# RANITIDINE IN THE ACUTE TREATMENT OF DUODENAL ULCER — A DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

I YAP
S J LaBrooy
H H Tay
R Guan
J Y Kang

**University Department of Medicine
National University of Singapore
Singapore General Hospital
Singapore 0316**

I Yap, MBBS, MMed (Int Med)
Lecturer

S J LaBrooy, MBBS, MRCP
Senior Lecturer

R Guan, MBBS, MRCP
Senior Lecturer

J Y Kang, MBChB (Hons), MRCP, FRACP
Senior Lecturer & Consultant Physician

## SYNOPSIS

**Sixty patients with endoscopically proven duodenal ulcer were entered into a double-blind study comparing the effects of ranitidine and placebo on acute ulcer healing. Forty-seven patients completed the trial. Twenty-three patients received ranitidine 150 mg bid and 24 patients received placebo. Repeat endoscopy at four weeks showed that the ulcers have healed in 19 patients (83%) receiving ranitidine and in 11 patients (46%) receiving placebo. This difference was statistically significant (P 0.025). The reduction in daytime pain during the first week of treatment was greater in the ranitidine group. Amongst patients given ranitidine, non-smokers healed their ulcers better than smokers. The use of ranitidine was not associated with any adverse effects.**

## INTRODUCTION

Ranitidine has been show to be superior to placebo in healing duodenal ulcers in Western populations. However, its efficacy in ulcer healing has not previously been studied amongst Singaporean patients. The aim of the present study was to compare the use of ranitidine with placebo in the acute treatment of duodenal ulcer patients in Singapore.

## METHODS

### Patient Selection

Adult patients with duodenal ulcer confirmed endoscopically within the previous seven days were included in the study. The following categories of patients were excluded: (1) pregnant and lactating mothers and females likely to conceive (2) patients with severe concomitant diseases (3) patients who had received treatment with histamine $H_2$ receptor antagonists or ulcer therapy other than antacids in the month perior to entering the study and (4) patients with concomitant gastric or oesophageal ulceration. Informed consent was obtained.

### Trial Design

Patients received either ranitidine 150 mg bid or an identical placebo tablet bid according to a randomised code. They were also given a supply of antacid tablets (Rennies, Nicholas) to take as required for pain. Diary cards were kept to record pain and antacid usage. The patients were assessed at two weeks and four weeks. After four weeks (28 ± 3 days) endoscopy was repeated and the ulcers assessed as healed or not healed: Gastric secretory testing, as well as pre and post treatment haematological and biochemical evaluation were performed.

### Statistical Analysis

Group means were compared using student's t tetst. Differences in the incidence of ulcer healing were assessed by the $X^2$ test with Yate's correction or by Fisher's exact probability test depending on the number of patients involved.

## RESULTS

Out of the 60 patients who were entered into the trial, 13 were withdrawn. Eleven patients defaulted follow up while in two the study protocol was not adhered to. Therefore 47 patients were available for analysis: 23 of them received ranitidine 150 mg bid and 24 received placebo one tablet bid. There were no significant differences between the two groups with respect to sex, race, age, duration of disease, alcohol consumption or gastric acid output (Table 1). Although there were fewer smokers in the ranitidine group this difference did not reach statistical significance ($P > 0.10$).

### Ulcer Healing

At four weeks 83% of patients treated with ranitidine 150 mg bid healed their ulcers compared to 46% of patients treated with placebo. This difference was statistically significant ($P < 0.025$) (Table 2).

**TABLE 2**
**INCIDENCE OF DUODENAL ULCER HEALING ON RANITIDINE AND PLACEBO**

| | Ranitidine | Placebo |
|---|---|---|
| Healed | 19 (83%) | 11 (46%) |
| Not Healed | 4 (17%) | 13 (54%) |
| Total | 23 | 24 |

$X^2 = 5.379$ ($P$ 0.025)

### Symptomatic Relief

The two groups were comparable in terms of pain experienced prior to entry into the trial. Ninety-five percent of patients in each group complained of daytime pain prior to treatment. The mean number of days per week with pain was 5.2 for the ranitidine group and 5.3 for the placebo group. The ranitidine group experienced more pain relief during the first week ($P < 0.05$). Over the next three weeks of treatment, however, symptoms improved equally in the two groups (Figure 1).

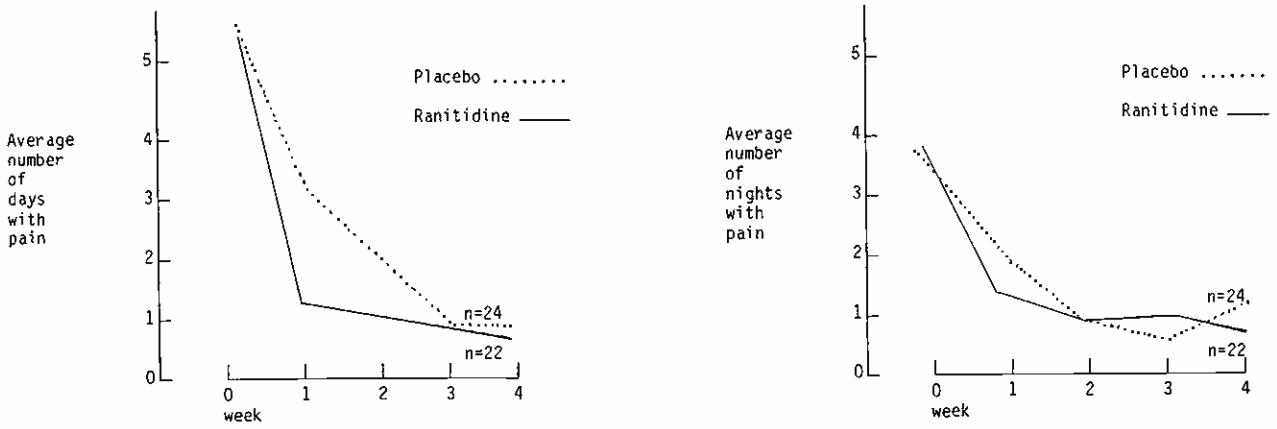
Sixty-eight percent of patients in the ranitidine group and 70% of patients in the placebo group complained of night-time pain prior to entry into the study, the mean numbers of nights per week with pain being 3.8 and 3.6 respectively. There was no difference between the two groups in the reduction of night-time pain over the four-week trial period (Figure 1).

