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Effect of Equimolar Amounts of Long-Chain Triglycerides and Medium-Chain Triglycerides on Small-Bowel Transit Time in Humans

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ABSTRACT. Background: The use of medium-chain triglycerides in diets is limited by the frequent occurrence of diarrhea or crampy abdominal pain. Because these symptoms may result from an accelerated transit time induced by medium-chain triglycerides, we investigated the effect of equimolar amounts of long-chain triglycerides and medium-chain triglycerides on small-bowel transit time in 10 healthy subjects. Methods: Small-bowel transit time was measured by the lactulose hydrogen breath test after intraduodenal administration of lactulose. Results: Intracoduodenal administration of 20 mmol of long-chain triglycerides per hour for 90 minutes did not alter small-bowel transit time compared with control (77 ± 11 minutes vs 77 ± 10 minutes, respectively), whereas intraduodenal infusion of an equimolar dose of medium-chain triglycerides significantly accelerated small-bowel transit time (59 ± 6 minutes) compared with long-chain triglycerides and control (p < .05). In six individuals, small-bowel transit time was shorter during the administration of medium-chain triglycerides compared with control, and three of these subjects experienced abdominal symptoms. Plasma cholecystokinin levels increased significantly (p < .05) during the administration of long-chain triglycerides, from 2.6 ± 0.3 pmol/L to a maximum of 4.3 ± 0.6 pmol/L. No significant alterations were observed in plasma cholecystokinin levels during administration of medium-chain triglycerides or in the control experiment. Conclusions: Although it significantly increases cholecystokinin secretion, the intraduodenal infusion of long-chain triglycerides does not affect small-bowel transit time, whereas the infusion of medium-chain triglycerides accelerates small-bowel transit time, independent of cholecystokinin. (Journal of Parenteral and Enteral Nutrition 19:5-8, 1995)

Medium-chain triglycerides contain fatty acids with a chain length varying from 6 to 12 carbon atoms. Compared with long-chain triglycerides, these triglycerides exhibit some favorable physicochemical characteristics that result in rapid intraluminal hydrolysis and absorption. Medium-chain triglycerides are therefore attractive as a calorie source for patients with impaired fat digestion or absorption. However, the use of medium-chain triglycerides in diets is limited by the frequent occurrence of gastrointestinal symptoms such as borborygmi, crampy abdominal pain, and diarrhea. It has been suggested that the diarrhea is secondary to the rapid hydrolysis of medium-chain triglycerides, and it results in the formation of osmotically active fatty acids. Although the gastrointestinal symptoms occurring after medium-chain triglyceride ingestion could be explained by an accelerated intestinal transit, this possibility has never been investigated. Therefore, the aim of the present study was to determine the effects of equimolar amounts of long-chain and medium-chain triglycerides on small-bowel transit time. To exclude the influence of variable gastric emptying, small-bowel transit time was measured during intraduodenal administration of fat, using the lactulose hydrogen breath test after intraduodenal administration of lactulose.

A second aim of the study was to investigate the role of cholecystokinin on small-bowel transit time inasmuch as cholecystokinin is released after ingestion of long-chain triglycerides but not after ingestion of medium-chain triglycerides.

Subjects

Ten healthy subjects (seven men, three women) (mean age, 25 years; range, 19 to 30 years) were studied. Informed consent was obtained from each individual, and the protocol was approved by the ethical committee of the Leiden University Hospital. None of the subjects had a history of gastrointestinal symptoms or surgery, and none were taking drugs that could possibly influence gastrointestinal motility or the intestinal flora.

Test Procedure

Each subject participated in three experiments performed on separate occasions in random order with an interval of at least 7 days. After an overnight fast, the subjects were intubated at 8 AM with a single-lumen polyurethane feeding tube (Flocare Ch10, Nutricia, Zoetermeer, The Netherlands) that was positioned under fluoroscopic control in the horizontal part of the
duodenum. An IV cannula was inserted into an antecubital vein of one arm for blood sampling.

