

TREATMENT OF ACUTE DUODENAL ULCERS WITH FAMOTIDINE AND ITS COMPARISON WITH OTHER H₂ BLOCKERS

Pages with reference to book, From 136 To 137

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ABSTRACT

Famotidine, a new H₂ antagonist in a dose of 40 mg qhs was tried in a clinical trial for the treatment of duodenal ulcer in 25 patients and compared with other H₂ antagonists. Cimetidine 800 mg qhs and Ranitidine 300mg qhs used in a similar number of randomised patients. Patients were evaluated clinically, biochemically and endoscopically. At the end of eight weeks, the healing rate with Famotidine was 96%, Cimetidine 92% and Rantidine 96%. No significant side-effects were noted with any of these drugs. In conclusion, Famotidine (40 mg qhs) is an effective and generally well-tolerated drug In the treatment of acute duodenal ulcer (JPMA 40: 136, 1990).

INTRODUCTION

The introduction of histamine (H₂) receptor antagonists in 1972 by Black et al¹ ushered in a new era in the management of peptic ulcer disease. The wide use of these agents since that time has not only increased our understanding of their benefits, but has also led to further therapeutic advances. Famotidine differs chemically from Cimetidine and Ranitidine, by the presence of a guanythiazole ring, it shares neither the imidazole ring of the former nor the furane ring of the latter. On a equimolar basis, Famotidine has been reported to be 2(Y to 160 fold more potent than cimetidine and 3-20 fold more potent than ranitidine². Antisecretory activity persists for approximately 12 hours following a 40mg nocturnal dose of famotidine³. At equipotent doses, famotidine has been shown to have a arger duration of antisecretory activity than either cimetidine or ranitidinein the Zollinger-Ellison Syndrome⁴. Fanmtidine has an excellent steady profile, in particular, it does not interfere with drug metabolism via the cytochrome P450 oxidative enzyme system⁵, therefore, it does not interfere with the hepatic oxidative metabolism of theophylline, phenytoin, warfarin, or diazepam. It has not been noted to exhibit antiandrogenicc effects⁶. This study was carried out to evaluate the efficacy and tolerance off dine in the tr nt dacute duodenal ulcer arni to make a omparative study with cimetidine and rankidine manopentrial.

PATIENTS AND METHODS

Seventy five patients having clinical symptoms within the previous 2 weeks and endoscopically varified duodenal ulcer above 5mm and less than2 5cm in diameter measured with open biopsy forceps were included in the study. Patients younger than 18 or older than 70 years were excluded, as were pregnant women, lactating mothers, or women trying to become pregnant, patients with pyloric stenosis, hiatal hernia, reflux oesophagitis, those on NSAIDs or having history of ulcer complications, previous gastric surgery (except simple closure of perforation within previous 3 months) concomitant gastric ulcer, neoplasm, cirrhosis of the liver, renal insufficiency; or acute paucratitis, prior treatment with H₂ receptor antagonists or other drugs with antiulcer like activity, anticholinergics, antidepressants during the seven 'days, before study started, hypersensitive to H₂ receptor antagonist,

significant pulmonary disease, congestive heart failure, myocardial infarction, arrhythmias within past six months, uncontrolled diabetes or hypertension and any other significant condition such as nervous system impairment were excluded from the study. Any impediment to endoscopy was also considered to be a criteria for exclusion. Endoscopy and baseline studies were performed within three days of the start of treatment including history, physical examination and laboratory tests. Follow up endoscopies were performed on 14th day, 28th day, and 42nd day of the treatment, 14th day endoscopy was omitted if the symptoms were persistent. On the days of follow up endoscopies, ulcer symptoms and any side-effects were recorded, and laboratory tests were repeated (blood count, ESR, platelet count, total bilirubin, SGOT, SGPT, alkaline phosphatase, urea, creatinine, glucose, faecal occult blood and urine analysis). Each patient was given a diary card for recording day and night pain, the severity of pain, and the number of medications and antacid tablets taken each day. Pain severity was scored as zero (0) for none, 1 for mild, 2 for moderate or 3 for severe, and whether or not the pain caused insomnia. Diary card checked and tablet counts were performed at each visit to determine compliance. Clinical and laboratory data were evaluated at each visit for possible adverse experiences. Twenty five patients received 40mg Famotidine qhs, 25 patients Cimetidine 800mg qhs and 25 patients 300mg Ranitidine qhs. Randomization was done in blocks of five patients each. The study was terminated for patients with endoscopically proven ulcer healing observed on any of the follow up dates. Patients were evaluated for success of treatment after eight weeks of therapy. Statistical evaluation of results were done with Kruskal-Wallis comparison test.

RESULTS

Age and sex distribution of 75 patients along with the duration of disease is shown in Table-1.

TABLE-1. Baseline characteristics of patients in three groups.

	Famotidine	Cimetidine	Ranitidine
No. of patients Enrolled	25	25	25
Sex (M/F)	22/3	21/4	23/2
Age (Yrs, mean $\pm$ SD)	44.3 $\pm$ 10.2	42.6 $\pm$ 12.0	43.6 $\pm$ 12.6
Duration of disease (Yrs, mean $\pm$ SD)	4.6 $\pm$ 6.8	5.0 $\pm$ 7.5	4.8 $\pm$ 7.0

During the first, second to fourth and fourth to eighth weeks of treatment, approximately 35%, 25% and 15% of patients respectively took antacids in addition to test medications. After eight weeks of treatment, the evaluated success with Famotidine 40mg qhs, Cimetidine 800mg qhs and Ranitidine 300mg qhs was 90%, 92% and 96% respectively (Table- II),

**TABLE-II. Duodenal Ulcer Healing Rates with Famotidine
Cimetidine, and Ranitidine.**

Duration of Treatment (WK)	Famotidine (%)	Cimetidine (%)	Ranitidine (%)
4	80	76	84
8	96	92	96

considered as good to excellent efficacy. Complete relief of day pain was achieved in a median time of 6,7 and 6 days and night pain relief was achieved in 3.5, 3 and 4.0 days by the treatment of Famotidine, Cimetidine and Ranitidine respectively. The percentage of patients taking antacids at any time during the eight weeks study period was similar in all groups. There were no clinical or laboratory adverse experiences with Famotidine, Ranitidine or Cimetidine. One patient had headache and one dyspepsia with Famotidine but none of the patients was withdrawn from the study because of any adverse experience.

DISCUSSION

Famotidine in single daily dose of 40mg given at bed time, accelerates duodenal ulcer healing to the same extent as does Cimetidine and Ranitidine. In the current study, the healing rates after six weeks were in the range of 90 percent. In the multicenter, USA trials⁶ and Austrian, Italian and German multicenter trials⁷ showed the effectiveness of one dose Famotidine therapy and its comparative equivalence with the Ranitidine bid therapy. Dam-mann et al⁸ showed the effectiveness of single dose of the three H₂- antagonists Cimetidine, Ranitidine and Famotidine specifically and recommended that the entire daily dose be administered once in the evening. Symptomatic response was excellent in all the treatment groups. There was no significant side-effects noted in this trial. In conclusion, Famotidine (40mg at bed time) is a highly effective and generally well tolerated therapy in the treatment of acute duodenal ulcer disease.

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