Colonic Inhibition of Gastric Secretion in Man


The effect of colonic infusion of various solutions on submaximal pentagastrin-stimulated gastric secretion was determined in healthy volunteers. Hypertonic (823 mOsm/kg) glucose, mannitol, and saline, and also isotonic glucose significantly induced a marked and sustained inhibition of gastric acid secretion of 74%, 66%, 79%, and 54%, respectively. A similar degree of inhibition was obtained for pepsin secretion with hypertonic glucose and mannitol. Isotonic triglycerides and isotonic saline solutions had no significant effect on gastric acid secretion. Hypertonic glucose, mannitol, and saline infusions significantly increased plasma concentrations of enteroglucagon, whereas other solutions had no effect. No correlation, however, was found between the percentage rise of enteroglucagon and the percentage inhibition of gastric secretion obtained from any of the three hypertonic solutions. The physiological significance of these findings remains to be established.

During the last few years many studies have been involved in the demonstration of an intestinal regulation of gastric secretion (reviewed by 1). Nearly all of them have been concerned with the small intestine, and the role of the colon has not been studied in man. However, the colonic mucosa contains several types of endocrine cells (2-4), the hormonal product of some of them such as enteroglucagon (5, 6) having as yet unknown effects. The purpose of the present study was to determine the effect of different intraluminal colonic stimuli (glucose, triglycerides, osmolarity, distension) on pentagastrin-stimulated gastric secretion in man. Changes in plasma levels of gastrointestinal hormones induced by these stimuli were also assessed and correlated with those of gastric secretion.

MATERIALS AND METHODS

Sixteen healthy volunteers, 10 males and 6 females, aged 19–31 years, participated in these studies after giving informed consent.

Tubes, Gastric and Colonic Stimulations. Gastric secretion was collected via a double-lumen nasogastric tube (Salem sump tube No. 16). In order to assess gastric juice recovery, polyethylene glycol 4000 (PEG) solution (50 g in 0.13 mol/liter saline) was perfused at a constant rate of 0.2 ml/min by means of an additional thin tube cemented to the Salem sump tube placed 5–10 cm below the cardia. A 5-lumen tube was used for the colonic infusion. It consisted of a mercury-air bag at the end of a tube, to which were cemented four radiopaque thinner tubes, each terminating 25 cm shorter than the next.

Gastric secretion was stimulated by pentagastrin (Pep-tavlon) by a constant intravenous infusion at the submaximal dose of 0.1 μg/kg/hr. The colonic stimuli were performed by infusing solutions into the colon at a constant rate of 20 ml/min. Hypertonic glucose (400 ml at 823 mOsm/kg) was perfused first. It was found to be a potent inhibitor of gastric secretion. The effects of the glucose and of the hypertonicity were therefore separated (1) by infusing an identical glucose load in an isotonic solution, ie, 1200 ml at 300 mOsm/kg; and (2) by infusing identical...
volumes of both equimolar hypertonic mannitol and hypertonic saline, ie. 400 ml at 823 mOsm/kg. Furthermore, the possibility that the effect observed with various solutions could be due merely to colonic distension was investigated. This distension resulted from both the volume infused and, for the hypertonic solutions, the fluid drawn into colonic lumen by the osmotic gradient. The effect of the 400 ml of hypertonic saline was therefore compared with that of 1200 ml of isotonic saline, this latter volume corresponding to the theoretical maximal distension induced by the hypertonic saline. The effect of emulsified isotonic triglycerides (400 ml of Intralipid® at 300 mOsm/kg) was also tested. Finally, we performed control gastric secretion studies without colonic perfusion (nonperfusion studies) to evaluate the possible fade in the secretory response of the stomach under the prolonged pentagastrin infusion and assess variability with time.

**Day 1 Procedure.** The colonic tube was swallowed by the fasting volunteer who was thereafter allowed to eat normally. Tube progression was checked fluoroscopically at intervals. When the mercury bag reached the duodenum, it was inflated with air to accelerate its progression, and the balloon was deflated when the bag reached the colon (within 24 hr of ingestion in every case).

