

Cimetidine in Treatment of Duodenal Ulcer

Pages with reference to book, From 55 To 58

Huma Qureshi, Sarwar J. Zuberi (PMRC Research Centre, Jinnah Postgraduate Medical Centre, Karachi.)

Abida Ahmad (Smith Kline & French, Site, Karachi.)

Abstract

One hundred patients with endoscopically confirmed duodenal ulcer were treated with cimetidine (Tagamet) in dosage of 1G/day or 400 mg b.d. for six weeks and 400 mg nocte for further 6 weeks. Eighty-five patients completed twelve weeks of cimetidine treatment. Eighty (94%) of these were symptom free and ulcers healed at the end of 12 weeks treatment; fifteen patients were lost to follow up. One patient died of associated renal disease and four patients failed to improve. The drug was well tolerated and no serious side effects were recorded. Routine laboratory tests revealed no persistent abnormalities. It is concluded that cimetidine is effective in the treatment of duodenal ulcer and in giving effective symptomatic relief (JPMA 34 : 55, 1984).

Introduction

The effectiveness of cimetidine and H₂receptor antagonist in healing duodenal ulcers has been demonstrated in many controlled trials (Bank et al., 1976; Bardan et al., 1979; Binder et al., 1978; Blackwood et al., 1976; Bodemar et al., 1977; Gillespie et al., 1977; GiUies et al., 1977; Gray et al., 1977; Hetzel et al., 1978; Northfield and Blackwood, 1977; Peter et al., 1978; Ubiluz, 1979). Although the daily dosage of cimetidine varied between 800 and 2000 mg, healing rates in the majority of these studies were remarkably similar.

The standard daily dosage of 1 G cimetidine divided in four doses is based on the results of pharmacological studies which show that 200 mg cimetidine with meals inhibits the mean intragastric hydrogen ion activity by 57 per cent (Pounder et al., 1977) and inhibition of nocturnal acid secretion is most marked with bedtime dose of 400 mg (Blackwood and Northfield, 1977). The daytime acid secretion could similarly be reduced by a single morning dose of 400 mg (Burland et al., 1980). It has not been proved that the degree of acid inhibition is an accurate predictor of the magnitude of the therapeutic response. Previous studies in a small number of subjects comparing 800 mg cimetidine with either 1.2 or 1.6 G cimetidine daily did not reveal any significant difference in duodenal ulcer healing (Blackwood et al., 1976; Bodemar et al., 1977). It has now been confirmed by various clinical trials that potency of the drug or higher dose does not influence the healing of an ulcer as long as optimal acid inhibition is obtained with a pharmacological dose of the drug (Langman et al., 1980; Northfield et al., 1977).

The present study was conducted to assess the value of cimetidine in patients with uncomplicated duodenal ulceration.

Method

Between December 1978 to April 1983, one hundred out patients with endoscopically proven duodenal ulcer were studied to assess the efficacy of cimetidine in giving symptomatic relief as well as healing of the duodenal ulcer.

These patients were attending the PMRC Research Centre at Jinnah postgraduate Medical Centre, Karachi, and were randomly allocated to either the standard dose of 1 G cimetidine divided in four doses (200 mg three times a day with meals and 400 mg at bedtime) or 400 mg cimetidine twice daily

at breakfast and bedtime for six weeks followed by 400 mg nocte for further six weeks in both groups. No other treatment was allowed except antacids which could be taken as frequently as required for the relief of ulcer pain which was not controlled by trial medication. Each patient was interviewed and a detailed clinical history was recorded and examined physically. Laboratory screening included Hb, TLC, DLC and Liver function tests in some cases before treatment and at the end of 6 weeks. Patients entered the trial on the day when duodenal ulcer disease was confirmed by fibre optic endoscopy. They were then interviewed at fortnightly interval for symptomatic assessment. At six weeks of treatment endoscopy was repeated. Ulcer healing was defined as complete disappearance of ulcers and erosions. It was done by the same investigator (SJZ) each time on the same patient. If the ulcer had healed at six weeks then such patients were put on cimetidine 400 mg nocte for another six weeks with a view to prevent recurrence of the ulcer and also to assess the efficacy of the maintenance dose and a third endoscopy was then performed. When the ulcer had not healed at six weeks Q.I.D. or B.I.D. regime was again repeated for further six weeks and then endoscopy was done to see the response.

