Relationship Between Small Bowel Transit Time and Absorption of a Solid Meal
Influence of Metoclopramide, Magnesium Sulfate, and Lactulose

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The times taken for a radiolabeled solid meal to empty from the stomach and terminal ileum and the absorption of the components of that meal were measured in 14 patients with terminal ileostomies under control conditions and after administration of either lactulose (40 g) or metoclopramide (20 mg tds), or magnesium sulfate (0.1 g/kg body weight). Absorption of each of the components of the meal was determined by chemical analysis of the ileostomy effluent. The radioisotope proved an excellent marker for the delivery of fat, protein, and carbohydrate residues. All three agents significantly reduced the time taken for the meal to empty from the ileum. This was associated with significant reductions in the absorption of fat, carbohydrate, protein, water, and electrolytes in the case of lactulose and magnesium sulfate. Although metoclopramide reduced transit time to the same degree as the other agents, its effect on absorption of fat, fluid, and electrolytes was much less, and absorption of protein and carbohydrate was unaffected. We therefore conclude that, although agents that accelerate postprandial transit of a meal may diminish absorption of the components of that meal in the small bowel, the extent to which this occurs cannot be predicted by a knowledge of transit kinetics alone and depends on the means by which transit is altered. The action of lactulose on the small intestine causes fluid and fat losses, sufficient to result in diarrhea and steatorrhea in a normal subject.

The degree of absorption of nutrients from the human small intestine is thought to be related to the efficiency of the digestive and epithelial transport mechanisms and the area of the intestinal mucosa presented to the luminal contents. However, studies in patients with diarrhea have suggested that rapid transit of food through the small intestine may also limit absorption by reducing the time that food remains in contact with the absorptive epithelium (1). We have investigated this possibility by studying the effect of three agents which reduce small bowel transit time by different mechanisms on the absorption of the components of a solid test meal in 14 healthy volunteers equipped with a terminal ileostomy.

MATERIALS AND METHODS

Subjects. Studies were carried out on 14 volunteers (4 male, 10 female; aged between 28 and 76 years), each of whom had been equipped with a terminal ileostomy for ulcerative colitis for at least nine months. All of the subjects were otherwise healthy and had normally functioning ileostomies. Fourteen healthy volunteers, who did not have ileostomies, were also studied (4 male, 10
female; aged between 18 and 71 years). Each subject gave written, informed consent for the study to be carried out and the protocol was approved by the Ethical Subcommittee of the Sheffield Area Health Authority (Southern District) on June 12, 1981.

**Studies in Ileostomy Patients.** Measurements of gastric emptying, small bowel transit time, and composition of ileostomy effluent were carried out in each patient under control conditions and after ingestion of either lactulose (Duphalac, Philips-Duphar, Weesp, Holland); metoclopramide (Maxolon, Beecham Research, Middlesex); or magnesium sulfate (BPC). All fourteen patients underwent control studies; seven underwent a further study with lactulose, six with magnesium sulfate, and nine with metoclopramide.

Lactulose (40 g) and magnesium sulfate (0.1 g/kg body weight) were added to the drink which accompanied the test meal. Metoclopramide was administered in three oral doses of 20 mg each, one at 8 PM on the day preceding the study and two on the day of the study, one at 8 AM and the second at noon.

All the subjects were instructed to have no food after 6 PM on the day preceding the test. At 9:30 AM on the test day, they ate the standard meal consisting of 100 g boiled lean ham, 218 g mashed potato (30 g potato powder and 188 ml de-ionized water), 100 g washed, blended baked beans (75 g beans, 25 ml de-ionized water), and 25 ml corn oil. Fifty microcuries of $^{99m}$technetium sulfur colloid (half-life = 6 hr) were added to the water that reconstituted the mashed potato. The constituents were mixed together before being eaten. Each subject drank 100 ml water containing a soluble calcium tablet (Sandocal, Sandoz) containing 0.4 g calcium. All subjects were urged to eat the meal within 10 min, and the time taken to finish the meal was noted. Immediately after ingestion, all patients rested in a semirecumbent position on a couch. A single crystal scintillation detector was positioned over the abdomen at the site of maximum radioactivity, and the rate of gastric emptying was monitored by counting over this point for 1 min out of every 10 min (1, 2). The counts were corrected for decay of the isotope, and counting continued until the correct counts had fallen to less than half of their original value. A value of the half time for gastric emptying was derived from the graph of count rate versus time, taking the count 20 min after ingestion as the initial value.

