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The effect of loratadine in exercise-induced asthma

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Exercise induced asthma (EIA) is defined as a reduction of 15% or more in forced expiratory volume in one second (FEV1) after exercise, and is known to occur in 70–80% of asthmatic children.1 Loratadine is a long acting, highly selective histamine H1 receptor antagonist, and possesses some anti-inflammatory activity. Loratadine is protective against histamine induced bronchoconstriction, and inhibits allergen induced early and late phase airway obstruction in asthmatics. Recent studies have shown that loratadine produces a mild bronchodilatation, and is effective in the long term treatment of allergic asthma.2

We investigated the effect of a 10 mg oral dose of loratadine, once daily for three days, on EIA in children, as we are unaware of any studies of its effects on EIA in the paediatric population.

METHODS

Fourteen children (eight boys, six girls; mean age 11.45 (SE 0.87) years, range 7–17) with bronchial asthma, diagnosed within the past month, were studied. All patients were judged atopic on the basis of positive skin tests to common allergens other than pollens, and increased serum concentrations of total and specific IgE. All patients had a history of exercise induced asthma, and had been previously shown to develop airway obstruction after exercise on a treadmill. To avoid the probable influences of seasonal allergies, patients with pollen allergies were excluded. Patients were excluded if they had symptoms or physical signs suggestive of renal, hepatic, or cardiovascular disease.

The lung function entry criterion on the exercise test days was an FEV1 above 85% of predicted normal. The inhaled corticosteroids were stopped at least 12 hours before each test.

Airway responses were assessed by measuring FEV1 with a water seal spirometer (System 2400 Computerized Pulmonary Function Laboratory, Sensor Medics, Yorba Linda, California, USA). The study protocol was approved by the Blacksea Technical University Hospital Ethical Committee. Informed consent was obtained in writing from parents before participating in the study.

Patients were asked to take loratadine or matched placebo at 0800 for three days (10 mg once daily) and to return to the laboratory on the third day. FEV1 was measured two hours after the last dose and the patient was then exercised. Exercise testing consisted of running on an inclined motor driven treadmill (5.3°) for six to eight minutes. Speed was adjusted during the run to achieve a steady state heart rate of at least 80% of calculated maximum age related heart rate for the last four minutes of the running time. FEV1 measurements were repeated immediately (0 minutes), and two, five, 10, 15, and 30 minutes after exercise. Heart rate was monitored throughout the exercise and before/after blood pressure measurements were performed. Room temperature and relative humidity were measured on the study days. The procedure was repeated with the alternate treatment after a washout period of at least two weeks.

The Wilcoxon rank sum test was used to compare the mean percentage differences from baseline between treatments; a value of p < 0.05 was considered significant.

RESULTS

Of the 14 patients enrolled, 11 completed the study with full data available for analysis. Two patients did not fulfill the lung function entry criteria on the first exercise test day and were excluded. One patient dropped out as an acute attack necessitated the use of a systemic steroid.

Mean FEV1 of the remaining 11 patients was 81% (SE 3.7%) of predicted at entry to the study. Mean pre-exercise (baseline) FEV1 was 2.16 (0.19) litres on the loratadine day, and 2.08 (0.16) litres on the placebo day. There was no significant difference between the mean percentage fall in FEV1 after exercise in placebo treated children (p > 0.05). The mean percentage fall in FEV1 after exercise was reduced significantly by loratadine at two, five, 10, 15, and 30 minutes when compared with placebo (p < 0.05; table 1). However, the mean decrease in FEV1 after exercise at five minutes was more than 15% of baseline in the loratadine group.

The difference between mean blood pressure values before and after exercise was not significant. There was no significant differences in temperature and humidity on study days.
**DISCUSSION**

The use of antihistamines in EIA has generally been disappointing. This may be related to failure to achieve a sufficient concentration of antihistamines at lung H1 receptor sites, as older antihistamines could not be given in high doses because of their sedative and anticholinergic side effects. However, results of studies with the more potent, newer H1 receptor antagonists in EIA have been varied. Inhaled cetirizine, oral azelastine, and higher doses of terfenadine have been reported to protect against EIA, whereas ketotifen failed to show any effect.

In the present study, the fall in FEV1 after exercise was statistically reduced by loratadine. Based on the results, however, loratadine was not effective in the prevention of exercise-induced asthma, as in the loratadine group, the mean decrease of FEV1 after exercise was more than 15%. We therefore conclude that loratadine, once daily for three days, reduces exercise-induced bronchoconstriction but does not prevent it.

The airway response to histamine, which is known to be increased in asthmatic patients, is widely used to measure airway responsiveness. However, the inhibitory effect of a compound on histamine-induced bronchoconstriction may not be predictive of its therapeutic efficacy. Obviously, exercise, in contrast to inhaled histamine, is a natural bronchoconstrictor, so the prevention of EIA is of greater clinical value. Although loratadine produced a reduction in EIA, we only studied a limited number of patients, and did not compare various compounds, such as β2 adrenergic agonists or cromolyn sodium, known to be effective in EIA. We suggest that further clinical studies are required to determine the therapeutic role of loratadine in EIA.

**ACKNOWLEDGEMENTS**

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**REFERENCES**


**Table 1** The mean percentage fall in FEV1 after treatment with placebo and loratadine

<table>
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<th>Time (min)</th>
<th>Placebo % (SE)</th>
<th>Loratadine % (SE)</th>
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