Results

One hundred adults with confirmed duodenal ulcer were included in the study. The study was carried out on outpatients basis. Of 100 patients 90 were males and 10 females (M:F 9: 1) with their ages ranging from 18 years to 74 years (Mean age of 40.63 years) as shown in Fig.

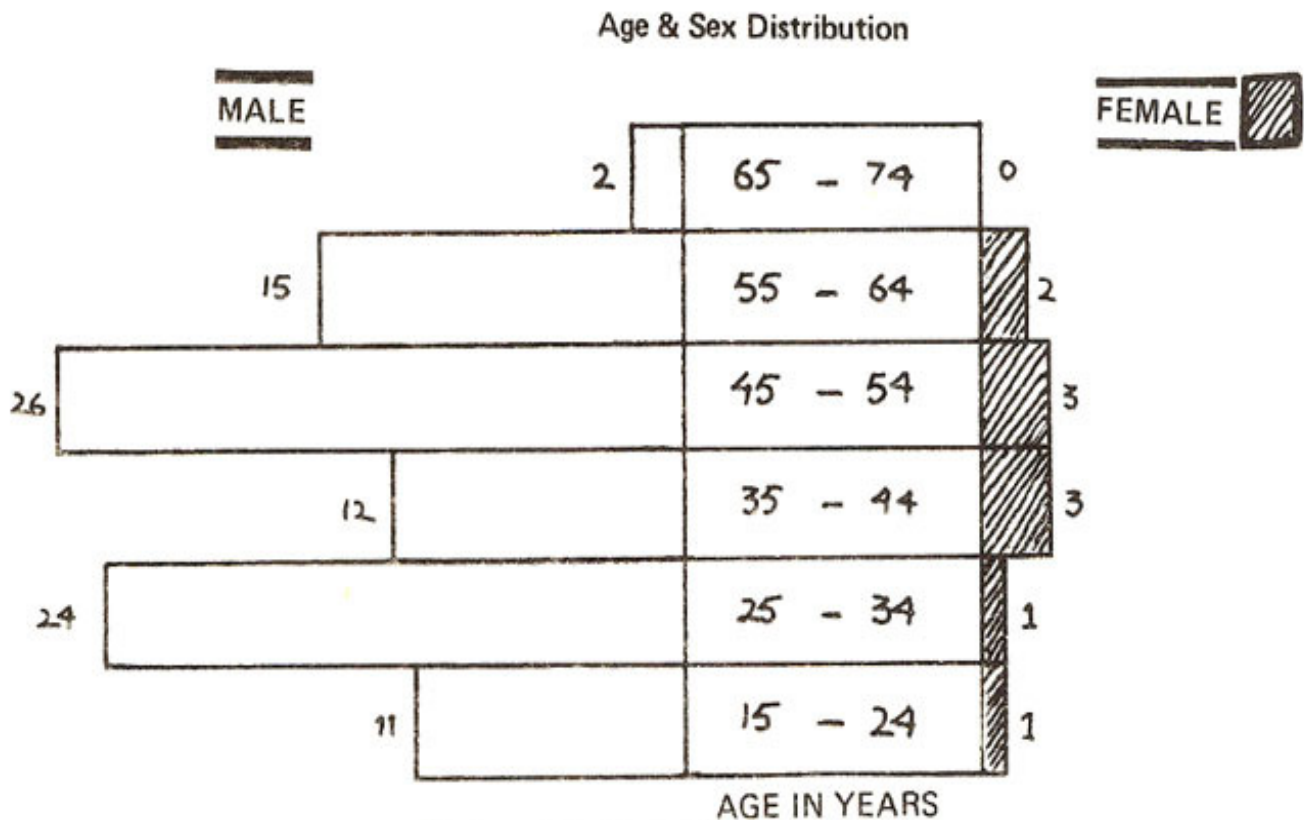


Fig. Age and Sex distribution.

