Original Articles

ORAL CIMETIDINE IN DUODENAL ULCERATION

Haziq-ul-Yaqin and Nafisa Razvi

Abstract

Twenty-four patients with duodenal ulceration were treated with 1 G Cimetidine daily for six weeks. Two patients left the trial at the end of four weeks and were free of symptoms. Twenty-two patients completed six weeks of Cimetidine treatment and twenty of these were symptom free, one patient failed to improve and another had symptoms at the end of trial. The drug was well tolerated and no serious side effects were recorded. Routine laboratory tests revealed no persistant abnormalities. It is concluded that Cimetidine is effective in healing duodenal ulceration (JPMA, 29:184, 1979).

Introduction

Cimetidine, an H -receptor antagonist is known to reduce basal as well as meal stimulated gastric secretion in man (Henn et al., 1975; Pounder et al., 1975) and hence the drug has been used extensively in duodenal ulceration (Groake and Fitz Gerald, 1976; Pounder et al., 1975).

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

Material and Methods

Each patient was interviewed and a detailed clinical history was recorded and examined physically. Screening including haemoglobin estimation, PCV, total and differential leucocyte count, total red cell count, blood urea, serum creatinine, bilirubin, alkaline phosphatase, transaminases and urine analysis were carried out prior to trial and then at weekly interval throughout the period of trial.

The patients were investigated for ulcer dyspepsia and only those confirmed as duodenal ulceration were included in the study. The diagnosis of duodenal ulcer was based on clinical history, radiography and endoscopy. Patients were also referred by other hospitals and specialists. All the patients were able to

K. V. SITE Hospital, Manghopir Road, Karachi.

read or write and were included in the trial after full assurance was obtained that they will be able to complete the trial. An informed consent was obtained from each patient. Pregnant and lactating patients were excluded from the study. No restrictions were put on the diet, smoking and drinking.

Pentagastrin stimulated gastric analysis, x-ray chest, Barium meal x-rays and endoscopy were done prior to the end of the trial.

At the start of the treatment each patient was explained in detail about the use of drug and they were allowed to consume antacids (Gelusil) as and when required. A diary was given to each patient so that they could record their symptoms and consumption of antacids or any other drug. Weekly supply of drug was given with instructions to return at the end of each week. Cimetidine 1 G was given daily in the form of 200 mgm tablets in four doses (one tablet t.i.d. and 2 tablets at bedtime). Diary cards were returned and occurrence of ulcer pain during the preceding week was recorded. Patients were told to report any untoward reaction.

Results

Twenty-four adult patients with confirmed duodenal ulcer were included in the study between October, 1977 and July, 1978. Of these 24 patients, one also had a gastric ulcer. The study was carried out on an out-patient basis. Of the 24 patients 20 were males and four females with their ages ranging from 18 years to 52 years (Table I). The place of birth was recorded in each patient and is shown in Table II. Endoscopy was done in patients both prior to and at the end of the study (Table III). Barium meal studies were performed in all the 24 patients prior to trial and in 22 patients at the end of the study. Pentagastrin stimulated gastric analysis was carried out in patients before and at the end of the study and the results are shown in tables IV and V.

Table I: Distribution of Ulcer Patients by Age and Sex

Age in years	*Male*	*Female*	*Total*
15-24	5	2	7
25-34	4	1	5
35-44	8	1	9
45-54	3	—	3
Total:	20	4	24

Table II: Distribution of Patients by Place of Birth

Place of birth	*Number of cases*	*Percentage*
Karachi	1	4.17
Punjab	2	8.34
Gilgit	1	4.17
Hazara/Swat	3	12.50
South India	4	16.66
South West India	3	12.50
North India	5	20.83
Central India	1	4.17
Not recorded	4	16.66
Total:	24	100

Table III: Endoscopy

Pre-trial Endoscopy	*Post-trial Endoscopy*	*No. of patients*
Duodenal Ulcer	Healed	16
Duodenal Ulcer	Not healed	1
Duodenum not negotiated	Duodenum not negotiated	2
Ulcer	Left the trial at 4 weeks	1
Not done	Not done	4
Total		24

Table IV: Pre-Treatment (Gastric Analysis)