Basal blood and breath samples were obtained at 30, 15 and 0 minutes before the start of the experiment. The experiment was started within 2 minutes by administration of 6 g of lactulose (Legendal; Inpharzam, Amersfoort, The Netherlands) in 70 mL of water (osmolality, 280 mOsm/kg) into the duodenum to determine small-bowel transit time by hydrogen breath analysis. Thereafter, intraduodenal infusion was started with long-chain triglycerides (corn oil, 93% C16-C18), medium-chain triglycerides (Ceres medium-chain triglycerides dietary oil, 98% C8-C10) (Van den Bergh en Jurgens BV, Rotterdam, The Netherlands), or saline (control) at an infusion rate of 20 mmol/h for 90 minutes (medium-chain triglycerides, 15 g for 90 minutes; long-chain triglycerides, 30 g for 90 minutes).

Small-Bowel Transit Time

Small-bowel transit time was determined by lactulose hydrogen breath analysis, as described by Bond and Levitt. Hydrogen gas is generated by bacterial flora from unabsorbed carbohydrates in the colon. Arrival of the nonabsorbable carbohydrate lactulose in the colon can be detected by an increase in pulmonary hydrogen excretion. Samples of end-expiratory breath were taken under basal conditions and every 5 minutes after intraduodenal lactulose administration until a sustained increase in breath hydrogen excretion was observed. The samples were collected in 25-mL plastic syringes and were immediately analyzed in a hydrogen breath-test unit (Lactoscreen, Hoekloos, The Netherlands). Small-bowel transit time was defined as the time between lactulose administration and a sustained rise in breath hydrogen concentration of at least 10 ppm above basal level. In our department, the mean coefficient of variation for duodenocolic transit time using the lactulose hydrogen excretion test was 12% ± 5%.

Blood Samples

Blood samples for determination of plasma cholecystokinin levels were obtained at 15-minute intervals, starting from time -30 minutes to 120 minutes. Blood samples were collected in tubes containing EDTA and were kept on ice during the experiment. Plasma cholecystokinin was determined by a sensitive and specific radioimmunoassay that used antibody 63K-7.8 This antibody binds to all carboxy-terminal cholecystokinin peptides containing the sulfated tyrosyl region. The detection limit of the assay was 0.5 pmol per liter of plasma. The intra-assay variation ranged from 4.6% to 11.5%, and the interassay variation ranged from 11.3% to 26.1%.

Statistical Analysis

The results are expressed as mean ± SEM. Plasma cholecystokinin levels are expressed in picomoles per liter. Differences in small-bowel transit time and in plasma cholecystokinin levels between the three treatment groups, and for plasma cholecystokinin levels within the three groups, were analyzed for significance of difference by analysis of variance. When this indicated a probability of less than 0.05 for the null hypothesis, Student's Newman-Keuls analyses were performed to determine which values differed significantly. The significance level was set at p < 0.05.

RESULTS

Small-Bowel Transit Time

Fasting hydrogen breath levels were below 12 ppm in all subjects. A sustained increase in the pulmonary hydrogen secretion of 10 ppm after administration of lactulose was observed in all subjects. Mean small-bowel transit time during intraduodenal infusion of saline was 77 ± 10 minutes. The transit time during infusion of long-chain triglycerides (77 ± 11 minutes) was not significantly different and was identical with that observed in the control experiment. Administration of medium-chain triglycerides, however, resulted in a significant acceleration of transit time (59 ± 6 minutes) compared with transit time after administration of long-chain triglycerides and of saline (p < .05). The individual data of the transit times are presented in Table I and Figure 1. Compared with saline infusion, small-bowel transit time was accelerated during administration of medium-chain triglycerides in six subjects and was equal in three subjects; small-bowel transit time was prolonged in one subject. Three of the six subjects with an accelerated small-bowel transit time experienced mild symptoms of borborygmi and diarrhea after administration of medium-chain triglycerides. Compared with administration of long-chain triglycerides, small-bowel transit time was accelerated during administration of medium-chain triglycerides in seven subjects and was equal in two subjects; small-bowel transit time was prolonged in one subject. No side effects were reported after administration of long-chain triglycerides or saline infusion.