Barium Meal was performed in forty seven patients and ulcer niche/deformed cap was demonstrable in 39 (83%) but X-rays were inconclusive in 12 patients. Endoscopy was done in all including those in whom radiology was inconclusive.

The symptoms of ulcer pain varied from under one year to 10 years. Fifty four patients gave history of

either malena or haematemesis or both in the past and 63 presented with haematemesis or malena or both.

Symptomatic relief to cimetidine therapy were graded as follows:

1. Excellent if patient become symptom free.
2. Good if symptoms were substantially reduced.
3. Poor - when there was no relief of symptoms.

There was excellent to good symptomatic relief following administration of the drug within two weeks of starting cimetidine in eighty patients while poor response in five patients (Table I).

Table 1 Symptomatic Relief.

Evaluation	No. of patients
Excellent	30
Good	50
Poor	5
Lost to follow up	15

Fifteen patients on Q.I.D. regimen were lost to follow up after entering into the trial for unexplained reasons. Eighty five patients thus completed six weeks of cimetidine therapy. At the end of six weeks 56 (91.8%) patients out of 61 patients had endoscopically proven healed ulcer on 1G/day Q.I.D. regime while on 800 mg B.I.D. regime 18 (75%) out of twenty four patients had healed ulcers. At the end of twelve weeks cimetidine healing rate were 98% and 83% respectively with Q.I.D. and B.I.D. regimen (Table II).

Table II
Results of Endoscopic Examination at 6 weeks.

Cimetidine dosage	No. of patients	6 weeks healed	12 weeks healed	not-healed
1G/day (Q.I.D.)	61	56(91.8%)	60(98.3%)	—
800 mg/day	24	18(75%)	20(83%)	4(17%)

In four patients on B.I.D. dosage healing was not achieved. They were referred to surgery. One patient died of associated renal disease therefore healing could not be further assessed.

Antacids were used only by 17 patients throughout the trial.

Apart from mild adverse reactions such as diarrhoea, headache and dizziness seen in four patients, cimetidine was well tolerated and no serious adverse reactions were recorded. No significant change was observed in the haematology and blood bio-chemistry at the end of the trial.

Discussion

The positive effect of cimetidine in the short term treatment of duodenal ulcer disease now seems to be without doubt and present study seems to substantiate the findings of other workers (Bardan et al., 1979; Bodemar et al., 1979).

It was interesting to note that radiology was inconclusive in twelve patients while endoscopy confirmed the presence of duodenal ulcer disease in them thus proving that endoscopic evaluation in the diagnosis is superior to radiology perhaps because of the fact that in most of the hospital and private X-ray centres barium studies are done by X-ray technicians without fluoroscopy. Similarly, in the assessment of healing of ulcer endoscopy is superior to radiology as it is difficult to see radiological evidence of healing in deformed duodenum. Symptomatic relief was excellent to good response in majority of the patients by end of six weeks cimetidine treatment. Antacid consumption was very low as compared to other reported series and our observations were similar to Gray et al. (1977) and Semak et al. (1977) that the consumption of antacid is considerably reduced in patients on cimetidine.

The healing rate of 92% following six weeks treatment with cimetidine 1G/day is better than the results from trials of similar methodology as reviewed by Bardhan (1978). The 75% healing rate on cimetidine 400 mg b.d. is similar to Q.I.D. regime as patient population was not strictly comparable. As expected the incidence of healing increased with the longer duration of treatment to cumulative proportions of 98% and 83% respectively at twelve weeks with both regimens.

