Inhibition of nocturnal acidity

Sir,—We read with interest the paper by Professor Bianchi Porro and his coworkers (Gut 1990; 31: 397–400) indicating that inhibition of nocturnal acidity is important, but not essential, for duodenal ulcer healing. We also have expressed the view that inhibition of nocturnal acidity is by no means paramount in the healing of duodenal ulcers. This was, however, more in agreement with surgical treatment than simple treatment of duodenal ulceration and some of our data on H. pylori receptor antagonists and inhibition of acidity are at variance with that of the authors. In a study published in the British Journal of Surgery we compared the effects of ranitidine 300 mg nocte with highly selective vagotomy in subjects with duodenal ulceration. We were able to show that, as expected, ranitidine given at night had a profound effect on nocturnal acidity but that highly selective vagotomy was much more potent inhibitor of daytime than night time acidity. From these data we suggested that inhibition of 24 hour acidity was important in the healing of duodenal ulcers and more particularly inhibition of nocturnal acidity as first suggested by Dragstedt. Ranitidine is particularly effective in inhibiting 24 hour acidity when given at night and, similarly, highly selective vagotomy is effective in reducing 24 hour acidity but may not be so effective if given during the day. Because of these findings we were particularly interested to know whether ranitidine given in the morning would be as effective in the inhibition of 24 hour acidity as when given at night. In a study of 16 normal subjects, we compared the effect of ranitidine 300 mg at night with 300 mg in the morning in normal subjects. This showed that although the median 24 hour pH was not markedly different between the two treatment groups, the reduction in acidity afforded by night time ranitidine was significantly better than that afforded by the morning dose. This is in contrast to the conclusions of Professor Bianchi Porro et al, who were unable to show such a difference.

One reason for the difference between our findings and those of the authors may relate to the totally inappropriate method used by the authors to assess acid inhibition. The authors have calculated the area under the curve of pH v time. Since pH units are on a logarithmic scale an analysis of this type has little meaning, as Walt has indicated. The appropriate method of analysis is to measure the area under the curve of the hydrogen ion activity v time. The area under this curve is a measure of the 24 hour acidity and, when active medicine is compared against placebo, the percentage reduction in acidity can be calculated. This is not possible using any method which involves the pH. In addition, the authors have derived means and standard deviations from the areas under the patients’ individual curves in spite of this being inappropriate for any value derived from pH units. An additional criticism is that these individual values are expressed to three decimal places despite being derived from a pH electrode calibrated at room temperature. The use of parametric statistical methods for analysis, such as the Student’s t test is also inapplicable as Walt has indicated. Indeed, it seems likely that if the authors’ data were analysed correctly as described by Walt and appropriate statistical methods applied, the conclusions would be in agreement with our own.

It is our hypothesis that although the suppression of nocturnal acidity is not the sine qua non in the healing of duodenal ulcers, ranitidine given at night is more potent than ranitidine given in the morning because it has a superior effect on suppression of 24 hour acidity. The authors’ clinical results also tend to support this view, since the nocturnal treatment was superior in respect of the healing rates at two weeks. This difference did not achieve statistical significance, but as the authors indicate, this is not unexpected with such small numbers in the study. To settle this matter would require a clinical study with large numbers of patients since meta analyses would predict that the difference in healing rates between the two regimens would be quite small.

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