A comparison of 4-week peptic ulcer healing rates following treatment with antacids and ranitidine

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Summary

Eighty-eight patients with endoscopically proven gastric and duodenal ulceration were treated with ranitidine (Zantac; Glaxo) or an antacid preparation containing aluminium hydroxide and magnesium trisilicate (Gelusil; Warner) over a 4-week period to assess healing. Clinical, haematological and biochemical assessment and endoscopy were performed at the beginning and at the end of this period.

Of the duodenal ulcers, 74% healed on ranitidine therapy and 63% on Gelusil. This difference was not statistically significant ($\chi^2_{(1)} = 0,55$). Of the gastric ulcers 58% healed on ranitidine therapy and 35% on Gelusil, but this difference did not reach statistical significance ($\chi^2_{(1)} = 1,79$). There was no significant difference between the two therapies with regard to symptomatic relief in the duodenal ulcer group, but ranitidine produced significantly better results in the gastric ulcer group. No side-effects were noted in either group.

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Antacids have been used for symptomatic relief of gastric and duodenal ulceration in clinical trials assessing the safety and efficacy of the H_2-receptor antagonist ranitidine (Zantac; Glaxo), but there has been no direct comparison of the two types of treatment. We report a trial comparing ranitidine with a regulated dose of a preparation containing aluminium hydroxide and magnesium trisilicate (Gelusil; Warner) in the short-term healing of gastric and duodenal ulceration.

Ranitidine, an H_2-receptor antagonist, is a substituted amino-alkyl furan and therefore unlike cimetidine, which has an imidazole ring common to histamine.[1] It is a more potent acid inhibitor than cimetidine.[2,3] Ranitidine need only be given twice a day for effective reduction of acid secretion.

Patients and methods

Patients attending Tygerberg Hospital, Parowvallei, CP, for outpatient investigation of dyspeptic symptoms were considered for entry into the trial, in which it was intended to compare treatment with ranitidine 150 mg twice a day, and Gelusil (magnesium trisilicate 500 mg and dried aluminium hydroxide gel 250 mg), 2 tablets 1 and 3 hours after meals and a further 2 at bedtime when staying up late at night (12 - 14 tablets per day). The neutralizing capacity of a Gelusil tablet is 8,2 mEq acid.

Eighty-eight patients with endoscopically proven gastric or duodenal ulceration entered the study. Patients outside the age range 18 - 80 years were excluded from the trial, as were those who had both duodenal and gastric ulceration, had previously undergone lower oesophageal or gastric surgery or had pyloric stenosis. Recent perforation of an ulcer, pregnancy or a possibility of conception during the trial, and breast-feeding were also grounds for exclusion.

The trial was approved by the Ethical Committee of Tygerberg Hospital, and informed, signed consent was obtained from the patients following explanation of the purpose of the study and the endoscopic procedure.

After an initial clinical, haematological and biochemical assessment, endoscopy was carried out to confirm the presence and site of ulceration. Consecutive patients were allocated to one of the two treatment groups according to a previously determined randomized schedule, and the endoscopist was not aware of which treatment any patient was receiving.

At 4 weeks the baseline investigations were repeated, the patients' symptoms were assessed and the remaining tablets were counted to assist in determining compliance. Healing, defined as complete epithelialization of the ulcer, was assessed by endoscopy.

The two treatment groups were compared with regard to ulcer healing and resolution of symptoms. Two-sided Mantel-Haenszel chi-squared tests without continuity correction were used with significance declared at the 5% level.

Results

Duodenal ulceration

Forty-seven patients with duodenal ulceration entered the trial. One in the Gelusil group and 3 in the ranitidine group did not keep the 4-week follow-up appointment, and a further patient who had received ranitidine attended for assessment but did not undergo endoscopy. These 5 patients have been excluded from the analysis. The background data and results for the patients who completed the trial are presented in Table I.

After 4 weeks' treatment the ulcers had healed in 17 of the 23 patients who had received ranitidine (74%) and in 12 of the 19 who had received Gelusil (63%). The difference was not statistically significant ($\chi^2_{(1)} = 0,55$) (Table I). There was also no significant difference regarding the symptomatic relief provided by ranitidine and Gelusil following 4 weeks of treatment (Tables I and II).

