11. EFFECT OF ATROPINE ON EXPERIMENTALLY INDUCED BRONCHOCONSTRICTION

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In man, both histamine- and antigen-induced bronchoconstriction has been modified in some, though not all, studies by pretreatment with atropine. However, it may be that this modification simply reflects the initial relief of bronchomotor tone, rather than implicating the parasympathetic nervous system as a mediator of the histamine- and antigen-induced bronchoconstriction. The present study attempts to resolve this question.

Bronchial challenge with histamine acid phosphate was performed on 18 non-atopic and 18 asthmatic subjects and with appropriate antigen, on nine atopic asthmatic subjects. The challenge aerosol was inhaled from a Hudson nebulizer attached to a breath-actuated ‘dosimeter’. The response was monitored by specific airways conductance, sGaw, measured in a body plethysmograph. Serial concentrations of either histamine or antigen aerosols were inhaled until a definite response occurred. A dose–response curve was then constructed for each challenge. Histamine and antigen challenges were repeated, on separate days, 30 min after pretreatment with either saline, placebo or atropine methonitrate aerosol (1.5 mg). This dose of atropine had previously been shown to abolish the response to inhaled methacholine in the same subjects. Analysis of variance compared the effects of placebo and atropine on the mean histamine and antigen responses.

Atropine raised the baseline sGaw by a mean of 32% in the non-atopic and 68% in the asthmatic subjects. Baseline sGaw was not significantly changed by placebo. In individual subjects, the difference between sGaw after premedication with placebo and with atropine was less than 25%. Atropine significantly antagonized the effect of histamine in both non-atopic subjects and asthmatics and the effect of antigen, whereas placebo had no significant effect on either.

In conclusion, it appears that the parasympathetic nervous system may play an important role in the bronchial response to both histamine and antigen.

12. EFFECT OF AN INHALED ANTIHISTAMINE ON EXERCISE-INDUCED ASTHMA

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Ten adults with reproducible exercise-induced asthma were studied on 2 separate days. Six were male, nine were atopic and their ages ranged from 24 to 45 years (mean 35). Submaximal exercise was performed for 8 min on a cycle ergometer on two occasions at each visit, with an interval of 120 min between tests. The first test was performed without prior medication; the second was preceded by inhalation of 1-0 ml of saline placebo or 0.05% clemastine fumarate from a disposable Hudson nebulizer. These were given 90 min before exercise, single-blind and in random order.

All four tests for each patient were closely matched in terms of oxygen uptake and ventilation, which were monitored throughout exercise. Ventilatory function was assessed from FEV1 and PEFR. Results have been expressed as the % fall in FEV1 or PEFR after exercise and compared by paired t-test. A protection index has also been used to compare the % falls after the first and second tests each day.

The mean falls in FEV1 and PEFR were 22.0% and 25.4% respectively after placebo, and 12.2% and 12.6% after clemastine (P < 0.005). The protection indices after clemastine were 46-2% for PEFR and 47-7% for FEV1 compared with -3.0% and 15-2% after placebo. All subjects demonstrated an improvement in exercise-induced asthma after clemastine. We conclude that histamine plays an important role in the genesis of this condition. The importance of other factors is not excluded and will be discussed.

13. CATECHOLAMINES IN EXERCISE AND HYPERVENTILATION-INDUCED ASTHMA

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The mechanism underlying exercise-induced asthma is uncertain but as catecholamines are released during exercise it has been postulated that there may be some abnormality in catecholamine release during exercise in asthmatic subjects. Previous studies where catecholamines have been measured with a fluorometrically have shown either no difference or an exaggerated rise in catecholamines when comparing asthmatics and normal controls.

Recently it has been shown that if the increased ventilation of exercise is matched with isocapnic hyperventilation at rest, then similar degrees of bronchospasm may be induced in asthmatic subjects. We have measured plasma catecholamines by a specific radioenzymatic assay (da Prada & Zurcher, 1976, Life Sciences, 19, 1161–1174) in exercise and matched hyperventilation in asthmatic subjects and matched controls.

Extrinsic asthmatic subjects (age 17.2 ± 0.7 years, mean ± SEM, n = 5) with known exercise-induced asthma and normal subjects without evidence of atopy (age 17.2 ± 0.4 years, n = 6) performed a standard treadmill running test (6 km/h, 6° slope, 6 min); peak expiratory flow rate and plasma catecholamines were measured before, during and 5, 15 and 30 min after exercise. All subjects developed bronchospasm after exercise (mean fall by 26% from baseline at 5 min). During exercise plasma noradrenaline rose from 1-8 ± 0-25 to 9-9 ± 0-6 nmol/l in controls and from 2-4 ± 0-6 to 4-5 ± 1-3 nmol/l in asthmatic subjects. Plasma adrenaline rose from 0-43 ± 0-06 to 1-39 ± 0-18 nmol/l in controls but showed no significant rise in asthmatic subjects: 0.63 ± 0.12 to 0.69 ± 0.06 nmol/l. Subjects were matched for age and sex and had similar heart rate and minute ventilation changes during exercise. None of the asthmatic subjects was taking regular treatment for asthma.

After 2 h rest the subjects hyperventilated at the same minute ventilation as during exercise and the end-tidal CO2 was kept constant by adding CO2 to the inspired air. A similar degree of bronchospasm was induced in the asthmatic subjects (mean fall by 25% from baseline at 5 min). There was no significant rise in plasma catecholamines either during hyperventilation or during the time of maximum bronchoconstriction.

These results suggest that catecholamines are unlikely to play an important role in exercise-induced asthma. However, the impaired rise in catecholamine concentrations during exercise in asthmatic subjects is difficult to explain.

14. TRANSIT TIME ANALYSIS OF THE FORCED EXPIRATORY SPIROGRAM IN NORMAL SUBJECTS AND IN PATIENTS WITH ASTHMA

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The analysis of flow–volume curves breathing gases of different densities (Despas et al., 1972, Journal of Clinical Investigation, 51, 3235–3243), and more recently the mean transit time