Effect of treatment with cimetidine for one year on gastrin cell and parietal cell function and sensitivity to cimetidine in patients with duodenal or gastric ulcers

H. P. M. FESTEN M.D.
A. TANGERMAN Ph.D.

C. B. H. LAMERS M.D.
J. H. M. VAN TONGEREN M.D.

Department of Medicine, Division of Gastroenterology, St Radboud Hospital, Nijmegen, The Netherlands

Summary
Twenty-two duodenal and 16 gastric ulcer patients were treated with 400 mg cimetidine twice daily for one year after their ulcers had healed. No change in gastric acid secretion was observed before and after treatment in 20 duodenal and 13 gastric ulcer patients. Similarly, the inhibitory effect of 200 mg cimetidine on gastric acid secretion was unaltered in 11 duodenal and 6 gastric ulcer patients studied and cimetidine blood concentration were unchanged in 9 duodenal and 4 gastric ulcer patients after one year. In 7 duodenal and 6 gastric ulcer patients the serum gastrin response to a standard test meal before and after treatment was identical.

Introduction
Maintenance treatment with cimetidine in a low dose is effective in preventing duodenal ulcer relapse (Bodemar and Walan, 1978; Blackwood, Maudgal and Northfield, 1978; Gumand-Hoyer et al., 1978; Burland et al., 1978; Gray et al., 1978; Hetzel et al., 1978). In the prevention of gastric ulcer relapse cimetidine seems equally effective (Machell et al., 1979; Birger Jensen et al., 1979). Treatment with cimetidine for short periods seems to be safe, but after-effects of such treatment on parietal and gastrin producing cells may become overt only during long-term treatment. Furthermore, it has to be demonstrated that inhibition of gastric acid secretion by cimetidine does not change with time. Some of these aspects have been studied in duodenal ulcer patients. (Hetzel et al., 1978; Forrest et al., 1979; Spence et al., 1978a, b; Sewing et al., 1978; Bodemar et al., 1979). In gastric ulcer patients, however, no studies of this kind have yet been done. This study was undertaken to assess the effect of one year's continuous treatment with cimetidine on gastrin-cell function (as determined by postprandial serum gastrin levels) and on parietal cell function (as assessed by basal and pentagastrin-stimulated gastric acid secretion) in duodenal and gastric ulcer patients. The inhibition of gastric acid secretion by cimetidine was also studied, before and after one year's treatment.

Patients and methods
Thirty-eight peptic ulcer patients without prior gastric surgery were studied, 22 of whom had a duodenal and 16 a gastric ulcer. One duodenal ulcer and 7 gastric ulcer patients were females. The mean age in duodenal ulcer patients was 48 ± 4 years and in gastric ulcer patients, 51 ± 3 years. All patients had endoscopically assessed healed ulcers before the start of maintenance treatment. Treatment with 400 mg cimetidine after breakfast and 400 mg at bedtime was continued for one year. To test patient compliance, a qualitative check on cimetidine in a urine sample was performed at each bi-monthly follow-up visit. The detection of cimetidine in the urine was performed by thin layer chromatography (Smith, Kline and French Laboratories, England; personal communication).

Immediately before the start of cimetidine treatment, several tests were undertaken in a number of patients. These tests were repeated one year later, between 3 and 7 days after cimetidine had been stopped. At repeat tests for gastric acid secretion and serum gastrin, concomitant blood cimetidine concentrations were assessed: these were all below detection level (<0.05 μg/ml).

Tests performed:
Gastric analysis was done in 20 duodenal and 13 gastric ulcer patients. After an overnight fast, an orogastric tube was positioned according to the method described by Hector (1968). Four 15-min basal secretory collections were aspirated and subsequently 4 15-min samples were collected after i.m. injection of 6 μg/kg pentagastrin. Peak acid output was calculated as the sum of the 2 consecutive highest 15-min samples multiplied by 2. Hydrogen
cimetidine treatment of ulcers

Gastric acid secretion and its inhibition by cimetidine

There was no difference between the pre- and post-treatment data neither in duodenal nor in gastric ulcer patients (Figs 1(a) and 1(b)).

