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Bronchodilator effects of the H₁ receptor antagonist—clemastine

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SUMMARY We investigated the specific H₁ receptor antagonist, clemastine, in 15 children with asthma. In the respiratory unit, clemastine was an effective bronchodilator but in a clinical trial we could not show any significant benefit compared with placebo.

Nogrady *et al.*¹ compared a nebulised solution of the specific H₁ receptor blocking antihistamine, clemastine, with salbutamol in adult asthmatics. Both drugs produced appreciable bronchodilatation, although the effect with clemastine was of slower onset but of more prolonged action. We have conflicting data on the bronchodilator properties of clemastine.^{2,3} This trial was designed to assess its clinical role in a group of schoolchildren in whom asthma was poorly controlled on conventional therapy.

Patients and methods

Fifteen asthmatic children aged 7 years 9 months to 13 years 10 months (mean age 10½ years) took part in the study. They were receiving beclomethasone dipropionate (9 children), sodium cromoglycate (3 children), ketotifen (2 children), and oral steroids (one child). All of them were also receiving varying doses of salbutamol by inhalation.

The study design was a crossover trial with 6-week periods on placebo and clemastine, 200 µg three times a day, delivered via a metered aerosol, in addition to the child's usual medications. Diary card records were kept of twice-daily peak expiratory flow rate (PEFR), total bronchodilator usage, and asthma symptom scores. The scoring system was a simple one with cough and wheeze graded separately by day and night. No symptoms scored zero and a

rising score (up to 3) reflected clinical deterioration. The worst possible daily score was twelve.

At the end of each 6-week treatment period, each child visited the respiratory laboratory with instructions to omit drug therapy for at least 4 hours before attendance. Baseline values were obtained for PEFR, forced expiratory volume in 0.75 seconds (FEV_{0.75}),⁴ and forced vital capacity, after which each child inhaled two puffs from the metered aerosol used in the previous 6 weeks. Lung function was measured during the next hour, after which a 6-minute run was performed and further readings made during the next 15 minutes. Results were expressed as percentage predicted for height⁵ and statistical analysis of lung function data was made by paired *t* tests. The last 28 days of each treatment period was compared by Wilcoxon's rank sum tests.

Results

In the respiratory unit, clemastine resulted in significant improvement in PEFR and FEV_{0.75} compared with initial values (Table 1). It did not protect against exercised-induced asthma with mean

Table 1 PEFR and FEV_{0.75} expressed as percentage predicted after clemastine and placebo

Time (min)	Clemastine (mean ± 1SD)		Placebo (mean ± 1SD)	
	PEFR	FEV _{0.75}	PEFR	FEV _{0.75}
0	76 ± 15	77 ± 16	74 ± 20	72 ± 23
5	78 ± 14	76 ± 17	74 ± 21	71 ± 24
15	81 ± 12*	77 ± 15	74 ± 21	71 ± 23
30	81 ± 12*	79 ± 14	74 ± 21	72 ± 23
60	84 ± 13*	82 ± 16†	75 ± 22	73 ± 24

*P 0.01; †P 0.02 } compared with initial.

Table 2 Asthma diary card scores for last 28 days of each treatment period

	Clemastine		Placebo	
	Mean	Range	Mean	Range
Symptom score	61.9	12–147	62.1	12–138
Symptom-free days	8.3	0–23	8.5	0–17
Doses of bronchodilator	77.1	8–260	81.4	0–203
PEFR (l/m)				
Morning	274	174–475	264	156–486
Evening	288	200–482	288	186–504

falls from baseline in PEFR and $FEV_{0.75}$ of 31% and 36% respectively, compared with falls after placebo of 33% both for PEFR and $FEV_{0.75}$.

We could not find any significant clinical benefit from clemastine as judged by symptom scores, asthma-free days, total bronchodilator usage, or twice-daily PEFR measurements at home (Table 2). The strongest trend noted was that 9 of the 15 children used fewer doses of salbutamol and other bronchodilators during the active period.

Discussion

Clemastine in a dose of 200 µg delivered by metered aerosol was a bronchodilator in these children. Our findings are similar to those reported by Nogrady *et al.*¹ in adult asthmatics in whom the maximum effect was reached slowly. In this study we did not find a significant improvement from baseline in $FEV_{0.75}$ until one hour after inhalation of clemastine (Table 1). This makes it unlikely that clemastine would ever find a role in the management of acute asthma in childhood.

We observed non-significant trends for the active drug period to be associated with less use of the bronchodilators, higher average morning PEFR at home, and higher baseline values for PEFR and $FEV_{0.75}$ in the respiratory laboratory. However, the overall results of the clinical trial (Table 2) are

discouraging with regard to the efficacy of the specific H_1 receptor antagonist as treatment for chronic asthma. Only one child was strikingly better on clemastine than placebo. He was matched by 2 others who showed the reverse trend. Furthermore, the poor clinical response at home was probably not due to inadequate dosage and poor inhalation technique because we were able to measure significant bronchodilatation when the children used the metered aerosol in the respiratory laboratory.

Although we have shown that clemastine is a bronchodilator in a group of children with residual symptoms despite conventional treatment for asthma, this study does not suggest that clemastine will be a useful addition to the management of their asthma.

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Relation between faecal fat and energy in preterm infants

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SUMMARY The energy measured in the faeces correlated highly ($r=0.93$) with faecal fat in 111 24-hour stool collections from 37 preterm infants. It is easier to measure faecal energy than faecal fat, and energy measurements provide a better indication of nutrient malabsorption than faecal fat alone.

Impaired energy balance and low energy digestibility are common in preterm infants.^{1,2} This is likely to be due mainly to fat malabsorption, but faecal energy is also derived from unabsorbed or endogenous protein and carbohydrate. The energy content of the faeces is fairly easy to measure by ballistic bomb calorimetry,³ whereas faecal fat