

Correspondence

Cimetidine versus ranitidine in short term healing of duodenal ulcers

SIR.—Quatrini *et al* (*Gut* 1984; **25**: 1113–7) refer to the now familiar difficulty of statistically proving differences, other than large ones, in comparative trials of ulcer healing drugs. In the 12 published studies which compared cimetidine and ranitidine in short term healing of duodenal ulcers (full references available upon request) the differences between the healing rates on the two drugs reached statistical significance only once.¹ In our own study,² we observed a higher rate of healing in the ranitidine group compared with the cimetidine group, although this difference also did not reach statistical significance (Fisher's exact test; $p=0.12$). Because of the small number of patients in the study, it was possible that we were constructing a type 2 or β error – that is, falsely accepting the null hypothesis. We therefore attempted to compare healing rates with cimetidine and ranitidine in all published trials in duodenal ulceration.

Of the 12 studies published, 10 reported higher healing rates in the ranitidine group. This is analogous to tossing a coin 12 times and getting 10 heads (or 10 tails); the probability of this happening, tested with the binomial distribution, is less than 0.05. We further analysed data only from those studies which were blinded, four week trials of cimetidine 1 g per day (as 200 mg tds, 400 mg nocte) versus ranitidine 300 mg per day (as 150 mg bd). Eight studies (1333 patients) fulfilled these criteria, and as far as we could ascertain from available data, they were comparable in design, mean age of patients, sex ratios, and percentages of smokers. This total number of patients approaches that calculated by Peterson and Elashoff³ to be needed to confidently show a 10% difference between two treatments when the less effective therapy is successful in 70% of patients. Of 657 patients receiving cimetidine, 450 were healed endoscopically at four weeks (68%) compared with 500 of 676 taking ranitidine (74%). Using χ^2 testing with Yate's correction, the difference in healing rate in favour of ranitidine is statistically significant ($\chi^2=4.61$, $p<0.05$).

With the reservation that any studies which favoured cimetidine over ranitidine might perhaps have been done, but not published, it seems likely that ranitidine is marginally more effective than cimetidine in short term healing of duodenal ulcers.

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- 2 Jones DB, Hanson RG, Mihaly GW, *et al*. Double-blind controlled trial of ranitidine versus cimetidine in the treatment of duodenal ulceration. *Aust NZ J Med* 1982; **12**: 547–9.
- 3 Peterson WL, Elashoff J. Placebo in clinical trials of duodenal ulcer: the end of an era? *Gastroenterology* 1980; **79**: 585–7.

Reply

SIR.—Jones and Yeomans pooled together the results of eight blind studies on four week treatments of 1333 duodenal ulcer patients, and found that ranitidine (150 mg bid) presents a 6% advantage on ulcer healing over cimetidine (200 mg tid, 400 mg nocte), which is statistically significant. With some reservations, these results and the method by which they were obtained are very probably valid. It should be pointed out, however, that with very large samples small differences can reach the level of statistical significance but the strength of association between the variables may still be quite weak.¹ Indeed the contingency coefficient C , calculated from Jones and Yeomans' figures, is only 0.06. This is connected with an important question which should be asked: is the difference found clinically important?

Before starting our study we were aware that the cimetidine and ranitidine healing rate probably did not differ greatly in short term treatments. What we did not know was if ranitidine would show a large advantage over cimetidine when the latter had failed to heal the ulcer previously. This possibility had been suggested by open studies and it would have been of practical as well as theoretical interest because it would have implied a possible, albeit improbable, difference in the mechanism of action of the two drugs.

Our study certainly does not exclude a difference between the two treatments in healing 'cimetidine-resistant' ulcers; it simply suggests that if a difference exists it is not a large one. Furthermore, it confirms that a most important variable in the healing of these ulcers is the duration of treatment.² To show a small difference is significant, a very large series is necessary; however, apart from the impossi-