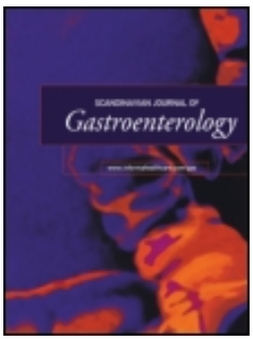

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Omeprazole: An Effective Drug for Zollinger-Ellison Syndrome

KE MCARTHUR, MJ COLLEN, JA CHERNER, JM HOWARD, PN MATON, RT JENSEN AND JD GARDNER
Digestive Diseases Branch, National Institutes of Health, Bethesda, Maryland, USA

Most patients with Zollinger-Ellison syndrome can be treated effectively with the histamine H_2-receptor antagonists cimetidine and ranitidine. To control gastric acid secretion, however, these drugs often have to be given in large doses at frequent intervals. Omeprazole inhibits gastric acid secretion by inhibiting the H^+K^+ATPase in the gastric parietal cell. Because omeprazole is a potent gastric antisecretory drug and has been shown to have a duration of action of up to 3 days in animals and humans, the present study was designed to evaluate the utility of this drug in the treatment of Zollinger-Ellison syndrome.

PATIENTS AND METHODS

Subjects for this study were 11 patients with Zollinger-Ellison syndrome (10 males, 1 female) who were representative of the larger group of 50 patients with this syndrome followed at the National Institutes of Health. All 11 patients had a positive serum gastrin response to infusion of secretin. Median basal acid output and maximal acid output were 44 mEq/hour (range 14–118 mEq/hour) and 53 mEq/hour (range 14–112 mEq/hour), respectively. The study protocol included four types of gastric secretory studies.

Acute effects

The acute effect of omeprazole, 60 mg, was examined in nine patients who had discontinued all antisecretory medication at least 24 hours earlier.

Maintenance dose

The maintenance dose of omeprazole was determined in all 11 patients. Patients took omeprazole once in the morning every 24 hours and gastric acid secretion was measured during the last hour before the next dose of medication. The maintenance dose was the minimal dose of drug needed to reduce gastric acid secretion to less than 10 mEq/hour during the last hour before the next dose of omeprazole. If gastric acid secretion was greater than 10 mEq/hour during the 24th hour after increasing the daily dose to 200 mg of omeprazole, the dose was divided and given every 12 hours.

Duration of action

The duration of action of omeprazole was examined in five patients by discontinuing omeprazole after several months of therapy and measuring gastric acid secretion at 8-hour intervals for 48 hours.

Long-term effectiveness

The long-term effectiveness and stability of maintenance dose requirements were examined in all patients by measuring gastric acid secretion during the last hour before the next dose, 1 week after starting omeprazole, at 3 weeks, at 2, 4, and 6 months and then at 3-month intervals.

The safety of omeprazole was assessed in all patients by measuring serum gastrin, thyroid functions, serum chemistry determinations, complete blood count, urinalysis and creatinine clearance. These tests were performed initially, at 1 and 3 weeks, 2, 4 and 6 months and then every 3 months. History and physical examination were performed initially, at 2, 4 and 6 months and then every 3 months. ECG, chest radiograph, upper gastrointestinal endoscopy and ophthalmological examination were performed initially and then every 6 months. There were no detectable side-effects and all examinations remained unchanged.

RESULTS

Maximal inhibition of gastric acid secretion occurred a mean of 4.7 hours after taking omeprazole (range 4–7 hours). The mean daily dose requirement for the 11 patients was 70 mg (range 20–160 mg). Ten patients required omeprazole once a day while one patient required omeprazole every 12 hours.

Gastric acid secretion was inhibited by more than 90% throughout the first 24 hours after omeprazole and by more than 50% throughout the 24–48 hour period after omeprazole. In follow-up studies, omeprazole has continued to control gastric acid secretion in all 11 patients.

All of the 11 patients had been treated with histamine H_2-receptor antagonists before omeprazole. Each patient required omeprazole less frequently (1–2 times/day) than cimetidine or ranitidine (3–6 times/day) and took fewer omeprazole tablets a day (1–6 tablets) than cimetidine or ranitidine ones (4–60 tablets).

CONCLUSION

These findings indicate that omeprazole is effective in the treatment of patients with Zollinger-Ellison syndrome, and offers a major improvement in convenience of therapy over the histamine H_2-receptor antagonists. If omeprazole proves safe for long-term therapy in humans, it promises to become the drug of choice for patients with Zollinger-Ellison syndrome.