Patients emptied their ileostomy bag before ingesting the meal, at 30-min intervals throughout the day until approximately 11 PM, and immediately on waking the following morning. Samples were collected in individual, labeled plastic containers, and these were stored in a refrigerator until the study was complete.

Drinks of bland, unsweetened fluids were allowed *ad libitum*, throughout the day, but no further food was eaten until approximately 6 PM, when the patients ate their usual evening meal, labeled with 100 g boiled beetroot as a marker.

**Measurement of Delivery of Ileal Residues.** On the morning following the test, each ileostomy sample was weighed and the radioactivity counted by inserting the container into the well formed by the inverted collimator and radiation detector. The counts were adjusted by applying a correction factor for the increased adsorption of counts caused by larger volumes in the container. The latter was determined by making up a solution of radioactive technetium in water. Increasing volumes of this solution were counted, and the results were plotted on a graph of volume vs counts. As more solution was added, the count deviated from a linear relationship due to adsorption of radioactivity (Figure 1). The factor which, when multiplied to the actual counts, was required to bring them up to the expected number was determined for each volume. Experiments were also carried out in which counts were repeated after addition of successive increments of mashed potato to a constant volume of solution. Addition of mashed potato did not decrease the count rate.

A graph of the cumulative counts in the ileostomy effluent was plotted, and values for the time taken for 10, 50, and 80% of the meal to empty from the ileostomy were determined.

**Preparation of Samples of Ileostomy Effluent.** After weighing and counting, all the samples containing radioactive isotope above background levels, but not containing beetroot, were pooled and reweighed. An aliquot of known weight was removed for fat analysis. The remainder was poured into an aluminum tray of diameter 18.3 cm and depth 1.5 cm. This was then placed in a chest freezer for approximately 8 hr before being dried to constant weight in a freeze drier (Edwards Modulyo, Crawley, UK). The dried material was weighed and an aliquot was removed for analysis of carbohydrate and protein. A further aliquot of dried material was removed, weighed, and ashed for 24 hr at 600°C in a muffle furnace. The ashed material was assayed for sodium, calcium, and potassium.

**Chemical Analysis.** Fat was estimated as stearic acid by a method adapted from van de Kamer (3). Protein was estimated by a modification of the micro-Kjeldahl method (4). Absorbable carbohydrate was assayed by hydrolysis with 0.5 M sulfuric acid, followed by incubation with glucose oxidase for 45 min at 37°C. Solutions were read at 420 nm on a Unicam SP600 spectrophotometer. Sulfate ions were assayed by the barium chloranilate method described by Lloyd (5).

For analysis of electrolytes, the ash was taken up in 10% hydrochloric acid and subsequently diluted with lanthanum chloride. Sodium and potassium concentrations were estimated using a flame photometer (Corning-Eel, model 435), while calcium and magnesium concentrations were estimated on an atomic absorption spectrophotometer (Perkin-Elmer, model 290b).

**Correction for Samples Contaminated by Residues of Second Meal.** Any samples which were stained with beetroot from the second meal were discarded and not analyzed. A correction was made for the presence of the test meal in those samples by multiplying the total amount of each constituent in the assayed samples, by the ratio of the total cumulative radioactivity in all the ileostomy samples to the total cumulative radioactivity in the samples which did not contain beetroot.

This correction assumed that the radioactive isotope provided an accurate marker of the rate of delivery of all the components of the meal. To validate this assumption,