Effect of omeprazole on plasma zinc levels after oral zinc administration

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Background: The intestines are the major site of zinc absorption and excretion. Reduced gastric acid secretion and elevated gastric pH is an important factor affecting intestinal mineral absorption. Methods: Gastric pH and volume, and basal and maximal acid outputs were measured in 14 healthy volunteers. Plasma zinc levels were then measured at baseline and 1, 2, 3 and 4 hours after oral administration of 300 mg zinc sulfate. The experiment was repeated after omeprazole administration (60 mg/day orally) for 7 days. Results: Omeprazole administration significantly increased fasting gastric pH (5.5 versus 2.4; p<0.001). Mean basal gastric acid output (1.6 vs 8.0 mEq/h; p<0.001) and maximal acid output (20.9 vs 105.6 mEq/h; p<0.001) decreased after omeprazole administration. Zinc absorption decreased after omeprazole administration (141 [34] mg/Dl/h) compared with pre-omeprazole values (245 [35]; p<0.01). Conclusion: Suppression of gastric acid secretion by omeprazole reduces intestinal absorption of zinc. [Indian J Gastroenterol 2002;21:216-218]

Key words: Omeprazole, zinc absorption

Zinc is an essential trace element for the human body, and is involved in many important body functions, including growth and development. The intestines are the major site of zinc absorption and excretion. Various factors influence absorption, including the amount of gastric acid secretion and the gastric pH.

Reduced acid secretion in humans has been associated with inhibition of intestinal absorption of iron and calcium. However, there are conflicting reports on the effect of hypochlorhydria on intestinal zinc absorption.6,7,8 We studied whether hypochlorhydria induced by the proton pump inhibitor omeprazole affects intestinal zinc absorption.

Methods

Fourteen healthy volunteers (aged 19-34 years; 8 women) participated in the study. The purpose of the study, its nature and the possibility of unpleasant effects of zinc sulfate and omeprazole were explained to them. There was no ethics committee in the university during the time of the study; all individuals gave informed consent to participate in the study, which was conducted according to the Helsinki Agreement. Before the study, all volunteers underwent physical, laboratory and upper abdominal ultrasonographic examination and esophagogastroscopey. Patients with organic disease, those taking non-steroid anti-inflammatory drugs, and those positive for Helicobacter pylori by urea breath test (AP2003 Mass Spectrometer INF1; Bochum, Germany) were excluded. Alcohol consumption was not allowed during the study period.

Following overnight fast, gastric juice was aspirated with a nasogastric tube inserted into the most dependent part of the stomach. Gastric juice pH was recorded using a ion-selective pH meter (Orion 920 A; Orion Research, Beverly, MA, USA). Basal acid output and maximal acid output in response to 6 mg/kg pentagastrin subcutaneously (Peptavlon; Zeneca, Cedex, France) were measured by aspirating the gastric contents for four consecutive 15-minute periods.

Zinc sulfate powder 300 mg (ZnSO₄·7H₂O; Sigma, Deisenhofen, Germany), equivalent to 68 mg of elemental zinc, was dissolved in 200 mL of physiological saline solution, and administered orally. Plasma zinc levels were measured at baseline and 1, 2, 3 and 4 hours after administration of zinc sulfate.9 Subjects were allowed only water during the test. Plasma zinc was estimated using inductively coupled plasma atomic emission spectrophotometer (ICP-AES Iy-24 Sequential Sperctrophotomer; Yobin Yvon, France).11 The experiment was repeated after 7 days of administration of omeprazole, 60 mg/day orally.

Statistical analysis

Areas under the serum concentration curves (AUCs) were calculated by trapezoidal rule during a 4-hour period, and the relative areas were obtained by subtracting basal values.

Significant statistical comparison was calculated with SPSS 9 software program (SPSS Inc. Chicago, IL, USA). To analyze the differences in the overall levels of plasma zinc levels and acid outputs before and after omeprazole treatment, a hierarchic multiple comparison procedure was done with Kruskal-Wallis one-way ANOVA test. This test compares three or more samples to determine if they came from similar populations. In case of significant differences, pair-wise comparisons were done using the
Figure 1

Fig 1: Effect of omeprazole treatment on plasma zinc concentration after oral administration of 220 mg zinc sulfate (values as mean [SD])

Bonferroni test. The effect of basal and maximal acid outputs on plasma zinc concentrations was evaluated by analysis of variance and regression analysis. To measure the linear relationship between two variables, Spearman's non-parametric correlation coefficients were calculated.

Results

Fasting gastric pH increased significantly after omeprazole therapy (5.5 vs 2.4; p<0.001). Mean basal gastric acid output (1.6 vs 8.0 mEq/h; p<0.001) and maximal acid output (20.6 vs 106.6 mEq/h; p<0.001) also fell after omeprazole administration.

Baseline plasma levels of zinc were not affected by the 7-day omeprazole administration (Fig 1). Subsequent mean plasma zinc levels were low when compared with pre-omeprazole levels, the lowest being at 3 hours. Significant reduction in AUC for zinc was evident after
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omeprazole (141 [34] mg/dL/h; p<0.01) as compared to the pre-omeprazole value (245 [35] mg/dL/h).

Positive correlation was observed between basal acid output and maximal acid output before and after omeprazole administration (r=0.694, p<0.01; r=0.549, p<0.05, respectively). Significant correlation was also found between plasma zinc concentration at 4 hours after administration, and basal and maximal acid outputs before and after omeprazole administration (Figs 2 and 3).

Discussion

Up to 70% of ingested zinc is absorbed in the proximal small intestine.2 Zinc absorption is influenced by various factors, including the form in which it is ingested,13 presence of other substances,14 and total body zinc pool.15 As in the case of iron and calcium, gastric pH also influences the passage of zinc through the intestinal cells by altering the ionic stage of the metal, the chemical structure of the ligands, or the enterocyte brush border membrane permeability.16 Stumilo et al17 showed that pharmacologic inhibition of gastric acid secretion induced a significant reduction in zinc absorption in healthy people. However, other authors have shown no direct effect of hyperchlorhydria on zinc absorption.7,8 We found that gastric acid secretion plays an important role in regulation of zinc absorption.

The reduced plasma levels of zinc after omeprazole administration could be attributed to change in the ionic stage of the zinc or to variations in the chemical and physical membrane features of the enterocytes. At pH 2, zinc is not bound to proteins with a molecular weight more than 10,000. As the pH increases, the solubility of zinc declines rapidly.17 At pH above 3, zinc may form large precipitates that inhibit its subsequent absorption in the small intestine. However, no studies have been published on clinically evident zinc deficiency during omeprazole therapy in man.

Thus, decreased gastric acid secretion by short-term omeprazole treatment decreases zinc absorption and may increase the risk for developing zinc deficiency due to mineral malabsorption.

References


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