LETTERS TO THE EDITOR

Omeprazole in gastric and duodenal ulcers

SIR,—In their interesting multicentre trial (*Gut* 1990; **31**: 653-6), the Cooperative Study Group concluded that omeprazole 40 mg heals gastric and duodenal ulcers more rapidly than ranitidine 150 mg twice a day, and this result may be due to the more effective control of gastric acid secretion by omeprazole. Although there is no doubt that omeprazole causes a more profound and prolonged acid inhibition than ranitidine at the above doses, part of the conclusion does not seem to be sustained by the experimental findings. In fact, while the differences in healing rates were significantly higher for omeprazole at both two and four weeks of treatment in duodenal ulcer patients, the same was not true at both four and eight weeks in gastric ulcer patients. It may be argued that the number of gastric ulcers was so small that a type II error is responsible for the lack of significant difference and, in fact, it was pointed out that the healing rates in the study are in accord with those obtained by Walan *et al*,[1] who showed in a much larger trial on gastric ulcer patients that omeprazole is significantly more effective than ranitidine.

We believe, however, that another critical point is worth emphasising. Once again we have a study which provides no information about the location of the ulcer crater in the stomach. In using a powerful antisecretory drug, such as omeprazole, it can be expected that its pharmacological effect is greater in cases associated with increased acid secretion. Unlike duodenal ulcers, gastric ulcers have normal or reduced levels of acid secretion compared to control subjects[2] and, although patients with gastric ulcer respond to antisecretory treatment, the relation between acid inhibition and gastric ulcer healing is not as clear cut as it is for duodenal ulcer.[3] The most plausible explanation for this is that acid plays a smaller part in the pathogenesis of gastric ulcers than in duodenal ulcers. The functional heterogeneity of gastric ulcers is particularly striking in relation to the site of the niche and, using continuous pH monitoring,[4] we recently found that the 24 hour gastric acidity of patients with ulcers located at or above the angulus is much lower than that of control subjects matched for sex and age[5] and of patients with prepyloric ulcers.[6] Thus the circadian acidity pattern[7] of proximal gastric ulcers should be clearly distinguished from that of distal ones, and assessing the efficacy of potent antisecretory drugs in the whole group of gastric ulcers, independently of their location in the stomach, may be misleading. This seems to be confirmed by the results of another recent large clinical trial comparing omeprazole 30 mg and cimetidine 1 g/day in patients with only gastric body ulcers.[8] There was no significant difference between the healing rates obtained with the two drugs, even though the dose of 30 mg omeprazole has been shown to cause a maximal decrease in 24 hour gastric acid secretion.[9] This means that extreme acid inhibition is of no help in conditions characterised by low acid secretion, and the differences in acid secretory patterns in the populations sampled in the various clinical trials are likely to be responsible for the conflicting results of the efficacy of omeprazole in gastric ulcers.[10]

Since we are still unable to give well defined guidelines for an aetiological treatment of peptic ulcer, antisecretory treatment should take into account at least the varying pathophysiological profiles of acid production in this heterogeneous disease. And there is increasing evidence that gastric ulcers can be subdivided according to their anatomic locations, which are associated with different circadian acidity patterns. Thus universal regimens with high doses of omeprazole, the most potent antisecretory drug, are unlikely to be valid for all patients with gastric and duodenal ulcers. On the other hand, individualised treatment related to the predominant pathogenetic mechanism in each patient remains at present a remote possibility. Therefore, a reasonable alternative may be to tailor the antisecretory regimen to several subsets of peptic ulcers established on the basis of their site and function.

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Reply

SIR,—Savarino and colleagues ask if healing rates in our patients with gastric ulcer could have been influenced by the ulcer site. The data on site and initial ulcer size are shown in the Table, but the numbers are too few for valid statistical analysis.

Gastric ulcer healing

	No				Healed (cum %)		
	L	M	S	Total	Week 4	Week 8	Not healed Week 8
Omeprazole:							
Body ulcer	2	8	3	13	10 (77)	1 (85)	2
Prepyloric ulcer	1	1	1	3	3 (100)	0 (100)	0
Ranitidine:							
Body ulcer	7	4	7	18	10 (56)	5 (83)	3
Prepyloric ulcer	1	3	2	6	4 (67)	1 (83)	1

L=large >15 mm; M=medium 10-15 mm; S=small 5-9 mm.

At week 4 seven of the nine prepyloric ulcers but only 20 of the 31 body ulcers had healed. There has been speculation that gastric body ulcers heal more slowly than prepyloric ulcers because they are generally larger. No conclusion can be drawn from our data, but of the four unhealed body ulcers one omeprazole and two ranitidine treated ulcers were large. The one ranitidine treated unhealed prepyloric ulcer was large.

Separation of the data for body and prepyloric ulcers gives healing figures essentially the same as those reported in our paper for the combined gastric ulcer group.

The gradient of acid secretory levels in the healing of duodenal, prepyloric, and gastric body ulcers has been discussed for a very long time.[1] We addressed this point in our paper by speculating that, even without initial hypersecretion, effective acid suppression in gastric ulcer patients could favourably affect the balance between aggressive and defensive factors. Because the common factor for omeprazole and ranitidine is the ability to inhibit acid secretion, with omeprazole the more effective, as acknowledged by Savarino and colleagues, we adhere to our original conclusion which is still compatible with the gastric ulcer data subdivided for ulcer site. Overall these results suggest that duodenal and gastric ulcers heal more rapidly during omeprazole treatment, which may be explained by a more effective control of gastric acid secretion.

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1 Smithies F. Gastric ulcer without food retention. A clinical analysis of one hundred and forty operatively demonstrated cases. *Am J Med Sci* 1913;**145**:340-57.

Screening for colorectal cancer in ulcerative colitis

SIR,—We read with great interest Dr Gyde's exhaustive and critical review on how to approach the risk of colon cancer in ulcerative colitis (*Gut* 1990; **31**: 1089–92). The criticism of how scarce resources are best spent seems pertinent in a disease where colon cancer, although the single most important risk factor in the longterm prognosis, accounts for only 5–14% of all deaths in ulcerative colitis.[1] The increased cancer risk is well established but probably lower than previously thought.[2–4]

The basic problem in evaluating screening procedures in cancer surveillance, as pointed out in the review, is the prospect that a true randomised prospective study will never be