Plasma Cholecystokinin Levels

Fasting plasma cholecystokinin levels were not significantly different among the three experiments: long-chain triglycerides, 2.6 ± 0.3 pmol/L; medium-chain triglycerides, 2.5 ± 0.3 pmol/L; and saline 2.5 ± 0.3 pmol/L (Fig. 2). Administration of long-chain triglycerides from time 0 to 90 minutes resulted in a significant (p < .05) increase in plasma cholecystokinin over basal level starting from time 15 minutes until 105 minutes. Plasma cholecystokinin levels during administration of long-chain triglycerides rose to a maximum of 4.3 ± 0.6 pmol/L at 75 minutes. Administration of long-chain triglycerides significantly (p < .05) increased plasma cholecystokinin levels from time 15 minutes to 105 minutes compared with control. No significant alteration in plasma cholecystokinin levels over basal was observed during administration of medium-chain triglycerides.

DISCUSSION

The present study shows that intraduodenal infusion of medium-chain triglyceride oil, as measured by lactulose hydrogen breath testing, significantly acceler-
...small-bowel transit time during intraduodenal infusion of equimolar amounts (20 mmol/h for 90 minutes) of long-chain triglycerides, medium-chain triglycerides, or saline.

<table>
<thead>
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<th>Subject</th>
<th>Long-chain triglycerides</th>
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<td>10</td>
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Mean ± SEM 77 ± 11 59 ± 09 77 ± 10

* Significant difference between medium-chain triglycerides and long-chain triglycerides or medium-chain triglycerides and saline (p < 0.05).

During the fasting period, a recurrent cyclic pattern of myoelectric activity, the interdigestive migrating myoelectric complex, is observed in the small intestine.

The mechanism responsible for the accelerated transit time by medium-chain triglycerides is not apparent; however, several mechanisms may be involved. It has been suggested that rapid hydrolysis of medium-chain triglycerides may lead to the formation of osmotically active fatty acids that increase flow through the small intestine. Alternatively, medium-chain triglycerides induce a direct secretory response of the small intestine.

This...
fasting pattern is disrupted by the ingestion of food, the constituents of which (especially fat) are capable of inducing a prolonged feeding pattern. In dogs, medium-chain triglycerides potently disrupt the interdigestive migrating myoelectric complex to a feeding pattern. In humans, however, a medium-chain triglyceride-oligopeptide mixture induces a motor pattern similar to the interdigestive migrating myoelectric complex. This may be explained by the inability of medium-chain triglycerides to stimulate cholecystokinin secretion, inasmuch as cholecystokinin is thought to be one of the hormonal factors involved in the conversion from a fasting to a fed motility pattern.

The effect of cholecystokinin on intestinal transit time is not fully understood. It has been reported that infusion of a cholecystokinin octapeptide accelerates intestinal transit. However, loxiglumide, the specific cholecystokinin receptor antagonist, does not affect small-bowel transit time as measured by lactulose hydrogen breath testing. In contrast to this observation is a recent report by Schmidt et al that demonstrates a prolonged orocecal transit time during loxiglumide infusion. Because loxiglumide accelerates gastric emptying, the prolonged orocecal transit time is thought to result from a delay in small-bowel transit during cholecystokinin-receptor blockade. Although in the present study endogenous cholecystokinin secretion was stimulated by intraduodenal long-chain triglycerides, no significant alteration in small-bowel transit time during infusion of long-chain triglycerides was observed. On the other hand, intraduodenal medium-chain triglycerides significantly accelerated small-bowel transit time without affecting cholecystokinin secretion, indicating that the effect of medium-chain triglycerides on small-bowel transit time is independent of cholecystokinin. Our observation that medium-chain triglycerides do not stimulate cholecystokinin secretion is in agreement with previous findings.

We conclude that intraduodenal infusion of long-chain triglycerides does not affect small-bowel transit time, although it significantly increases cholecystokinin secretion, whereas infusion of medium-chain triglycerides significantly accelerates small-bowel transit time, independent of cholecystokinin.

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REFERENCES