	Basal			*Post-Pentagastrin*		
	Male	*Female*	*Total*	*Male*	*Female*	*Total*
Volume (mls)	16.41 ± 1.66 (20)	22.45 ± 4.41 (4)	17.53 ± 1.62 (24)	27.02 ± 1.77 (20)	26.05 ± 2.45 (4)	26.94 ± 1.55 (24)
pH Value	2.51 ± 0.42 (20)	3.34 ± 1.70 (4)	2.63 ± 0.42 (24)	2.14 ± 0.22 (20)	1.59 ± 0.90 (4)	1.74 ± 0.16 (24)
Total Acidity (per hour)	10.58 ± 2.3 (20)	18.97 ± 0.13 (4)	11.63 ± 1.61 (24)	22.88 ± 2.12 (20)	24.01 ± 1.71 (4)	23.04 ± 2.56 (24)
Na^+ mEq/L	70.95 ± 3.20 (20)	81.72 ± 4.28 (4)	72.65 ± 2.93 (24)	37.23 ± 3.10 (20)	50.1 ± 4.12 (4)	39.13 ± 3.52 (24)
K^+ mEq/L	10.36 ± 0.9 (20)	12.32 ± 0.02 (4)	10.67 ± 0.56 (24)	11.06 ± 0.31 (20)	13.16 ± 0.42 (4)	11.37 ± 0.37 (24)

Mean ± S.E. of volume, pH, Total acidity Na^+ and K^+ of gastric secretion of basal and after Pentagastrin injection.

Table V: Post-Treatment

	Basal			Post-Pentagastrin		
	Male	*Female*	*Total*	*Male*	*Female*	*Total*
Volume (mls)	20.58 ± 2.01 (20)	21.59 ± 1.49 (4)	18.47 ± 1.31 (24)	26.45 ± 1.71 (20)	26.08 ± 1.69 (4)	23.38 ± 1.69 (24)
pH Value	2.45 ± 0.37 (20)	2.95 ± 0.90 (4)	2.55 ± 0.34 (24)	2.63 ± 0.71 (20)	1.65 ± 0.10 (4)	1.81 ± 0.18 (24)
Total Acidity per hour	12.40 ± 1.52 (20)	10.3 ± 0.76 (4)	12.07 ± 2.02 (24)	22.20 ± 3.10 (20)	20.96 ± 2.57 (4)	21.97 ± 2.31 (24)
Na^+ mEq/L	65.19 ± 3.2 (20)	80.13 ± 4.50 (4)	67.9 ± 2.31 (24)	34.8 ± 3.10 (20)	43.33 ± 2.10 (4)	36.37 ± 1.31 (24)
K^+ mEq/L	10.16 ± 0.32 (20)	10.7 ± 0.15 (4)	10.26 ± 0.19 (24)	9.92 ± 1.10 (20)	12.05 ± 0.91 (4)	10.45 ± 0.82 (24)

Mean + S.E. of volume, pH, Total acidity, Na^+ and K^+ of gastric secretion in basal and after Pentagastrin injection.

Two patients left the trial after four weeks Cimetidine therapy with a significant improvement as they had to leave town on account of their domestic problems. Twenty-two patients thus completed six weeks of Cimetidine therapy and the compliance was excellent.

The symptoms of ulcer pain varied from under one year to ten years (Table VI) and seven patients gave a positive history of either malaena or haemetemesis or both in the past. The number of relapses varied from one to several times. Antacids were used by all the patients prior to entering the trial. No significant change was observed in haematology and blood biochemistry at the end of the trial.

Cimetidine was tolerated well by patients and no serious adverse reactions were recorded and the drug was not discontinued in any patient. The mild adverse reactions were recorded in four patients and were transient headache, dizziness, diarrhoea and nausea and none of these patients required any specific treatment.

Antacids were used only by three patients throughout the trial.

At the end of six weeks treatment with Cimetidine, eighteen patients were free of symptoms, in four patients their symptoms had improved while no significant improvement occurred in two (Table VII).

Table VI: Duration of Symptoms in Years

Duration	*Male*	*Female*	*Total*
1 year	9	3	12
1-2 years	4	—	4
3-4 years	2	—	2
5-6 years	—	1	1
7-8 years	4	—	4
9-10 years	1	—	1
Total:	20	4	24

Table VII: Status After the Administration of Cimetidine

	Week-1	*Week-2*	*Week-3*	*Week-4*	*Week-5*	*Week-6*
Symptom-free			4	5	5	5
Improved					2	1
No significant improvement						2
Total:			4	5	7	8

Discussion

The present study seems to substantiate the findings of other workers that Cimetidine has a favourable effect on duodenal ulceration with a high rate of healing, quicker relief and low consumption of antacids.

