Mean Reduction in VC, FEV₁, and PEF_R ($\pm$ S.D.) Immediately after Inhalation Challenge after Pretreatment with Placebo and Active Drug

	Placebo	Doxantrazole	Difference*
VC (l)	0.76 $\pm$ 0.52	0.48 $\pm$ 0.24	0.28 $\pm$ 0.51 (N.S.)
FEV ₁ (l)	0.78 $\pm$ 0.65	0.45 $\pm$ 0.42	0.33 $\pm$ 0.35 (P < 0.05)
PEFR (l/min)	111 $\pm$ 72.2	63 $\pm$ 58.6	(48 $\pm$ 23.1 P < 0.001)

*P values were assessed with student's *t* test. N.S. = Not significant.

of bronchodilators after placebo in some patients. The initial mean values of VC, FEV₁, and PEF_R immediately before challenge after either pre-treatment were not significantly different. The mean percentage falls in FEV₁ and PEF_R in the placebo-treated group were 29.4 and 27.4% respectively, indicating that a significant response to challenge had occurred.

Discussion

These results in a few patients suggest that doxantrazole may be valuable in the treatment of asthma. A similar protection against asthma induced by allergen challenge has been reported for the orally administered compound AH 7725,³ but the value of disodium cromoglycate was proved by long-term trials⁴ rather than such single-dose studies. Further clinical trials are obviously needed to establish the long term efficacy of doxantrazole and determine which patients are likely to respond. Nevertheless, these preliminary findings are encouraging. Apart from difficulties with the Spinhaler an important disadvantage of cromoglycate is that it may cease to be effective in patients with severe airways obstruction because it is not effectively inhaled into their lungs.⁵ An orally active drug should be effective however severe the degree of airways obstruction.

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Double-blind Evaluation of Mazindol in Refractory Obesity

Mazindol (Teronac) is an isoindole compound with anorectic properties. It has been claimed that its pharmacological action is fundamentally different from that of the sympathomimetic amines, that it produces sustained weight loss, and that it helps to re-establish good eating habits. We undertook to evaluate its efficacy in patients with refractory obesity.

Patients, Methods, and Results

Fifty women, more than 20% in excess of their ideal weight, with refractory obesity were randomly divided into two groups. One group was instructed to take mazindol 2 mg 60 minutes before the midday meal and the other group to take an identical placebo tablet. All were given further dietary advice based on the principle of carbohydrate restriction. They had to attend every fortnight during the 12-week treatment period and again two weeks later. At each visit they were weighed, the blood pressure was recorded, and they were asked about side effects. The tablets were dispensed from the clinic and any patient failing to attend on two consecutive occasions was withdrawn.

Two patients receiving mazindol defaulted and six, four of them on mazindol, were withdrawn because of side effects. The mean age, ideal weight, and percentage in excess of ideal weight of the 23 patients receiving placebo and the 19 receiving mazindol who completed the study were comparable. The mean weight change in the placebo group during the treatment period was -0.3 kg (range +3.2 to -4.6 kg), 10 patients gaining and 13 losing weight. In the mazindol group the mean weight change was -1.4 kg (range +2.7 to -8.6 kg); 11 lost weight and only three lost more than 5 kg. The maximum weight loss on mazindol occurred at six weeks (see fig.). Only five patients with the greatest total weight losses (8.6, 6.8, 5.9, 4.5, and 3.6 kg respectively) lost any weight during the second six weeks. The 13 patients on mazindol who reattended two weeks after treatment stopped had regained a mean of +1.0 kg compared with +0.1 kg in the 16 women who had received placebo. Only four patients taking mazindol and one receiving placebo had suppressed appetites during the treatment period. There was no material change in blood pressure, and, generally, the side effects on mazindol were similar to those previously reported: five patients complained of excessive sweating and one had to be withdrawn.

Weight change in active and placebo groups.

Discussion

Though clinically unrelated to amphetamine mazindol is a central nervous system stimulant and its neuropharmacological action is comparable to that of amphetamine.¹ When given double-blind to amphetamine addicts it produces a subjective sensation similar to but less pronounced than that of amphetamine. Mazindol should be treated as a potential drug of abuse.

Studies have suggested that mazindol is an effective anorectic agent in the short term, causing weight loss comparable or superior to that achieved by phenmetrazine, dexamphetamine, and fenfluramine.²⁻⁴ We found, however, that the mean weight loss was disappointing, and only lasted about six weeks, and, when contrasted with findings in similar studies in comparable patients, was less than that achieved with chlorphentermine, phenmetrazine, phentermine, and fenfluramine.⁵ This is consistent with others' observations,²⁻⁴ and reports of more prolonged effects may merely reflect differences in patient selection.³ The rapid weight regain in our patients would refute the claim that mazindol helps to re-establish good eating habits. There is no firm evidence to suggest that anorectics will modify subsequent eating habits, and their role in the management of obesity is strictly limited. Mazindol's biochemical novelty does not confer on it any important clinical advantage over other anorectic agents.

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