Gastric ulceration

Forty-one patients with gastric ulceration entered the trial but 1 in the Gelusil group and 4 in the ranitidine group did not keep the 4-week follow-up appointment and have therefore been excluded from the analysis. Background data for the patients who completed the trial are presented in Table III.

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TABLE I. DUODENAL ULCERATION — BACKGROUND DATA AND RESULTS

	Ranitidine	Gelusil
Entered trial	**27**	**20**
Completed trial	**23**	**19**
Sex (M/F)	**16/7**	**13/6**
Age (yrs)		
Median	**55**	**39**
Range	**27 - 78**	**21 - 68**
Duration of dyspeptic history (wks)		
Median	**60***	**42†**
Range	**6 - 384**	**3 - 480**
Duration of current episode (wks)		
Median	**3‡**	**2**
Range	**1 - 12**	**1 - 18**
Smokers/non-smokers	**14/9**	**11/8**
Alcohol consumption higher than average	**2**	**4**
Symptoms resolved	**17 (74%)**	**13 (68%)**
Ulcer healed	**17 (74%)**	**12 (63%)**

*18 patients.
†14 patients.
‡21 patients.

TABLE II. SYMPTOMATIC RELIEF OF DUODENAL ULCERATION

	Gelusil	Ranitidine
Resolved	**13**	**17**
Not resolved	**6**	**6**
Total	**19 (68%)**	**23 (74%)**
Mantel-Haenszel $\chi^2_{(1)}$ =	**0,15 (not significant)**	
Improved/resolved	**17**	**21**
Unchanged/worse	**2**	**2**
Total	**19 (89%)**	**23 (91%)**
Mantel-Haenszel $\chi^2_{(1)}$ =	**0,04 (not significant)**	

TABLE III. GASTRIC ULCERATION — BACKGROUND DATA AND RESULTS

	Ranitidine	Gelusil
Entered trial	**23**	**18**
Completed trial	**19**	**17**
Sex (M/F)	**14/5**	**10/7**
Age (yrs)		
Median	**47**	**51**
Range	**19 - 75**	**29 - 66**
Duration of dyspeptic history (wks)		
Median	**24***	**24†**
Range	**11 - 96**	**6 - 60**
Duration of current episode (wks)		
Median	**2‡**	**3§**
Range	**1 - 12**	**1 - 12**
Smokers/non-smokers	**15/4**	**13/4**
Alcohol consumption higher than average	**4**	**3**
Symptoms resolved	**15 (79%)¶**	**4 (31%)**
Ulcer healed	**11 (58%)**	**6 (35%)**

*13 patients.
†11 patients.
‡18 patients.
§16 patients.
¶A significantly higher proportion of patients with gastric ulceration had experienced resolution of symptoms after 4 weeks' treatment with ranitidine ($P < 0,01$).

TABLE IV. SYMPTOMATIC RELIEF OF GASTRIC ULCERATION

	Gelusil	Ranitidine
Resolved	**5**	**15**
Not resolved	**11**	**4**
Total	**16*(31%)**	**19 (79%)**
Mantel-Haenszel $\chi^2_{(1)}$ =	**7,84; $P < 0,01$**	
Improved/resolved	**15**	**19**
Unchanged/worse	**1**	**0**
Total	**16*(94%)**	**19 (100%)**
Mantel-Haenszel $\chi^2_{(1)}$ =	**1,19 (not significant)**	

*Excluding 1 patient with unspecified data.

After 4 weeks' treatment the ulcers had healed in 11 out of the 19 patients who had received ranitidine (58%) and in 6 out of the 17 who had received Gelusil (35%); this difference was not statistically significant ($\chi^2_{(1)} = 1,79$) (Table III).

Symptomatic assessment before and after 4 weeks' treatment showed that symptoms had resolved in 79% of the patients who had received ranitidine and in 31% of those who had received Gelusil; this difference was statistically significant ($\chi^2_{(1)} = 7,84$; $P < 0,01$) (Tables III and IV).

Laboratory investigations

Haematological and biochemical values and the results of urinalysis before the commencement of treatment were compared with those after 4 weeks. There were no changes which could be attributed to treatment with either ranitidine or Gelusil.

