

Comparative Trial of Cimetidine 400 mg (BID) and 1G (QID) Conducted at Mayo Hospital, Lahore

Pages with reference to book, From 52 To 54

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Abstract

Forty patients with duodenal ulceration were treated with cimetidine for eight weeks, randomly allocated to a Q.I.D. (ig daily) or B.I.D. (800mg daily) regimen. Ten patients were lost to follow-up. Thirty patients completed eight weeks of treatment and 27 of these were symptom-free. Two patients on the B.I.D. and one patient on the Q.I.D. regimen failed to heal by eight weeks, though they had some improvement in symptoms and on endoscopy their ulcers were smaller. The drug was well tolerated and no serious side-effects were recorded. Routine laboratory tests revealed no persistent abnormalities. These findings are similar to the results of European studies and support the conclusion that the B.I.D. dosage of cimetidine is as effective as the Q.I.D. regimen in healing duodenal ulceration. Compliance Q.I.D. regimen, though the difference did not reach with B.I.D. dosage was better than that with the statistical significance (JPMA : 34: 52, 1984).

Introduction

The standard daily dosage of ig of cimetidine daily in divided doses (200mg three times daily with meals and 400 mg at bedtime) was established on the basis of the drug's plasma half-life and the flattening of the dose-response curve above ig daily (Pounder et al., 1975,1977). A 200 mg dose of cimetidine given with a meal was found to reduce gastric acid secretion in healthy subjects by about 60% during the two hours after administration (Pounder et al., 1976). Mean 24-hour intragastric hydrogen ion activity was reduced by 55% in duodenal ulcer with Q.I.D. dose (Pounder et al., 1975). Doubling the dose to 400mg Q.I.D. did not produce a much greater effect on daytime intragastric acidity, but did result in a more marked suppression of nocturnal acidity.

In healthy subjects, no significant difference was found in the average hourly reduction of gastric acidity over 24 hours between the standard ig/day dosage of cimetidine (200mg T.I.D. and 400mg at night) and 400mg 13.1.D. (Mills et al., 1982).

European studies have shown equivalent efficacy of the two dosage regimens in healing duodenal ulcers (Delattre, 1982). The present study was planned to compare healing of duodenal ulcers with the two dosage regimens in Pakistan.

Method

A total of 589 patients with epigastric pain, epigastric fullness, heartburn, nausea, haematemesis or anorexia and loss of weight were examined endoscopically. The patients were referred from all the general hospitals in Lahore and from the outpatient and emergency departments of the Mayo Hospital, Lahore. Forty patients were selected who had duodenal ulcers. The purpose of the study was discussed with them and their informed consent was obtained.

Each patient was interviewed, examined physically and a detailed clinical history was obtained. Before and at the end of the trial, haematological and biochemical tests were performed, including haemoglobin estimation, PCV, total and differential leucocyte count, total red cell count, blood urea, serum levels of creatinine, bilirubin, alkaline phosphatase and transaminases, urinalysis and a stool

occult blood test.

Duodenal ulceration was confirmed by clinical history, radiography and endoscopy. Pregnant and lactating patients were excluded.

Each patient was given detailed instructions about the use of the drug and a supply of antacids was provided to be taken when required to treat symptoms. A diary was also given to each patient so that they could record their symptoms and consumption of antacids or other drugs. A supply of cimetidine was provided each week and the patients were instructed to return any tablets remaining at the end of the week. They were also asked to report any untoward reactions.

Allocation to the Q.I.D. (1g/day) or B.I.D. (800mg/day) regimen of cimetidine was randomized.

Patients were re-endoscoped after four weeks and those who had not healed were examined again after eight weeks.

During treatment, patients were advised not to eat fried, fatty or spicy meals and to avoid analgesics for minor ailments.

Patients with severe haematemesis were initially given supportive treatment for excessive blood loss.

Intravenous cimetidine was included among the initial resuscitative measures.

Results

Of the 40 patients recruited, ten were lost to follow-up, leaving 30 who completed the trial. The male:female ratio was 3 : 1 and the mean age was 31.5 years. Seven patients had no relationship of pain to meals. The duration of symptoms was more than six months in 18 patients and less than six months in 22.

At four weeks, 12 out of 15 patients (80%) treated with the Q.I.D. regimen had healed ulcers, compared with seven of the 15 (46.7%) given the B.I.D. dosage (Table I).