The number of antacid tablets consumed decreased over the study period for both groups (Figure 2). While the ranitidine group took fewer antacid tablets (throughout the four weeks, the difference was not statistically significant.

**TABLE 1**
**PATIENT CHARACTERISTICS**

| | Ranitidine | Placebo |
|---|---|---|
| Number | 23 | 24 |
| Sex (M: F) | 14:9 | 16:8 |
| Race (Chinese: Indian: Malay: others) | 20:3:0:0 | 14:4:5:1 |
| Age: mean (range) | 43 (19-71) | 44 (18-79) |
| Duration of Disease in years Median (range) | 2.5 (<1-27) | 4 (<1-20) |
| Smokers (%) | 8 (35) | 12 (50) |
| Drinkers (%) | 2 (9) | 7 (29) |
| Basal Acid Output (mean mEq/hr) | 5.85 | 6.63 |
| Peak Acid Output (mean mEq/hr) | 30.23 | 30.39 |

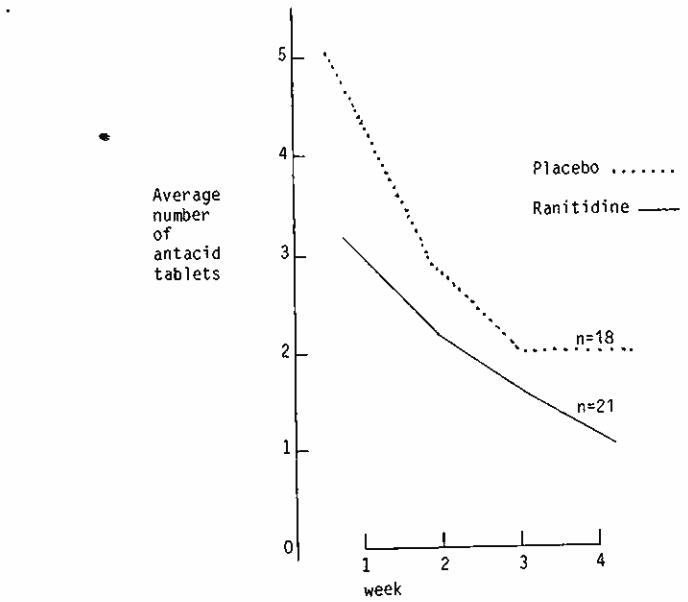
**Figure 1 Reduction in Pain**




(a) Mean number of days per week with pain

(b) Mean number of nights per week with pain

**Figure 2 Antacid Consumption**




### Effect of Smoking

Overall, 78% of non-smokers healed their ulcers compared to 45% of smokers ($P < 0.05$). Amongst those taking ranitidine the 100% healing rate of non-smokers is significantly higher than the 50% of smokers ($P < 0.02$). Smokers taking ranitidine had a healing rate similar to that of smokers and non-smokers taking placebo (Table 3).

### Adverse Effects

No significant clinical, haematological or biochemical events attributable to therapy occurred during the course of the trial.

## DISCUSSION

Recent studies from Europe and Australia have

**TABLE 3**
**THE EFFECT OF SMOKING ON DUODENAL ULCER HEALING**

| | Ranitidine | Placebo | All |
|---|---|---|---|
| Smokers | *4/8 (50%) | 5/12 (42%) | **9/20 (45%) |
| Non Smokers | *15/15 (100%) | 6/12 (50%) | **21/27 (78%) |

*P 0.02
**P 0.05

shown that ranitidine is more effective than placebo in promoting duodenal ulcer healing (1, 2, 3, 4). However, the rates of ulcer healing on various treatments including placebo vary from population to population. Hence, findings in one country cannot necessarily be extrapolated to another country (5, 6)

We have previously shown that duodenal ulcer healing rates in Singaporean patients taking cimetidine and placebo are similar to those reported from Western centres (7). The present study demonstrates that ranitidine too is superior to placebo in the acute healing of duodenal ulcer in Singaporean patients. The rates of healing on ranitidine and placebo (83% and 46% respectively) are similar to those reported in patients from Europe and Australia (1, 2, 3, 4).

Symptomatic improvement was observed more rapidly with ranitidine than with placebo for the first week. There was however no difference in the frequency of pain after the second week between the two groups. This reflects the natural history of duodenal ulcer.

Smoking has previously been demonstrated to be an adverse influence on duodenal ulcer healing (2, 8, 9. 10, 11). This effect is also evident in the present study.

Ranitidine therefore is safe for the acute treatment of duodenal ulcer in Singaporean patients. It is superior to placebo in promoting ulcer healing amongst non-smokers.

## ACKNOWLEDGEMENT

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