Correspondence

Nifedipine enhances the bronchodilator effect of salbutamol

SIR,—The data presented by Drs Lever, PA Corris, and GJ Gibson (August 1984;**39**:576–8) do not seem to support their title and principal conclusion. To determine whether the effect of salbutamol was enhanced by nifedipine comparison of FEV_1 readings should have been made with reference to the recordings at time 30 minutes—that is, immediately before salbutamol was given—and not with reference to the results at time zero. Similarly, the area under the curve measurements should have been made with reference to time 30 minutes.

The data as presented indicate that four hours after salbutamol was given the FEV_1 had returned to the pre-salbutamol level in both the placebo and the nifedipine groups, indicating no enhancement of salbutamol response. The data suggest that nifedipine had an effect of its own, which at 30 minutes failed to be significant at the 5% level but achieved significance at four and a half hours.

For the authors to make their conclusion additional data are required showing that for their subjects nifedipine did not have a prolonged action of its own in the absence of exposure to salbutamol. This step was not included in the design of the study. Without this evidence their conclusion is unfounded and should be withdrawn.

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** This letter was sent to the authors, who reply below.

SIR,—The point Dr Miller makes is implicit in the last paragraph of our paper, where we acknowledge that a small bronchodilator effect of nifedipine cannot be excluded. Several studies have, however, failed to demonstrate such an effect. In our study, although there was a larger change in FEV_1 30 minutes after nifedipine than after placebo, the difference was not significant and no difference was detectable in the post salbutamol measurements 15 minutes later. Our conclusion remains that the combined effect of nifedipine and salbutamol exceeds that of salbutamol alone. Since submission of our paper another study with similar conclusions has been published.[1]

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1 Svedmyr K, Lofdalel C-G, Svedmyr N. Nifedipine—a calcium channel blocker—in asthmatic patients: interaction with terbutaline. *Allergy* 1984;**39**:17–22.

Comparative trial of two non-sedative H_1 antihistamines, terfenadine and astemizole, for hay fever

SIR,—The invention of a drug with a new type of action is often followed by the production of analogues with a similar action. This imposes the need to evaluate the drugs to determine the differences of action, if any. Where drugs which are being compared act on the same receptors, any differences found in maximal effect may be due to differences in dosage. By adjusting the doses of two drugs which are being compared for their wanted effect, it is possible to make either one or the other yield a greater effect, or indeed to make their effects of equal magnitude.[1,2] Drs PH Howarth and ST Holgate (September 1984;**39**:668–72) describe their comparative trial of terfenadine and astemizole using the doses recommended by the manufacturers, and found the latter drug to be the more effective one. The choice of doses may not have been optimal. In the early days after the introduction of a new drug the manufacturer's recommended dose may need changing in the light of further experience. Further studies are needed to compare terfenadine and astemizole using a range of doses.

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1 Freedman BJ, Principles of comparative drug trials with special reference to bronchodilators. In: Burley DM, Clarke SW, Cuthbert MF, Paterson JW, Shelley JH, eds. *Evaluation of bronchodilator drugs*. Folkestone: Trust for Education and Research in Therapeutics, 1973:219–35.
2 Freedman BJ. The methodology of comparative drug trials with special reference to bronchodilators. *Int J Clin Pharmacol Res* 1981;**1**:187–97.

** This letter was sent to Dr Holgate, who replies below.

SIR,—Dr Freedman points out in his letter that one of the reasons why we observed the difference between terfenadine and astemizole in our recent comparative trial of these two histamine H_1-antagonists for hay fever was that the dose of terfenadine chosen for the comparison was too low. Clearly, this remains a possibility but in designing the trial we naturally chose the oral dose of terfenadine which was the maximum recommended for the treatment of allergic rhinitis. If practitioners are given a recommended dose by manufacturers then it is only reasonable that these dosages are chosen for initial clinical trial work. Clearly, the lack of efficacy demonstrated for terfenadine in our trial would make it worth trying a higher dose in a further comparative study.

Nevertheless, I should point out that astemizole offers some advantages over terfenadine in that it is a once daily medication, which on account of its long duration of action, lack of side effects, and H_1 antihistaminic potency makes it an ideal drug for the prophylaxis of hay fever. On the other hand, terfenadine with its shorter action may be more profitably used as required for the symptomatic treatment of hay fever symptoms rather than in long term prophylaxis. It should also be pointed out that both drugs are relatively ineffective against nasal obstruction in hay fever, and where this is a dominant symptom alternative treatment should be sought with nasal decongestants or local steroids.

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