Table I
Symptomatology.

	No. of patients
Haematemesis	3
Post prandial pain	30
Pain not related to food	7

Table II**Healing Rates.
(After four weeks)**

Total No. of Patients.	Ulcer completely healed	Ulcer not healed	Healing percentage.
Q.I.D. 15	12	3	80%
B.I.D. 15	7	8	46.7%

After Eight Weeks

Total No. of patients	Ulcer completely healed	Ulcer not healed	Healing percentage
Q.I.D. 15	14	1	93.3%
B.I.D. 15	13	2	86.7%

This difference was not statistically significant (X² test, p 0.1). At eight weeks, the figures had risen to 14 out of 15 (93.3%) and 13 out of 15 (86.7%) respectively. The three patients who remained unhealed did show a reduction in ulcer size by the end of the trial. Two patients who had not healed on the B.I.D. regimen were treated for another four weeks with the Q.I.D. dosage but still proved refractory and were subsequently referred for surgery. All the patients with bleeding ulcers responded well to treatment with either regimen.

Analysis of the results by stratifying according to age and smoking habits showed no significant difference in healing rates between the two regimens.

Symptomatic assessment (Table III)

Table III Symptomatic Assessment.

No. of weeks	No. of patients Q.I.D./B.I.D.	Symptomatic relief
1st week	30	10 Q.I.D. regime 7 B.I.D. regime
4th week	30	12 Q.I.D. regime 9 B.I.D. regime
8th week	30	14 Q.I.D. regime 13 B.I.D. regime

In 17 patients the duration of pain was over two hours and in 12 others it was up to one hour. Nocturnal pain was reported by seven patients. Three patients, who presented with haema. temesis, had no history of pain.

There was a marked improvement in symptoms within 48 hours with both regimens of cinietidine. The severity of pain was reduced and bloating and burning sensations had subsided by the end of the first week in ten out of 15 patients. At week four, complete relief of daytime pain and other symptoms was reported in 12 of the 15 patients treated with the Q.I.D. regimen and in seven of the 15 treated with the B.I.D. regimen. Complete relief from nocturnal pain was reported in 12/15 and 9/15 patients respectively.

In eight weeks complete relief of symptoms had been obtained in the 27 patients whose ulcers healed. In the other three (one in the Q.I.D. and two in the B.I.D. dosage groups), partial symptomatic improvement occurred.

Adverse reactions(Table IV)

Table IV
Adverse Reactions.

Number of patients reporting adverse reactions		Total patients	Percentage
Q.I.D.	None	15	
B.I.D.	1	15	3.33%

Both dosages of cimetidine were well tolerated, the only adverse reaction being mild diarrhoea, which did not necessitate discontinuation of treatment, in a patient in the B.I.D. dosage group. No abnormalities were noted in routine laboratory tests.

Compliance

Throughout the trial the patients were asked whether they had taken their doses at the correct times and whether any had been missed. Those on the B.I.D. regimen took all their doses correctly, while those on the Q.I.D. regimen who worked long hours occasionally missed daytime doses. Compliance was thus somewhat better with the B.I.D. dosage than with the Q.I.D. regimen.

Discussion

The results of the present study seem to substantiate the findings of other workers that cimetidine in a dosage of 400mg B.LD. is as effective in healing duodenal ulcers as the 1g/day regimen. Seven of the 15 patients treated with the B.I.D. dosage had healed ulcers at four weeks compared with 12 of the 15 receiving 1g/day, but this difference was not statistically significant and by eight weeks the healing rates were almost identical (13/15 and 14/15 respectively).

As might have been expected, patient compliance was somewhat better with the simpler B.I.D. dosage than with the Q.I.D. regimen. This fact together with the lower cost of the B.I.D. dosage make it an attractive alternative to the traditional Q.I.D. regime.

This study reaffirms the important place of cimetidine in the treatment of duodenal ulcer. It is well established that cimetidine in a Q.LD. dosage regimen achieves a high rate of healing in a short time (Bardan, 1978). The findings of this and other studies indicate that comparable results can be achieved with the simplified B.I.D. regimen (Delattre, 1982). Truly effective treatment includes not only healing of the ulcer but also prevention of relapse. There is now ample evidence that maintenance treatment with cimetidine at a reduced dosage of 400mg each night significantly reduces the rate of ulcer relapse (Bodemar, 1981).

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