**Procedure on Days 2 and 3.** The subject was studied on each day following an overnight fast and maintained a semireclined position throughout. Colonic infusion was performed via the thin tube whose tip lay nearest the hepatic flexure on fluoroscopy. The gastric tube was positioned so that its tip lay in the proximal antrum. Pentagastrin and PEG infusions and gastric aspiration were then initiated, and continued throughout the study. Gastric juice recovered during the first 60 min was discarded, then it was collected every 30 min during a 2-hr control period followed by a 4- to 6-hr test period starting from the beginning of the various colonic instillations. The gastric tube was withdrawn at the end of each study day. Blood samples were collected hourly from the beginning of the control period to the end of the study.

The volunteers were separated into four groups of four subjects each. The subjects who received on days 2 and 3, in a randomized order, hypertonic glucose and hypertonic mannitol formed group 1; hypertonic glucose and isotonic mannitol, group 2; hypertonic saline and isotonic triglycerides, group 3; isotonic saline and noncolonic infusion, group 4.

**Analytical Methods.** Volume, hydrogen ion concentration (by titration to pH 7), pepsin concentration (7), PEG [by the turbidimetric method of Hyden (8)] and osmolality (Fiske osmometer) were determined in each gastric juice sample. Hematocrit and blood glucose were measured in each blood sample.

 Plasma levels of gut hormones were measured by radioimmunoassay using conventional techniques in each hourly blood sample. The assays employed antisera to synthetic human gastrin I (9), ovine somatostatin, natural human pancreatic polypeptide (10), natural porcine motilin (11), gastric inhibitory polypeptide (12), vasoactive intestinal polypeptide (13), total and pancreatic glucagon (14, 15), and natural bovine insulin (Wellcome, UK) and neurotensin (16). The assays could detect the following changes in individual, adjacent unextracted plasma samples with 95% confidence: gastrin 2 pmol/liter, somatostatin, 0.5 pmol/liter, pancreatic polypeptide 4 pmol/liter, gastric inhibitory peptide 3 pmol/liter, vasoactive intestinal polypeptide 1.5 pmol/liter, pancreatic glucagon 2 pmol/liter, enteroglucagon 8 pmol/liter, insulin 6 pmol/liter, and neurotensin 5 pmol/liter. No significant cross-reaction was detectable between any of the peptides assayed, with the exception of enteroglucagon which was measured by subtracting pancreatic glucagon from total glucagon (15). Serotonin plasma concentrations were also determined by a spectrofluorometric method (17) before and after the colonic infusion of the three hypertonic solutions.

**Calculations and Statistical Analysis.** The volume of gastric secretion recovered during the control and test periods was corrected using the percentage of PEG recovery during this time. It was assumed that the percentage loss of gastric juice and PEG via the pylorus was identical. The percentage inhibition of gastric acid and pepsin concentration and output induced by the colonic stimulation was calculated by subtracting the mean concentrations and outputs during the test period (mean of 4 hr) from the mean of the control period (mean of 2 hr). Results obtained with the nonperfusion studies were expressed in the same way, ie, test period versus control period. All data are given as mean ± SEM.

Three kinds of statistical comparisons were performed. First, the absolute difference obtained between the test period and the control period was compared by the paired t test for each set of four experiments performed with a given solution. Second, the percent change observed with the various solutions was compared either by the paired or the unpaired Student’s t test. Third, for hypertonic saline and isotonic saline sets of experiments, the acid output found during each 30-min collection period was compared to that obtained during the corresponding collection period with the nonperfusion studies using the paired t test.

Mean plasma hormone levels obtained during the control period and the test period were also compared by the paired t test. Furthermore for the hypertonic glucose, mannitol, and saline experiments mean levels at each individual time of sampling were compared by the Student’s paired or unpaired t test.

**RESULTS**

**Gastric Secretion.** Good PEG recovery was observed with no significant difference between the control and test period; the mean osmolalities of the gastric juice samples obtained during the two periods were closely similar (Table 1). Mean acid outputs during the control period of all experiments, on days 2 and 3 were 17 ± 2 and 16 ± 2 mEq/hr, respectively; the difference was not statistically significant. In some subjects, diarrhea occurred after the end of the colonic infusion. This occurred in all subjects after hypertonic glucose, in three out of four subjects after hypertonic mannitol, two out of