Influence of Carbon Chain Length of Dietary Fat on Intestinal Alkaline Phosphatase in Chylous Ascites

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The long-term effects of chain length of dietary fat on intestinal lymphatic transport of alkaline phosphatase were investigated in two patients with chylous ascites due to leakage of intestinal lymph into the peritoneal cavity. Substitution of a medium-chain triglyceride diet for long-chain triglyceride resulted in a parallel fall in triglyceride and the intestinal isoenzyme of alkaline phosphatase in chylous ascites. The concentrations of lymph triglyceride were linearly related to lymph intestinal alkaline phosphatase levels, suggesting a positive relation between absorption of long-chain triglycerides and transport of mucosal alkaline phosphatase into lymph.

A functional relationship between intestinal alkaline phosphatase (IAP) and fat absorption has been suggested by: (1) an increase in alkaline phosphatase in thoracic duct lymph during fat absorption (1, 2); (2) a bidirectional translocation of brush-border IAP during fatty acid perfusion (IAP is released into the lumen along with an increased activity of IAP in the lamina propria) (3); and (3) the inhibition of oleic acid absorption by a specific inhibitor of IAP L-phenylalanine (4). Changes in location and activity of IAP (2, 3) were much less pronounced during absorption of medium-chain fatty acids (MCFA) (primarily transported via the portal venous system) than with long-chain fatty acids (LCFA) which utilize the lymphatic pathway (5).

To clarify the relationship between lymphatic transport of IAP and fat ingestion, we have studied two patients in whom leakage from the intestinal lymphatic system into the peritoneal cavity produced chylous ascites. This pathological situation made it possible to observe the effect of fatty acid carbon chain length on lymph IAP over a period of several weeks.

MATERIALS AND METHODS

Two patients with chylous ascites due to lymphatic obstruction were studied. The first patient (male, 55 years old) had a biopsy-proven reticulum cell sarcoma with obstruction of the abdominal lymphatics and leakage of dye into the peritoneal cavity as evidenced by lymphangiography. The second patient (female, 53 years old) had advanced ovarian carcinoma with metastasis to the mesenteric and retroperitoneal lymph nodes, diagnosed by laparotomy and later confirmed at autopsy.

Just prior to admission into this study, the kinetics of dietary fat entering the peritoneal cavity were investigated as part of another project (6). In these two patients, 21% and 26% of ingested labeled long-chain fat were recovered in ascitic fluid. More than 80% of this fat was incorporated into chylomicrons. Furthermore, the lipid composition of the ascites of both patients closely resembled that of intestinal lymph. The above evidence (in addition to clinical and radiological data) strongly suggest that chylous ascites in both patients most likely consisted of intestinal lymph leaking into the peritoneal cavity.
Procedure and Experimental Design

During baseline studies both patients were maintained on a standard hospital diet containing 100 g LCT (long-chain triglycerides, LCT diet), 90 g protein, and 182 g carbohydrate. A medium-chain triglyceride* (MCT) diet containing 110 g MCT, 230 g carbohydrates, and 56 g protein was substituted for the LCT diet for 13 and 8 days, respectively. After the MCT diet, both patients resumed the previous LCT diet for at least another 2 weeks. Both diets were equicaloric (2000 kcal). During the study period repeat paracentesis was performed to obtain serial samples of ascitic fluid (30 ml) for enzyme and lipid analysis. Total alkaline phosphatase activity was measured by an automated method previously described (7) and expressed in King–Armstrong (KA) units. Intestinal and liver isoenzyme activities were determined by selective inhibition using L-phenylalanine and L-homoarginine, respectively (7, 8). No Regan isoenzyme of alkaline phosphatase was found in serum or ascitic fluid of these patients as determined by starch-gel electrophoresis (9).

Analysis of triglycerides in ascites was performed by standard laboratory procedures (10). Further, the chylomicron fraction of the ascitic fluid was isolated (11), and its alkaline phosphatase activity was measured as outlined above.

RESULTS

Substitution of MCT for LCT in the diet produced a marked decrease of the triglyceride concentrations in chylous ascites which subsequently became cleared (Figure 1). The decrease in triglyceride concentrations was associated with a decrease in total alkaline phosphatase activity in chylous ascites. The decrease was due to a selective fall in the IAP fraction. With the resumption of the LCT diet, IAP, total alkaline phosphatase activity, and triglyceride levels returned to baseline levels. The liver isoenzyme of alkaline phosphatase remained unaffected throughout the study. No significant change in abdominal girth or body weight was observed in either patient during the study period.

IAP activity and triglyceride concentration in chylous ascites were linearly related in both patients, as shown by Figure 2. Less than 10% of alkaline phosphatase activity was found in the chylomicron fraction of chylous ascites.

DISCUSSION

The assumption that chylous ascites consisted primarily of intestinal lymph was supported by prior studies in both patients (6). These studies revealed that the lipid composition of their ascitic fluid resembled intestinal lymph and that at least 20% of labeled LCT incorporated into a test meal was recovered in ascites (almost entirely in ascitic fluid chylomicrons) as opposed to less than 1% of simultaneously ingested MCT. Absorbed LCT is incorporated into chylomicrons and transported by the lymphatics thereby increasing intestinal lymph flow, while MCT is primarily transported via the portal system (5). Thus, replacing dietary LCT by MCT should decrease chylomicron formation and reduce lymphatic triglyceride transport. As expected, ascitic triglyceride concentrations did decrease, and the ascitic fluid lost its milky appearance, an observation also reported by others (12, 13).

The concentrations of IAP in chylous ascites decreased linearly with triglyceride concentrations. Since the volume of ascites remained essentially unchanged (as evidenced by both stable weight and abdominal girth), the total amounts of IAP and triglyceride in ascites also decreased. Further, when LCT diet was resumed all parameters returned to their original levels, strongly suggesting that reduction in IAP and triglyceride in ascites had been induced by the MCT diet.

Previous information on the effect of dietary fat on lymph IAP in man has been limited to acute experiments. It has been found (1) that IAP in thoracic duct lymph increases after a fat-containing meal, correlating well with an increase in triglyceride concentration. Dietary protein or glucose did not show such stimulatory effects. The effect of MCFA has not been previously studied in man, but Lam and Mistilis (2) showed a two-fold higher increase in lymph IAP with LCFA as compared to MCFA in the rat. Our calculations of the data of Glickman et al (14) also showed a difference but of a lesser magnitude.

Our studies suggest that substitution of MCT for ordinary LCT in the diet decreases IAP and triglyceride transport in intestinal lymph. Thus, IAP activity in human intestinal lymph could depend on regular ingestion of LCT which stimulates lymphatic transport of both IAP and triglycerides. The significance of our observation is enhanced by the fact that MCFA is mainly transported by portal circulation rather than lymph and therefore not reesterified or incorporated into chylomicrons. Since the effects of MCFA on mucosal IAP are also much less pronounced than with LCFA (15), the evidence presented supports a possible role of IAP on LCFA

* MCT was given as a combination of a MCT margarine (Ceres margarine, supplied by Unilever Research Lab., Vlaardingen, Netherlands) and a commercially prepared formula (Portagen, Mead-Johnson and Co., Evansville, Illinois).