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Measurement of Gastrointestinal pH and Regional Transit Times in Normal Children

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Summary: Gastrointestinal pH and regional intestinal transit times of a capsule were measured in twelve healthy children aged 8–14 years using a radiotransmitting pH-sensitive capsule. The location of the capsule was determined by fluoroscopy. pH in the stomach was 1.5, but rose to 6.4 in the duodenum (mean values). pH gradually rose in the small intestine and reached an alkaline peak value of 7.4 in the distal part. pH dropped to 5.9 in the cecum but rose to 6.5 in the rectum. Median gastric residence time of the capsule was 1.1 h. Small intestinal transit time was 7.5 h, and colonic transit time was 17.2 h. pH profile and intestinal transit times found in the present study are almost identical to values found in studies on healthy adults. It is therefore concluded that the release pattern of pH-dependent sustained-release tablets in children is likely to be equal to that of adults. **Key Words:** Gastrointestinal pH—Gastrointestinal transit time—Small intestinal transit time—Colonic transit time—Children.

Several new tablets developed for the treatment of chronic inflammatory bowel diseases and other diseased conditions are constructed in order to release their active contents at a rate determined by gastrointestinal pH (1–5). Thus, the activity of these tablets is influenced by gastrointestinal pH and the transit times of the tablet through the different segments of the gut. Although these factors have been investigated in adults (6–9), information concerning children is scarce, and important differences may exist.

The development of small, radiotransmitting, pH-sensitive capsules (10–12) has provided a method that enables determination of intestinal pH under almost physiological conditions. The transit times of the capsule through the gut can be measured by repeated determinations of the location of the capsule by fluoroscopy.

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The purpose of this study was to determine the pH profile of the gut and to measure the regional intestinal transit times of a capsule in normal children.

MATERIAL AND METHODS

Subjects

We studied 12 healthy children, 5 boys and 7 girls, aged 8–14 years (median 12 years). All were without symptoms of gastrointestinal disease, and none received any medical treatment.

Informed consent from the children and their parents was obtained, and the study protocol, containing an estimate of the amount of radiation expected to be used, was approved by the local ethics committee.

pH Measurements

The pH-sensitive, radiotransmitting capsule used (Remote Control Systems, Ltd, London) measured

24 mm in length and 7 mm in diameter (Fig. 1). The frequency of transmission changes with the pH of the capsule's environment. Before use the capsule was allowed to stabilize at 37°C for 10–14 h and then calibrated using pH 1 and pH 9 buffer solutions at 37°C. Signals from the capsule were detected by an antenna and passed to the receiver. Determinations were made with the person standing, holding the antenna in place for ~15 s.

Localization of the Capsule

The location of the capsule was determined by fluoroscopy. An average of 10 s of exposure time was used for each determination. The median number of determinations was 25 (range of 17–32; estimated maximal surface exposure of 130 mSv).

When the capsule was located in the small intestine, a location in the upper left abdominal quadrant was designated "proximal," and a location in the right lower abdominal quadrant was designated "distal." The localization of the capsule in the colon relied upon the identification of bony landmarks and gaseous outlines (13).

Study Design

Studies began at 8 am on the first test day after a minimum fasting period of 8 h. After swallowing an untethered capsule, pH was measured every 10–15 min until the capsule emptied into the duodenum, an event marked by an elevation of pH to a value above 5. The study subjects continued to fast until this had occurred. pH and the location of the capsule was determined every half hour, until the capsule entered the cecum. The intervals between determinations were then increased to 2 h. If the capsule had not been passed by 11 pm, the study continued at 8 am on day 2. If the capsule still had not been passed by 11 pm on day 2, no further determinations were performed. All stools were examined until the capsule was recovered. Recalibration of the capsule was done after recovery, and corrections in pH calculations were made for frequency drift, which may have occurred during the study.

The children were not restricted to any dietary control either before or during the study.

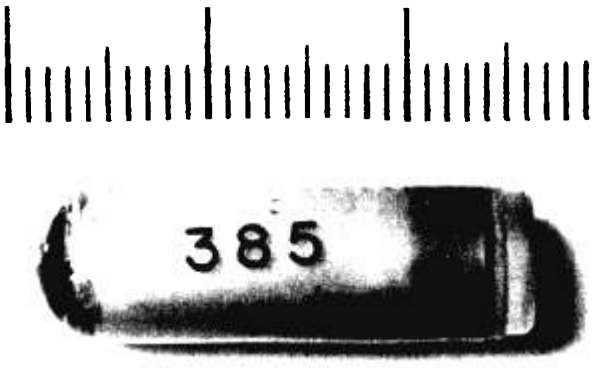

FIG. 1. The pH capsule.