Eight patients in this study had ulcer symptoms for over three years and would have been advised electric surgery, yet on Cimetidine treatment they seem to have obtained considerable relief. Similar results have been observed by Gillespie et al. (1977). The study was monitored throughout by haematological and biochemical blood analysis and no abnormalities were observed as has been reported by other workers (Semb et al., 1977; Gillespie et al., 1977).

At the end of three weeks Cimetidine treatment, four patients were free of symptoms while at four weeks another five patients became free of their pain. Thus at the end of four weeks 37.5 per cent were totally free of symptoms. A much higher percentage of healed ulcer has been reported by other workers at the end of three and four weeks (Gray et al., 1977; Peter et al., 1977).

In a study by Gray et al. (1977) at four weeks of Cimetidine therapy, 17 out of 20 patients had healed ulcer, while Peter et al. (1977) found that of their 15 patients, 11 had a healed ulcer at the end of 3 weeks. The reason for this difference might be due to a large number of patients with chronic duodenal ulcers in the present series. However, at the end of six weeks treatment 75 per cent patients were completely free of symptoms, 16.6 per cent had considerable improvement and 8.3 per cent had no improvement.

The consumption of antacids during the trial in this study was very low as compared to other reported series and only three patients had to take antacids during the initial weeks of Cimetidine therapy. Our observation is similar to Gray et al. (1977) and Semb et al. (1977) that the consumption of antacids is considerably reduced in patients on Cimetidine.

The Pentagastrin stimulated gastric secretory studies following Cimetidine therapy showed an insignificant decrease in volume, pH value and total acidity. The technique is already described (Razvi et al., 1978).

Radiology was done in all the patients before the trial and in 22 patients at the end of the trial as two patients left at the end of four weeks. Scarring of duodenal cap was noted in 20 patients as radiological evidence of healing is difficult to obtain in patients with deformed duodenum. Endoscopy is superior to radiology for assessment of healing.

Endoscopy was done before the start and at the end of six weeks of Cimetidine treatment. Endoscope could not be passed in two patients due to narrowing of duodenum and four patients refused examination and one patient left the trial at the end of four weeks without endoscopy. Of the 17 patients endoscoped 16 had a healed ulcer.

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 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 study, and would be highly desirable.

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References

Blackwood, W.S., Maudgal, D.P. and Northfield,

T.C. (1978) Prevention by bedtime Cimetidine on duodenal ulcer relapse. Lancet, 1:626.

Bodemar, G. and Walan, A. (1978) Maintenance treatment of recurrent peptic ulcer by Cimetidine. Lancet, 1:403.

Gillespie, G., Gray, G.R., Smith, I.S. et al. (1977) Short-term and maintenance Cimetidine treatment in severe duodenal ulceration. Proceedings of the Second International Symposium on Histamine H -receptor Antagonists. Excerpta Medica, 240-247.

Gray, G.R., McKenzie, I., Smith, I.S. et al. (1977) Oral Cimetidine in severe duodenal ulceration. A double blind controlled trial. Lancet, 1:4.

Gray, G.R., Smith, S., MacKenzie, S.I. and Gillespie, G. (1978) Long-term Cimetidine in the management of severe duodenal ulcer dyspepsia. Gastroenterology, 74:397.

Groake, J.E. and Fitz Gerald, O. (1976) Early clinical experience with Cimetidine in duodenal ulcer patients. Ir. J. Med. Sci., 145:172.

Henn, R.M., Isenberg, J.I., Maxwell, Y. and Sterdevant, R.A.L. (1975) Inhibition of gastric acid secretion by cimetidine in patients with duodenal ulcer. N. Engl. J. Med., 293:371.

Pounder, R.E., Williams, J.G., Milton-Thompson, G.J. et al. (1975) 24-hour control of intragastric acidity by cimetidine in duodenal-ulcer patients. Lancet, 2:1069.

Razvi, N., Yaqin, H., Baqai, M.U. et al. (1978) Pentagastrin Stimulated Gastric Analysis in Apparently Healthy Subjects. JPMA, 28:17.

Semb, L.S., Berstad, A., Myren, J. et al. (1977) A double blind multicentre comparative study of Cimetidine and Placebo in short-term treatment of Active duodenal ulceration. Proceedings of the Second International Symposium on Histamine H -receptor Antagonists. Excerpta Medica, 248-253.