THE USE OF TRIMIPRAMINE IN THE TREATMENT OF PEPTIC ULCER IN SINGAPORE

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SYNOPSIS

Forty-six patients with peptic ulcer were treated with trimipramine in an open study. Ulcer healing was assessed by endoscopy. At 6 weeks, 53% of gastric ulcer and 54% of duodenal ulcers had healed. All but one patient reported complete or partial relief of dyspepsia. Most patients developed drowiness but this was rarely severe. A controlled study to compare trimipramine against placebo or another agent of proven efficacy is required for formal evaluation of its ulcer healing properties.

INTRODUCTION

In recent years, several drugs have been shown to promote the healing of gastric and duodenal ulcers in outpatients. These include Cimetidine (1, 2), Ranitidine (3, 4), Colloidal Bismuth (5, 6), Carbenoxolone (7, 8), Sucrafate (9, 10) and Trimipramine (11, 12). However, all the cited work was carried out overseas. Little formal evaluation of anti-ulcer drugs had been carried out amongst Singapore or Malaysian patients. We report here an open study using Trimipramine in the treatment of gastric and duodenal ulcers in outpatients in Singapore.

MATERIALS AND METHODS

Forty-eight patients with peptic ulcer, proven on endoscopy, were entered into the study. Of these, 20 had gastric ulcer, 25 had duodenal ulcers and 3 patients had both gastric and duodenal ulcers. Forty-four patients (91%) had dyspepsia while 16 patients (33%) presented with upper gastrointestinal haemorrhage or iron-deficiency anaemia. The age, sex, length of history and other characteristics of the patients are shown in Table 1.

None of the patients had received any medication other than conventional dose antacids in the week prior to starting on the study. For the gastric ulcer patients, biopsies were carried out to exclude malignancy.

Within one week of the initial endoscopy, each patient was started on Trimipramine, 50 mg at night. The patients were reviewed after 3 weeks and enquiry was made regarding their dyspeptic symptoms and any side effects experienced. After 6 weeks (± one week) of treatment, repeat endoscopy was carried out to determine whether the ulcer had undergone complete healing. When a patient had more than one ulcer, he was considered to have healed only if every ulcer had undergone healing. All the endoscopies were carried out by one of us (JYK).

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Table 1: Patient Characteristics

	Gastric Ulcer	Duodenal Ulcer	Both Gastric And Duodenal Ulcer
Number	19	24	3
M : F	16 : 3	17 : 7	1 : 2
Age (mean ± SD)	48.1 ± 16.6)	38.3 ± 15.6	63+
Length of history (median years and range)	5(0-30)	3(0.3-20)	2(0-10)
Number (%) with dyspepsia	16(84)	24(100)	2(67)
Number (%) presenting with haemorrhage or anemia	9(47)	6(25)	1(33)
Smokers: Number (%)	8(42)	13(54)	0
Ulcer size (mean mm ± SD)	10 ± 6	10 ± 6	7+

+ **Number insufficient for analysis**

Two patients who did not complete protocol excluded

RESULTS

Two patients, one with gastric ulcer and the other with duodenal ulcer, were entered in the study but did not complete the protocol. Both withdrew due to severe drowsiness. One other patient who developed drowsiness on 50 mg nightly of Trimipramine was able to take 25 mg nightly for one week and then increased to 50 mg nightly for the next 5 weeks.

Excluding the two patients who withdrew, 13 out of the 24 duodenal ulcer patients healed completely at 6 weeks (54%). Of the gastric ulcer patients, 10 out of 19 had shown complete healing by the second endoscopy (53%). All 3 patients with both gastric and duodenal ulcers completely healed after 6 weeks of therapy (Table II).

Twenty-nine patients (63%) reported side-effects. Drowsiness occurred in 25 patients (54%) : dry mouth in 8 patients (17%) and constipation in 2 patients (4%). Although drowsiness was very common, it was usually mild and well tolerated, only 2 patients having to withdraw for this reason. One other patient, as described above, had to reduce his medication during the first week. Several patients welcomed the improved sleep they experienced while taking the drug.

Out of the 42 patients who had dyspepsia, all but one patient reported improvement of symptoms. In 23 patients, the relief of dyspepsia was complete (55%). In 19 patients (45%), the dyspepsia was improved but not completely abolished. Although the healed ulcer group amongst both the gastric and duodenal ulcer patients tended to be younger and to have smaller ulcers compared to the unhealed group, these differences were not statistically significant. Likewise, the smoking history, length of history and the site of ulceration (in the case of duodenal ulcers), did not appear to influence ulcer healing.

DISCUSSION

Trimipramine has previously been shown in formal controlled trials in Scandinavia to be superior to placebo in both gastric and duodenal ulcers (11, 12). In another trial, Cimetidine with antacids was compared to Trimipramine with antacids and both treatment were found to be equally effective.[13]

However, peptic ulcer patients from different populations behave differently. The incidence of duodenal ulcer healing after one course of placebo treatment, for example, varied from 19% — 60% in different series whereas between 52% — 93% of duodenal ulcer healed after a course of Cimetidine therapy. [1] Findings from one population cannot therefore necessarily be extrapolated to another. Very few formal studies on peptic ulcer therapy has been carried out in Singapore or Malaysia. Chelvam in Malaysia [14] used Cimetidine in the treatment of gastric and duodenal ulcers. At 6 weeks, 73% of the duodenal ulcer patients and 50% of the gastric ulcer patients healed. [14] These figures are comparable to those in the present study.

Open studies, however, have severe limitations. In particular, the incidence of ulcer healing on placebo is unknown. For definitive evaluation of any medication, a formal con-

Table 2: Incidence of ulcer healing at 6 weeks

	Gastric Ulcer	Duodenal Ulcer	Gastric And Duodenal Ulcer
Number	19	24	3
Number healed at 6 weeks	10	13	3
% healed	53	54	100

trolled trial comparing the drug to placebo is required. Our study, however, suggested that Trimipramine is well tolerated by our patients although healing rates achieved were on the low side. A controlled trial comparing Trimipramine against placebo or another agent of proven efficacy is required to formally assess its value.

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