Data Analysis

Individual median pH values for each segment of the gut were calculated, and the Wilcoxon rank test for paired data was used to test for differences in pH between different segments. Significance was considered at the 5% level.

RESULTS

All children completed the study, and none complained of any discomfort that could be related to the capsule.

The pH profile of the gut in the children studied is shown in Fig. 2. In all subjects, median pH values below 3 were found in the stomach. pH rose to a mean value of 6.4 in the duodenum and hereafter

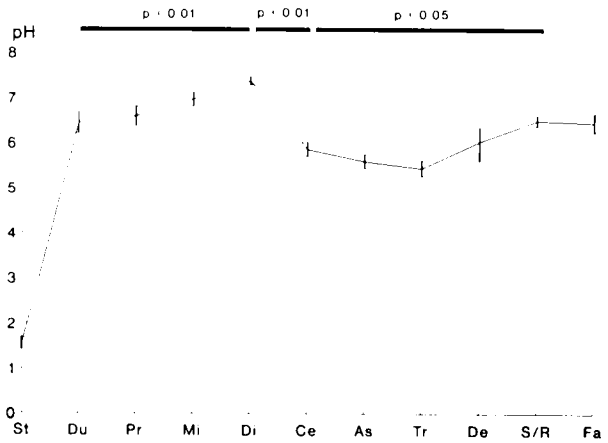

FIG. 2. Gastrointestinal pH profiles (mean ± SEM) of the 12 children studied. Statistical significant differences in pH between segments of the gut are shown. St, stomach; Du, duodenum; Pr, proximal small intestine; Mi, mid-small intestine; Di, distal small intestine; Ce, cecum; As, ascending colon; Tr, transverse colon; De, descending colon; S/R, sigmoid colon and rectum; Fa, feces.

gradually increased, reaching a peak alkaline value of 7.4 in the distal part of the small intestine. pH dropped to 5.9 in the cecum, but a significant tendency towards neutral pH in the left colon was observed. pH in the sigmoid colon and rectum was measured to be 6.5 Fecal pH was 6.4.

The median gastric residence time of the capsule was 1.1 h (range of 0.2–2.3 h). Median small intestinal transit time was 7.5 h (range of 5.1–9.2 h). Judged by the number of observations in each segment of the small intestine, the capsule was located in the duodenum for 8%, in the proximal part for 5%, in the mid part for 12%, and in the distal part for 75% of the time. Median colonic transit time was 17.5 h (range of 6.2–54.7 h). For 43% of this time, the capsule was located in the cecum.

DISCUSSION

Very few studies on gastrointestinal pH in children have been published. Barbero et al. (14) investigated pH in stools and intestinal fluids obtained by aspiration technique in infants up to 3 months of age. They found median pH levels between pH 6 and 7 in the small intestine, which corresponds well to the levels found in our study. However, Barbero et al. found that pH reached an alkaline peak between pH 7 and 8 in the cecum before it tended to fall in the distal part of the colon. In our study, the lowest pH levels were found in the cecum and in the right part of the colon, and the levels were ~2 pH units lower than the values reported by Barbero et al. (14). The diverging results almost certainly are due to differences in food consumption and colonic bacterial composition between the two different age groups of children studied. The gastrointestinal pH profile found in the present study corresponds well with results obtained in studies on adults (6,7,15).

In our study, mean fecal pH was 6.4, which is in agreement with the results reported by Walker et al. (16). They also found that the acidity of feces in children could be increased by raising the crude fiber content in the diet. This effect has also been demonstrated in adults (17). Supplementation of the diet with protein, fat, and sugar foods did not significantly change the fecal pH level (16). This indicates that the acidity of colonic contents and feces is caused by bacterial fermentation of nonabsorbed carbohydrates such as cellulose. To our knowledge, the gastrointestinal transit of a single unit such as a tablet or a capsule has not been studied in children. In adults, it has been shown that one of the most important factors affecting the gastric residence time of a particle >2 mm is the presence or absence of food in the stomach (18). A particle >2 mm taken with a meal most often will be retained in the stomach until it is empty of food. In the present study, the capsules were taken during a fasting state, and the gastric residence time found is almost identical to values measured in adults (19). The small intestinal transit time of 7.5 h is considerably longer than values reported from other studies using different methods (20,21). The value, however, is in accordance with values in adults, measured with the same method as used in the present study (6,7). The capsule was located in the distal part of the small intestine for 75% of the small intestinal transit time, which demonstrates that the ileo-cecal transit is prolonged for larger particles.

The results of the present study correlate well with results obtained from studies in adults. This indicates that the release pattern of pH-dependent sustained-release tablets in children is likely to be identical to that of adults.

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