PAPERS AND ORIGINALS

Cimetidine and ranitidine in duodenal ulcer

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Summary and conclusions

Two histamine H₂ antagonists, cimetidine and ranitidine, given in doses of 1 g daily and 200 mg daily to 18 and 20 patients respectively proved equivalent in promoting healing of duodenal ulcer. No adverse effects occurred during the trial, though serum urea and creatinine concentrations tended to rise slightly during treatment with cimetidine but not ranitidine.

Choice between the two drugs is likely to be influenced by overall patterns of adverse effects rather than considerations of individual potency.

Introduction

Evidence shows that the histamine H₂ antagonist cimetidine is effective against duodenal ulcer. Ranitidine is a molecular variant in which substitutions have been made: the imidazole ring has been replaced and there are minor changes in the cyanoguanidine side chain. Experimental evidence suggests that ranitidine is at least five times as powerful as cimetidine on a molar basis in inhibiting secretion of gastric acid.¹ We have therefore compared the clinical value of these two drugs in patients with duodenal ulcer.

Method

Patients presenting with endoscopically proved duodenal ulceration were treated with cimetidine, 200 mg three times daily and 400 mg each night, or ranitidine, 100 mg twice daily. Treatments were allocated according to a prearranged randomised schedule using coded envelopes, so that the investigators did not know beforehand which

treatment a patient would receive. Treatment regimens clearly differed, and thus endoscopies to assess healing were performed whenever possible and on almost all occasions by different investigators from those who inquired about the patients' clinical progress.

Treatment was given for four weeks and continued for a further four weeks if healing as assessed endoscopically had not occurred. Patients attended at two-weekly intervals, when they were asked about their symptoms and blood samples were collected for measurement of haematological indices and blood urea, creatinine, and electrolyte concentrations, and for liver function tests.

Results

Thirty-eight patients were treated, 18 with cimetidine (two women, 16 men) and 20 with ranitidine (six women, 14 men). Patients receiving ranitidine tended to have slightly longer symptomatic histories than those given cimetidine, but the groups were otherwise well matched in their clinical characteristics (table I). Six patients, three in each group,

TABLE I—Clinical characteristics of patients treated

	Cimetidine	Ranitidine
Mean age (years)	44	45
Median duration of current attack (weeks)	4	6
Median duration of total history (years)	4	7
Median number of cigarettes smoked per day	15	15

TABLE II—Outcome of treatment

	Cimetidine (n = 18)	Ranitidine (n = 19)
No with healed ulcer:		
At four weeks	13	12*
At eight weeks	17	17†
Median time to symptom relief (days)	13	12

*One patient received cimetidine during the next four weeks; the ulcer did not heal.

†One patient with an unhealed ulcer received cimetidine for the next four weeks without effect.

were treated initially as inpatients because of recent acute bleeding or anaemia, all being discharged home within seven days. All patients completed the first four weeks of treatment except one initially given ranitidine, who proved to have Crohn's disease of the duodenum and ileum.

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During the first four weeks over two-thirds of the ulcers healed irrespective of the treatment given, and after a further four weeks all except three of the ulcers had healed; the percentage healing in the two groups was almost identical (94% with cimetidine and 89% with ranitidine). These results were matched in general by prompt symptomatic responses, patients becoming pain free after an average of 13 days with cimetidine and 12 days with ranitidine (table II).

The ulcers ultimately healed in all except three patients, two receiving ranitidine and one cimetidine. Of the patients given ranitidine, one treated early in the trial was given cimetidine for four weeks after only four weeks of ranitidine, but without inducing ulcer healing. The other was given four weeks' treatment with cimetidine after eight weeks with ranitidine, but again without effect.

