

The effect of histamine H₂-receptor blockade with metiamide on serum gastrin levels in man

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SUMMARY Metiamide, an histamine H₂-receptor antagonist which inhibits gastric acid secretion, does not lower basal serum gastrin concentration in man. Serum gastrin responses after stimulation by food were marginally higher when the stimulus of food was preceded by metiamide.

Histamine H₂-receptor antagonists (Black, Duncan, Durant, Ganellin, and Parsons, 1972) inhibit basal (Milton-Thompson, Williams, Jenkins, and Misiewicz, 1974; Thjodleifsson and Wormsley, 1974) and stimulated (Wyllie, Hesselbo, and Black, 1972) human gastric acid secretion. Unlike certain hormonal inhibitors of gastric acid secretion, eg, secretin (Hansky, Soveny, and Korman, 1971) and glucagon (Hansky, Soveny, and Korman, 1973; Becker, Reeder, and Thompson, 1973), the H₂-receptor antagonists, burimamide and metiamide, do not depress basal (Barbezat, Daniel, Bank, Grant, and Vinik, 1974) or food-stimulated (Konturek, Tasler, Obtulowicz, and Rehfeld, 1974) serum gastrin levels

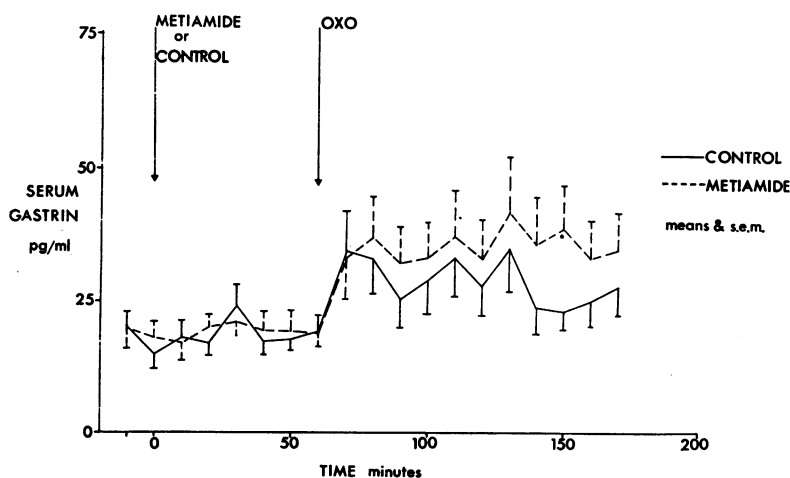
in dogs. This study was performed to investigate the effect of oral metiamide on basal and food-stimulated serum gastrin levels in man.

Methods

Studies were performed on 10 healthy volunteers 17-35 years old (mean 22.7 years). After a 10-hour overnight fast 5 ml blood was taken from a forearm vein using a thin-walled siliconized needle which was left *in situ* for the remainder of the study. Ten minutes later, after drawing another blood sample, 200 mg metiamide, a dose shown to produce significant inhibition of pentagastrin-stimulated gastric acid secretion in man (Barbezat, Bank, Clain, Novis, and Marks, 1974) followed immediately by 100 ml tap water, was given orally to five subjects. The other five subjects were given water only. One

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hour later, each subject drank a solution of warm meat extract (Oxo, four cubes in 150 ml water). Blood was taken every 10 minutes throughout the test. Studies were repeated on the following day. Subjects who received only water on the first day were given metiamide on the second day and vice versa. Serum was separated by centrifugation and stored at -20°C for later estimation of gastrin levels by radioimmunoassay.

Results

Mean basal serum gastrin levels were similar on both control and test days (17.9 and 18.4 pg/ml respectively). In the first hour after oral metiamide basal serum gastrin levels remained unchanged. After Oxo subjects who received metiamide had consistently higher serum gastrin concentrations than controls. Using Student's test for paired values, this difference only reached statistical significance at 150 minutes ($P < 0.05$).

Discussion

As in the dog, metiamide does not depress serum gastrin levels in man. It could be claimed that one hour is too short a time to judge its effect on basal serum gastrin concentration, but previous studies have shown therapeutic blood levels of metiamide one hour after the oral ingestion of a 200 mg dose. It is also difficult to detect a lowering of basal gastrin concentrations when these are at the lower levels of sensitivity of the immunoassay. Serum gastrin levels were, however, consistently raised after oral Oxo, but this increase was greater in subjects who had received metiamide. Similarly, patients given intravenous atropine before a test meal have previously been shown to produce greater increments in serum gastrin concentration than those receiving the test meal alone (Walsh, Yalow, and Berson, 1971). This is therefore a non-specific response to certain inhibitors of gastric acid secretion.

Since performing this study, two reports have been received of reversible granulocyte depression in patients who were taking metiamide. This drug was used in an open clinical trial in 10 patients in our unit, but no adverse reactions were detected despite weekly haematological and biochemical monitoring. As a precautionary measure the drug has been temporarily withdrawn from clinical use in South Africa.

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