Effective treatment for duodenal ulcer does not only include healing of the ulcer but prevention of relapse. It is now well established that cimetidine achieves a high rate of healing in a short period of time. The incidence of relapse is being studied currently and hence there is a lot of interest in long term cimetidine therapy in the hope that the rate of relapse could be controlled (Blackwood et al., 1978;

Gillespie et al., 1977). Bodemar and Walan (1978) have reported their experience on maintenance treatment in recurrent peptic ulcer and found that of the 32 patients receiving cimetidine for one year only six had recurrence as compared to 30 patients out of 36 on placebo. Similarly Gray et al. (1977) found that 80% of their patients on placebo suffered from recurrent duodenal ulceration as compared to 27% on low dose long term cimetidine therapy. The rate of recurrence after short term cimetidine treatment and the effect of long term maintenance therapy need further assessment and would be highly desirable.

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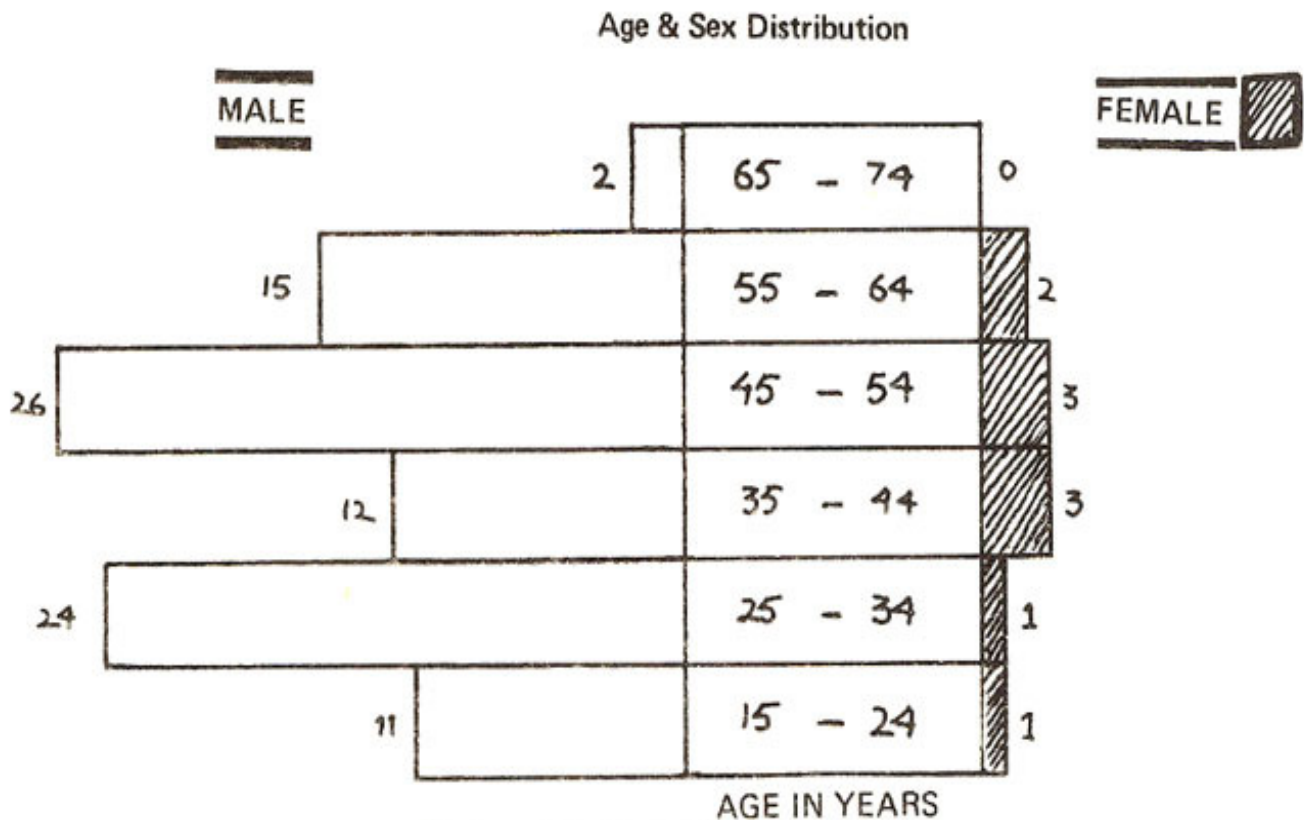


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