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Omeprazole, a Gastric 'Proton Pump Inhibitor': Lack of Effect on Renal Handling of Electrolytes and Urinary Acidification

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Summary. Omeprazole has previously been shown to be a potent inhibitor of gastric acid secretion in man. In a new study, oral omeprazole 60 mg/day was given to 8 healthy male subjects for 8 days. The daily urinary electrolyte output and urine pH in response to ammonium chloride were not significantly altered. This provides further support for the specificity of its action on gastric acid secretion.

Key words: omeprazole; H^+/K^+-ATPase, ammonium chloride, urinary acidification, gastric acid secretion inhibitor, renal electrolyte excretion

Omeprazole, a substituted benzimidazole, causes dose-dependent inhibition of gastric acid secretion in animals and man [1, 2, 3]. It does not act as an antagonist of cholinergic or histamine receptors, but does appear to be a non-competitive inhibitor of H^+/K^+-ATPase in parietal cells [4].

Although the mode of action of omeprazole has been claimed to be highly specific and limited to the parietal cell, it is important to demonstrate that it does not interfere with H^+ handling by the kidney, and thus with renal electrolyte turnover and urinary acidification.

Materials and Methods

Eight healthy male subjects (mean age 25, range 19–29 years) gave their informed, written consent to the study, which was approved by the Research and Ethical Committee of the Greater Glasgow Health Board, Northern District. Prior to the study, each subject collected a 24 h urine sample for electrolyte measurements. Three of the subjects were given dietary advice to try to bring the 24 h urinary sodium output into the range of 130–180 mmol, and the 24 h urinary potassium output within the range 50–80 mmol.

Each subject received placebo and omeprazole 60 mg daily for 8 days according to a randomised double blind crossover design. The treatment periods were separated by at least 7 days. 24 h urine collections and measurements of serum electrolytes were made on the sixth day of each treatment period. Urinary acidification in response to ammonium chloride was measured at the end of each treatment period. In the test of urinary acidification, subjects were given placebo or omeprazole capsules following an overnight fast. Two hours later they were given oral ammonium chloride 100 mg/kg body weight in gelatin capsules. Following the ammonium chloride, subjects were allowed to take fluids "ad libitum", and urinary pH was measured at 2,4 and 6 h.

Statistical comparisons were made with Wilcoxon's signed rank test for paired data, and by repeated measures analysis of variance where appropriate. Data are presented as mean ± SEM.

Results

There were no significant differences in serum electrolytes or urinary electrolyte excretion following omeprazole or placebo (Table 1).

Three subjects were unable to complete both ammonium chloride tests because of nausea and vomiting. Of the 5 who successfully completed both tests, all attained a urine pH of 5.3 or less at some time within the 6 h period. Mean urinary pH measured 6 h after ammonium chloride was 4.96 after omeprazole and 5.02 after placebo. Repeated measures anal-

Table 1. Urine pH and urine and serum electrolytes following omeprazole and placebo: mean ± SEM; $n = 8$

	Omeprazole	Placebo	P.
Urine pH	6.23 ± 0.18	6.41 ± 0.10	N.S.
Na^+ output [mmol/24 h]	146 ± 12.9	150 ± 25.1	N.S.
K^+ output [mmol/24 h]	51.8 ± 5.0	52.5 ± 8.8	N.S.
Cl^- output [mmol/24 h]	156 ± 12.6	197 ± 25.9	N.S.
Serum Na^+ [mmol/l]	142 ± 0.6	141 ± 0.7	N.S.
Serum K^+ [mmol/l]	4.16 ± 0.16	4.06 ± 0.08	N.S.
Serum Cl^- [mmol/l]	104 ± 1.0	105 ± 0.7	N.S.
Serum HCO_3^- [mmol/l]	26.0 ± 0.5	25.1 ± 0.6	N.S.

ysis of analysis of variance did not show any difference in the urine pH response following omeprazole.

Apart from nausea related to ammonium chloride ingestion, none of the subjects reported any adverse effect, either spontaneously or on direct questioning during omeprazole treatment. There was no significant alteration in biochemical or haematological indices in any subject.

Discussion

In a previous study [3], a single oral dose of 60 mg omeprazole was shown to reduce basal acid output by 91.7% and pentagastrin-stimulated acid output by 95.3%. Following 7 days of this treatment both were inhibited by about 99%. Secretion of pepsin was not significantly altered, however, suggesting that omeprazole had a selective effect on acid secretion. This would be in accordance with its proposed mode of action on H^+/K^+ ATPase.

In the present study no effect of omeprazole on renal tubular handling of acid could be demonstrated. Although only 5 of the subjects could tolerate both ammonium chloride tests, all achieved a urine pH of 5.3 or less at some time in the 6 h after its ingestion, indicating a normal response [5].

The H^+/K^+-ATPase enzyme has not been identified in renal tissue. In animal studies [6] an antibody raised to this enzyme cross-reacted with gastric fundus and the thyroid, and weakly with the thymus. As there was no demonstrable effect on renal electrolyte excretion or renal acid handling in the present study, it is considered that this is further evidence of the specificity of action of omeprazole on parietal cells.

The lack of side effects, or of any alteration in serum electrolyte concentrations is consistent with the findings in the previous study [3]. In trials of omeprazole in the treatment of duodenal ulcer a healing rate of 93% after 4 weeks has been reported [7].

Thus, omeprazole may be a useful agent in peptic ulcer disease. It is a potent inhibitor of gastric acid secretion, without any demonstrable effect on the renal handling of acid.

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