Blood cimetidine concentrations

There was no difference between the data of the duodenal and the gastric ulcer patients studied and so they were pooled. The mean cimetidine blood level between 60 and 135 min after oral medication with 200 mg before treatment was 0.83 ± 0.08 μg/ml and after one year 0.88 ± 0.08 μg/ml (n.s.). The mean peak blood concentrations were 1.05 ± 0.10 and 1.11 ± 0.10 μg/ml (n.s.) respectively.

Serum gastrin

In duodenal ulcer patients the fasting and meal-stimulated serum gastrin concentrations before and after one year’s treatment were not significantly different; the fasting concentrations being 42 ± 5 and 47 ± 5 pg/ml (n.s.) and the IGR 5.8 ± 0.8 and 6.1 ± 1.4 ng/ml at 120 min (n.s.) respectively. In gastric ulcer patients, the fasting serum gastrin concentration before treatment was 42 ± 7 pg/ml and after therapy 58 ± 11 pg/ml (n.s.). The IGRs were 6.4 ± 1.2 and 7.0 ± 1.3 ng/ml at 120 min (n.s.) (Fig. 2) respectively.

Discussion

The present study shows that one year’s treatment with cimetidine does not influence gastric acid secretion. Other investigators reported similar findings in duodenal ulcer patients (Bodemar and Walan, 1978; Forrest et al., 1979; Spence et al., 1978a). This study shows that gastric acid secretion in gastric ulcer patients is also unaltered. Whatever mechanism causes the relative hyposecretion of gastric acid in gastric ulcer patients, it was unchanged after one year’s treatment with cimetidine while the ulcer remained healed. The basal and post-prandial serum gastrin concentrations in duodenal and gastric ulcer patients were unaltered after one year’s treatment with cimetidine. Other reports on serum gastrin in duodenal ulcer patients after the long-term use of cimetidine have been conflicting (Forrest et al., 1979; Spence et al., 1978b; Sewing et al., 1979). There are no other reports on serum gastrin in gastric ulcer patients after the long-term use of cimetidine.

It might be assumed that possible after-effects of long-term cimetidine treatment on gastrin cell function and on parietal cell function will become manifest earlier in gastric ulcer patients than in duodenal ulcer patients owing to the significantly lower gastric acid secretion after cimetidine in this condition (Festen, Lamers and van Tongeren, 1978). Such an effect, however, was not demonstrated in this study.

Results

Patient compliance

No patient failed to attend any of the follow-up visits during maintenance treatment. Bi-monthly urine cimetidine checks were, with 14 exceptions (6%) in different patients, all positive.
Fig. 1(a) (20 duodenal ulcer patients)

Basal acid output (mmol H⁺/hr)

Maximal acid output (mmol H⁺/hr)

Peak acid output (mmol H⁺/hr)

after 200 mg cimetidine 

n=11

Fig. 1(b) (13 gastric ulcer patients)

Basal acid output (mmol H⁺/hr)

Maximal acid output (mmol H⁺/hr)

Peak acid output (mmol H⁺/hr)

after 200 mg cimetidine 

n=6

Fig. 1. Gastric acid secretion before and after 200 mg cimetidine (mmol H⁺/hr; mean±s.e. mean) and resulting percentage inhibition (mean±s.e. mean) before (□) and after (■) one year's treatment with cimetidine.
Cimetidine remained effective during one year's continuous treatment: blood concentrations of cimetidine and inhibition of gastric acid secretion were unchanged.

It is concluded that after one year's maintenance therapy with cimetidine in duodenal and gastric ulcer patients no rebound phenomena, or after-effects on gastric acid secretion, or serum gastrin concentrations were observed. The acid inhibitory effect of cimetidine did not change.

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References


