Letters

Intragastrointestinal acidic serum and gastrin after sufdotinide

Sir,—The recent paper by Smith and Pounder (Gut 1990; 31: 291–3) shows that the new competitive H₂ receptor antagonist sufdotinide, taken in doses of 600 mg H₂, induces virtually 24 hour gastric acidity. Thus its antisecretory effect closely resembles that of the proton pump inhibitor omeprazole.

The study, however, is not without relevant methodological problems. The gastric acid secretion was not studied in basal conditions, but rather only during meals. It is known that the resting acid output is lower in patients with duodenal ulcers than in normal controls and that the acid output during meals is even lower than the basal acid output. Therefore, the authors found a statistically significant difference in the mean acid output observed in the two groups of patients. However, the difference may be unreliable.

The use of the trapezoidal rule is another type of "smoothing"—certainly the integration of observed values of either acidic or gastrin provides an easily understood measure of individual 24 hour response.

The samples for 1000 and 2000 hours were not aspirated, because they occurred immediately after a main meal and oral dosing with either sufdotinide or placebo. We did not want to remove any active drug from the stomach. We know that intragastric acidity in either patients or healthy subjects is overwhelmed at these times by food buffer (see the similar value for 1400 hours in the same experiments). The substituted values tend to underestimate the antisecretory effect of sufdotinide.

The results of dosing with sufdotinide 600 mg/day to clear that statistical analysis is almost superfluous, although we agree that the p values in Figures 2 and 4 are incorrect, and should be <0.01 and <0.05, respectively.

A wide range of techniques can be used for the mathematical and statistical analysis of 24 hour data. We believe that the advantages of our technique are that it is simple to perform and the mathematical presentation produces a clear result—some statisticians tend to overinterpret 24 hour data.

Y R MAHIDA
Department of Therapeutics, University Hospital, Queen's Medical Centre, Nottingham NG7 2UH

D P JEWELL
Gastroenterology Unit, Radcliffe Infirmary, Oxford


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, based on a simple trial of a single dose of ranitidine and some of our data on H2 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 high 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 high selective vagotomy was a 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 made a particularly high level of nocturnal acidity as suggested by Dragsedt. Ranitidine is particularly effective in inhibiting 24 hour acidity when given at night and, similarly, high selective vagotomy is effective in reducing 24 hour acidity but much of the effect seems to be 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,1 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 medication 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.

J N PRIMROSE
M R ROGERS
University Department of Surgery,
St James’s University Hospital,
Leeds LS9 7TF

REFERENCES


NOTES

Register of Primary Immune Deficiencies

In line with other European countries, a register of all patients in the United Kingdom with primary immune deficiencies is being compiled. This is organised by Dr J Goos, Immunology Department, Blood Transfusion Service, Bridle Path, Leeds LS15 7TW. In order to gain complete coverage we should be grateful if any physicians or general practitioners, who have not already been contacted and who are currently managing such patients, could send details of their patients to Dr Goos. Registration forms are available on request from Dr J Goos (tel: 0532 645091) or Dr H Chapel (tel: 0865 817305), Immunology Department, John Radcliffe Hospital, Oxford OX3 9DU.

Hopkins’ Endoscopy Prize

The Hopkins’ Prize is offered annually for a paper on any topic relating to endoscopy. Applicants are invited to submit a three page summary of the proposed paper to the Endoscopy Committee of the BSG who will recommend to Council the recipient of the 1991 award. The closing date for entries is Friday, 14 December, 1990.

Further information from: Dr N Krasner, Department of Medicine, Walton Hospital, Rice Lane, Liverpool L9 1AE.

Pancreatic Society of Great Britain and Ireland

Symposium on ‘Pathogenesis of Pancreatitis’ to be held 15 November 1990. Details from Joan M Braganza, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL.

Course in gastroenterology

A course designed for consultants and registrars, including those who do not specialise in gastroenterology, will be given on 6–9 January, 1991 in Oxford, and cover topics of current interest in relation to the normal functioning of the digestive system and its diseases. Course fee £100. Closing date for applications 1 December, 1990.

Details from Dr D P Jewell, Radcliffe Infirmary, Oxford OX2 6HE. Tel: 0865 816829.

American Association for the Study of Liver Diseases Postgraduate Course

Annual Postgraduate Course, Common Liver Problems: An Update on Practice and Science, at the Marriott Hotel in Chicago, Illinois, 3–4 November 1990. The postgraduate course will be followed by the 41st Annual Meeting of the American Association for the Study of Liver Disease on 5–6 November 1990. For further information contact: Registration Manager, Slack Inc, 6900 Grove Road, Thorofare, NJ 08086–9447 USA. Tel: (609) 848–1000.

North American Society for Pediatric Gastroenterology and Nutrition

2–3 November, 1990, The Palmer House Hotel, Chicago, Illinois. For further information, registration, and housing forms, please contact: NASPGN Registration Manager, c/o Slack, Inc, 6900 Grove Road, Thorofare, NJ 08086–9447 USA. Tel: (609) 848–1000.

Sir Francis Avery Jones BSG Research Award 1991

Applications are invited by the Education Committee of the British Society of Gastroenterology who will recommend to Council the recipient of the 1991 award. Applications (15 copies) should include:

(1) a manuscript (2 A4 pages only) describing the work conducted;
(2) a bibliography of relevant personal publications;
(3) an outline of the proposed content of the lecture, including title;
(4) a written statement confirming that all or a substantial part of the work has been personally conducted in the United Kingdom or Eire.

The Award consists of a medal and a £100 prize. Entrants must be 40 years or less on 31 December 1991 but need not be a member of the BSG. The recipient will be required to deliver a 40 minute lecture at the Spring Meeting of the Society in Manchester in 1991.

Applications (15 copies) should be made to: The Honorary Secretary, BSG, 3 St Andrew’s Place, Regent’s Park, London NW1 4LB by 1 December 1990.

1 Savarino V, Mela GS. Comparison of gastric aspirate pH monitoring with antimony electrode: methodological remarks. Digestion (in press).