Correspondence

Effect of cimetidine and omeprazole on aspirin and taurocholate—induced gastric mucosal damage

Sir,—The study by Utley et al (Gut 1985; 26: 770–5) concludes that cimetidine, but not omeprazole can protect the pylorus ligated rat against gastric mucosal injury induced by topical aspirin or taurocholate. These conclusions are not strictly valid, because the gastric mucosal injury was only assessed macroscopically. If a study is designed to investigate and compare the cytoprotective qualities of two drugs, then surely a histological assessment of the gastric mucosal injury is mandatory.

The omission of histology in the earlier studies by Robert et al.,1 which first described cytoprotection, caused much confusion over the definition and depth of cytoprotection by prostaglandins. A subsequent histological investigation2 of the gastric mucosal injury in these experiments revealed that prostaglandins did not provide complete cytoprotection of the gastric mucosa, and surface mucosal injury was evident. Histological studies of the aspirin induced gastric mucosal lesion by St John et al.3 and by Rowe et al.4 have shown the presence of microscopic ulcerated lesions in macroscopically normal areas.

The rat model described in Utley’s study also has two serious omissions, particularly concerning the aspirin induced gastric mucosal injury.

(a) It is important to measure the gastric luminal pH at the end of the experiment. Aspirin is a weak acid with a pK of 3.5. The drug is absorbed in its unionised, lipid soluble form, and its absorption and the subsequent gastric mucosal injury aided by back diffusion of acid is strongly dependent on the luminal pH as shown by Rowe et al.5

(b) An increasing loss of mucosal protection was observed with doses of cimetidine that caused progressive inhibition of acid secretion. Was the absorption of aspirin in these different groups of rats similar, or does cimetidine effect the absorption of aspirin? A measurement of the serum salicylate at the end of the experiment would answer this and, with the additional luminal pH data, provide evidence that each group of rats was exposed uniformly to the drugs producing gastric mucosal injury.

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References

Reply

Sir,—I was interested to read the comments by Mr Rowe and his colleagues. They are quite correct in that our article dealt with macroscopic assessment and a detailed histological study was not performed. It is conceivable that microscopic damage has escaped notice but the term cytoprotection is an operational one and the fact remains that significant differences in macroscopic damage were observed under the experimental conditions stated.

We were fully aware of the effects of luminal pH on absorption of aspirin. The experiment was designed to keep luminal pH well beneath the pKa of aspirin and exogenous acid was added to the luminal fluid for this purpose. In fact data are available for luminal pH at the end of the experimental period and it is exceptional for pH to rise above 2.5. We have not observed luminal pH values in excess of 3.5.

I have difficulty understanding their last point and can only assume that they have misread our article. We did not observe ‘increasing loss of mucosal protection with doses of cimetidine that caused progressive inhibition of acid secretion’. In fact increasing cytoprotection against injury induced by topical acidified aspirin was observed with doses of cimetidine that caused progressive inhibition of acid secretion in the dose range 2–100 mg/kg. On the other hand, increasing loss of protection was observed with doses of cimetidine that caused progressive inhibition of acid secretion when acidified sodium taurocholate was used as the injurious agent.

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Gut 1986 27: 589
doi: 10.1136/gut.27.5.589

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