Adverse symptoms

One patient in the ranitidine group developed swollen, tender cervical lymph nodes after 2 weeks' treatment. The condition resolved completely within 1 week in spite of the fact that the drug was not withdrawn. At the routine follow-up visit a full blood count was normal and the Paul-Bunnell test for infectious mononucleosis was negative. A causal relationship with ranitidine is considered unlikely.

One patient was entered into the trial in spite of the fact that liver function tests indicated the development of alcoholic hepatitis. At the 4-week follow-up visit the patient was frankly jaundiced and carcinoma of the head of the pancreas was diagnosed. This was not related to treatment with ranitidine.

Discussion

The present study shows that Gelusil compares favourably with ranitidine in the healing of both duodenal and gastric ulcers. In addition, in patients with duodenal ulceration there was no

significant difference between the two drugs with regard to symptomatic relief, but ranitidine provided superior relief in those with gastric ulceration.

No physical, haematological or biochemical side-effects appeared to be related to either of the two drugs.[4] Ranitidine is known to be relatively free of side-effects, and no androgenic manifestations have been reported to date. Relative freedom from interference with hepatic drug metabolism and transient increases in serum transaminase concentrations have been reported; the latter resolved on treatment.[5] Drug side-effects may only become apparent after further prolonged use, but to date ranitidine has proved to be a safe drug with good ulcer-healing properties.

Possible influences of sex and smoking status

Duodenal ulceration

Table V shows the effects of treatment, sex and smoking status on healing rates. Some of the categories involve very few patients. After allowing for the overall effect of smoking status and the interaction of this factor with sex and treatment, there was some evidence that the difference between healing rates on Gelusil and on ranitidine depended on sex ($\chi^2_{(1)} = 6{,}27$; $P < 0{,}05$). Ranitidine produced a higher observed healing rate than Gelusil in males, but the reverse was true in females. It should be emphasized that the differences between the sexes as regards treatment results were not statistically significant; sex merely appeared to influence the effect.

TABLE V. EFFECTS OF TREATMENT, SEX AND SMOKING STATUS ON DUODENAL ULCER HEALING RATES

	Ranitidine		Gelusil	
	No.	%	No.	%
Males	**12/16**	**75**	**7/13**	**54**
Smokers	**8/11**	**73**	**7/9**	**78**
Non-smokers	**4/5**	**80**	**0/4**	**0**
Females	**5/7**	**71**	**5/6**	**83**
Smokers	**3/3**	**100**	**2/2**	**100**
Non-smokers	**2/4**	**50**	**3/4**	**75**
Smokers	**11/14**	**79**	**9/11**	**82**
Non-smokers	**6/9**	**67**	**3/8**	**37**

After allowing for the overall effect of sex and its interaction with smoking status and treatment, there was some evidence that the difference between Gelusil and ranitidine depended on smoking status ($\chi^2_{(1)} = 5{,}84$; $P < 0{,}05$). There was little difference between results of the two treatments in smokers, but the non-smokers in the ranitidine group fared better than those in the Gelusil group. Again the treatment differences within smoking categories were not statistically significant, but smoking seemed to affect results.

Gastric ulceration

The overall healing rates were 35% (6 out of 17 patients) for Gelusil and 58% (11 out of 19 patients) for ranitidine, a difference which was not statistically significant ($\chi^2_{(1)} = 1{,}79$).

Neither sex nor smoking status was important in determining the outcome of treatment. Table VI shows the healing rates classified according to treatment, sex and smoking status. Although most of the categories involve very few patients, there were no significant differences between Gelusil and ranitidine healing rates for any of the subgroups of patients with regard to sex or smoking status.

TABLE VI. EFFECTS OF TREATMENT, SEX AND SMOKING STATUS ON GASTRIC ULCER HEALING RATES

	Ranitidine		Gelusil	
	No.	%	No.	%
Males	**8/14**	**57**	**4/10**	**40**
Smokers	**7/12**	**58**	**4/9**	**44**
Non-smokers	**1/2**	**50**	**0/1**	**0**
Females	**3/5**	**60**	**2/7**	**29**
Smokers	**2/3**	**67**	**2/4**	**50**
Non-smokers	**1/2**	**50**	**0/3**	**0**
Smokers	**9/15**	**60**	**6/13**	**46**
Non-smokers	**2/4**	**50**	**0/4**	**50**

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