TABLE III—Mean ($\pm$ SD) concentrations of urea and creatinine with the two drugs

	At entry	2 weeks	4 weeks
<i>Urea (mmol/l)</i>			
Cimetidine	4.5 $\pm$ 1.2	4.8 $\pm$ 0.9	4.8 $\pm$ 0.9*
Ranitidine	4.9 $\pm$ 1.3	5.1 $\pm$ 1.1	4.7 $\pm$ 0.9
<i>Creatinine (μmol/l)</i>			
Cimetidine	89.8 $\pm$ 10.5	98.1 $\pm$ 12.0†	95.8 $\pm$ 13.8
Ranitidine	92.2 $\pm$ 18.0	89.4 $\pm$ 15.8	89.6 $\pm$ 16.5

Conversion: SI to traditional units—Urea: 1 mmol/l $\approx$ 6 mg/100 ml.
Creatinine: 1 μ mol/l $\approx$ 0.01 mg/100 ml.

*t = 2.2, p < 0.05.
†t = 2.5, p < 0.05.

No clinical adverse effects occurred that were attributable to the treatments. In addition there were no significant changes in haematological indices or in serum activity of alkaline phosphatase, transaminase, and γ -glutamyl transpeptidase or concentrations of calcium, sodium, potassium, and bicarbonate. Serum urea and creatinine con-

centrations rose slightly but significantly in patients given cimetidine but not in those treated with ranitidine (table III).

Discussion

The results obtained in this clinical trial show that cimetidine and ranitidine give equivalent results in patients with duodenal ulcer. The overall healing rates of about 90% were equivalent to those we obtained with cimetidine during earlier studies. The difference in clinical responses between 89% and 94% for the two treatments is clearly trivial, and if this was a fair sample trebling or quadrupling the total numbers treated would not show any statistically significant difference. Failure of response to ranitidine was matched in the only two patients in whom it occurred by failure of response to cimetidine, again suggesting clinical equivalence in their effects. Choice between the drugs in treating duodenal ulcer is likely to be influenced by their proneness to cause adverse effects rather than by their effect on healing.

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Reference

- 1 Peden NR, Saunders JHB, Wormsley KG. Inhibition of pentagastrin-stimulated and nocturnal gastric secretion by ranitidine. *Lancet* 1979; ii: 690-2.

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Continuous ambulatory peritoneal dialysis: one year's experience in a UK dialysis unit

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Summary and conclusions

Thirty-two patients aged 8-63 years trained to manage themselves by continuous ambulatory peritoneal dialysis for end-stage renal failure achieved better steady-state serum biochemistry and much higher haemoglobin and lower serum phosphate concentrations than during treatment with haemodialysis up to one year before. Two patients, however, returned to intermittent haemodialysis because of recurrent peritonitis. Costs of the technique during the first year were less than half those incurred in the first year of home haemodialysis. Nevertheless, the major advantage was the ease with which patient independence and rehabilitation could be achieved.

This technique is an appreciable advance over other forms of management for end-stage renal failure.

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Nevertheless, until it is more refined and long-term problems have been assessed it should probably be used only in established renal units where back-up treatments are available.

Introduction

Continuous ambulatory peritoneal dialysis for end-stage renal failure was first described by Popovich *et al.*¹ Potential advantages of the technique, however, were offset by an unacceptable incidence of peritonitis and the use of cumbersome glass bottles.² Oreopoulos *et al.* therefore modified the technique by using polyvinylchloride bags, making the procedure simpler and safer.³ Subsequently it gained increasing acceptance and is now used worldwide.⁴

The technique requires a peritoneal dialysis solution to be present in the peritoneal cavity continuously except for periods of 20-40 minutes when the patient exchanges the equilibrated solution for fresh solution through a permanent soft indwelling catheter implanted through the anterior abdominal wall into the peritoneal cavity. This differs from "conventional" peritoneal dialysis, in which 2 exchanges of dialysis fluid are performed hourly for 48-72 hours a week. In continuous ambulatory peritoneal dialysis the long dwell times of the dialysis fluid (four to eight hours between exchanges) result in a high degree of