CIMETIDINE FOR CHRONIC DUODENAL ULCERATION SHORT TERM CLINICAL TRIAL

PANIR CHELVAM & ZULKIFLI AHMAD

INTRODUCTION

CIMETIDINE is an effective drug for the short term treatment of duodenal ulcer. In the eight prospective randomised double blind placebo-controlled studies available in the published world literature (Winship, 1978) healing occured in 57 to 87 % of duodenal ulcer patients compared to a healing rate of 19 to 60 % in placebo-treated patients. The duration of treatment was for 4 to 6 weeks and the dose ranged from 0.8 to 2.0 g per day.

We present here a preliminary report of a short term clinical trial of cimetidine treatment of 26 Malaysian patients with chronic duodenal ulceration, using a dosage of 1 gm per day for six weeks.

METHOD

The trial was carried out at the General Hospital, Kuala Lumpur by the Department of Medicine, National University of Malaysia. Patients entering the trial had symptomatic and endoscopically proven duodenal ulcer (26 patients). Endoscopy using the Olympus GIF type K, JF type B2 and GIF type P2 instruments was carried out in the week before the commencement of treatment. The endoscopy was repeated by the same endoscopist in the first week after the 6 weeks of treatment. Ulcers were recorded as healed or unhealed. All patients were treated as outpatients with regular follow-up at 2 weeks intervals for the period of treatment. The dose of cimetidine used was 200 mg three times a day immediately before meals and 400 mg at night. Antacid tablets were allowed for symptom relief. During a pretreatment interview a detailed history and physical examination was performed. Baseline studies performed pre-treatment included haematological and biochemical blood studies (haemoglobin, haematocrit, red blood cell count, total white blood cell count, differential and platelet count, blood urea, serum creatinine, bilirubin, alkaline phosphatase, SGPT) and urinalysis. These studies were repeated during follow-ups in most of the patients.

At each follow-up a history and physical examination was performed with particular reference to ulcer symptoms, amount of antacids consumed and to side effects of cimetidine.

Department of Medicine,
University Kebangsaan Malaysia, Kuala Lumpur.

PANIR CHELVAM, M.R.C.P. (U.K.)
Lecturer in Medicine.

ZULKIFLI AHMAD, M.R.C.P. (U.K.)
Associate Professor and Head

RESULTS

Patient profile:

Twenty-six patients entered the trial. Of these, 18 were males and 8, females. The racial distribution consisted of 6 Malays, 8 Indians and 12 Chinese. The ages of the patient ranged from 16 years to 64 years, the mean age being 46 years.

Symptom relief with Cimetidine

The duration of symptoms ranged from 6 months to 12 years with a mean duration of 6.0 years. The most consistent symptom was burning epigastric pain (in 22 patients out of 26), relieved by antacids and/or meals, aggravated by fasting. Sixteen patients out of the 26 had night pains disturbing their sleep in the early hours of the morning.

There was improvement of symptoms in 25 patients out of the 26. The pain relief was complete in 15 patients after the first week of treatment; in another 6, after the second week of treatment; in another 1, after the fourth week of treatment. There was partial relief of pain (i.e. decreased frequency and intensity of pain) in 3 patients, almost no improvement in 1 patient. The use of antacids during the course of treatment could be reduced in all patients except one. All patients with night pain (16 out of 26) had relief of their nocturnal symptoms whilst on cimetidine.

Ulcer healing with Cimetidine

Nineteen out of the 26 patients (73%) had complete healing of the ulcer (proven endoscopically) after 6 week of Cimetidine treatment. In the remaining 7 patients, 3 had partial healing and 4 had no healing at all.

Although 22 patients had complete relief of pain after the fourth week of treatment, only 19 patients had complete ulcer healing. Two of the 15 patients, where pain had disappeared after the first week of treatment, had no evidence of ulcer healing at the end of the six weeks treatment. There was no definite correlation between ulcer healing and symptom relief.

Of the 7 patients whose ulcers did not heal with Cimetidine the ages ranged from 16 to 52 years of age. Also the duration of the duodenal ulcer disease did not seem to affect the healing.

Side-effects of Cimetidine

There were no serious side-effects in all our patients. All patients tolerated the drug well.

Change of bowel habit was the most frequent untoward side-effect noted in our series. 8 out of the 26 patients complained of constipation; 4 complained of loose to soft stools. No patient developed nausea or vomiting. None had dizziness or headache while on the drug. There was no gynaecomastia or galactorrhoea in our patients. Laboratory investigations did not reveal any evidence of agranulocytosis in all the patients. Of the 20 patients who had serial liver function tests done, none had any elevation of liver enzymes. Of the 18 patient none showed any elevation of the serum creatinine above 2.0 mg % (i.e. clinically significant).

DISCUSSION

Cimetidine, the most recent and most promising of the histamine H -receptor antagonists is a potent inhibitor of gastric acid secretion in normal subjects, and in patients with duodenal ulcer, (Henn, 1975; Longstreth *et al.*, 1976) hence the main indications for the drug are duodenal ulceration and the Zollinger-Ellison Syndrome (Malagelada, 1978). (Useful indications include treatment of gastric ulcer and pancreatic insufficiency; possible indications are prevention of gastrointestinal bleeding and treatment of peptic oesophagitis).

In 300 placebo-treated patients with duodenal ulcers a healing incidence of 37% has been reported in the world literature (Winship, 1978). The healing incidence of 73% in our series using 1gm of Cimetidine per day confirms the significantly higher healing rate. This healing rate is in agreement with experience elsewhere in the world (Banks *et al.*, 1976; Hetzel *et al.*, 1978).

Cimetidine relieved pain completely in 21 out of our 26 patients. However 3 of these patients showed no healing of ulcer endoscopically at the end of treatment, indicating that symptom relief does not indicate ulcer healing. Ippoliti *et al.* (1978), in his series, states that ulcer healing was not necessary for symptom relief as 18 of 36 patients with endoscopic evidence of ulcer or erosion were asymptomatic.

We did not experience any serious side-effect of the drug. Bowel habit alterations especially constipation was observed in 12 of our patients. Although gynaecomastia, raised serum trausaminares and creatinine have been observed we detected none in our series. Serum prolactin levels have been reported to be raised in patient with Cimetidine. Prolaction levels were not measured in our patients.

We conclude that Cimetidine is an effective drug for ulcer healing and symptom relief for the short term treatment of duodenal ulceration.

SUMMARY

26 patients with endoscopically proven chronic duodenal ulceration were treated with Cimetidine 200mg three times a day and 400mg at night for 6 weeks. In 19 out of the 26 patients (73%) the ulcer was endoscopically healed at the end of the treatment. All patients received antacids only for symptom relief. Symptomatic relieve did not correlate to ulcer healing. No significant side effects were noted in the 26 patients. This study demonstrates the efficacy of short term Cimetidine in healing of chronic duodenal ulcer and in relieving ulcer symptoms.

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