at sensory nerve endings.

Dr Ichinose and his colleagues studied 10 patients aged between 18 and 55 years with asthma. In a double blind, crossover trial each patient received inhaled bradykinin in gradually increasing doses beginning 25 minutes after the inhalation of either FK-224 or placebo. The bronchoconstrictor response as shown by the fall in specific airway conductance (sGaw) measured by whole body plethysmography was less severe after FK-224. The mean cumulative concentration of bradykinin needed to produce a 35% fall in sGaw was 5.3 µg/ml after placebo and 40 µg/ml after FK-224 ($p < 0.001$). Coughing induced by the inhalation of bradykinin was prevented by pretreatment with FK-224.

The results give support to the hypothesis that neurogenic inflammation mediated by tachykinins might be involved in the asthmatic process and tachykinin antagonists could prove to be useful in the treatment of asthma.

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