Preliminary Communications

Medium-chain Triglyceride Diet: Its Use in Treatment of Liver Disease*

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Three years ago, when starting an investigation of infants with neonatal hepatitis or biliary atresia, we observed that some of these babies passed stools which appeared to contain excessive fat. Balance studies in these infants confirmed the presence of severe steatorrhoea. The slow growth seen in children with liver disease has traditionally been attributed to "poor liver function." Our findings suggested that steatorrhoea might be an important factor even in those patients whose bowel motions were not so obviously abnormal.

Fat-balance studies were therefore made in all our patients with liver disease investigated during the past two years. This group comprised nine infants with biliary atresia, 17 with neonatal hepatitis, and six older children with chronic liver disease. Thirty-one of these 32 patients excreted more than 5 g. of fat daily, and absorption ranged from 20 to 80% of ingested fat. In 17 less than 60% of the dietary fat was absorbed. Although it seemed likely that the absence of biliary secretions from the intestine was responsible for the steatorrhoea, no correlation was found between the presence of complete biliary obstruction and the amount of fat excreted. Studies of the possible mechanism of the malabsorption are in progress, and will be reported later.

Attempts to improve fat-absorption seemed worth while. Death may result from infection in an emaciated infant with neonatal hepatitis, and impaired healing of the wound is an important cause of morbidity after operations on babies with obstructive jaundice. In adults with steatorrhoea and liver disease, supplements of bile salts, pancreatic extract, and bicarbonate have produced variable results, but, overall, the response to these measures has not been encouraging (Summerskill and Moertel, 1962). Similarly, this therapy caused no consistent change in the fat-absorption of our patients. Another approach to the management of these children was suggested by reports that medium-chain triglycerides having a chain length of 8–12 carbon atoms are more easily absorbed than the usual dietary long-chain fats in a number of diseases associated with malabsorption (Fernandes *et al.*, 1962). Medium-chain triglycerides are absorbed by a different mechanism from that for long-chain fats. In the absence of pancreatic and biliary secretion, the absorption of long-chain fats is poor, but that of medium-chain triglycerides is less severely affected (Isselbacher, 1966).

Investigation of the value of medium-chain triglycerides in these patients was undertaken in two ways. After changing to a diet in which a large proportion of the fat was in the form of medium-chain triglycerides, faecal-fat excretion was measured during a period of at least three days, and in more-prolonged feeding trials the growth rate was recorded. Balance studies were repeated in 18 patients who presented after a preparation of medium-chain triglycerides became available 18 months ago. In every case the faecal-fat excretion decreased greatly (see Table).

Initially a medium-chain triglyceride oil (E. F. Drew Co.) was used, but 12 months ago a palatable milk (Mead Johnson) containing most of its fat as medium-chain triglycerides became available to us. This milk formula has been well tolerated, and long-term feeding trials are now in progress.

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CASE 1

The first patient managed in this way was a 13-year-old girl with chronic liver disease who was referred for investigation because of her failure to grow. Jaundice had first developed on the second day of life, and the diagnosis of neonatal hepatitis was made by needle biopsy of the liver at 2 months of age. Growth rate was slow. Jaundice did not clear until 2½ years, after which her growth rate increased. She had then remained well until the age of 11 years, when jaundice had recurred during an epidemic of infectious hepatitis. The jaundice had persisted throughout the succeeding two years and no growth had occurred. Extreme tiredness, which had prevented her attending school for more than three days each week, and severe itching had been major problems. Prednisolone had been given intermittently for the first year and then in a dose of 5–10 mg. daily during the second year. For one month before her admission to the Royal Children's Hospital, at the age of 13, stanolone (Anabolex) had been given, but had failed to affect her growth or well-being.

On examination she was small for her age and icteric, and her skin was thickened and excoriated. Her liver and spleen were mildly enlarged. Serum bilirubin level varied between 11 and 24 mg./100 ml., serum glutamic oxaloacetic transaminase (S.G.O.T.) 66 S.F. units, serum glutamic pyruvic transaminase (S.G.P.T.) 47 S.F. units, cephalin flocculation ++, and serum alkaline phosphatase 13 King-Armstrong units. A needle liver biopsy showed mild active inflammatory changes with moderate fibrosis and a great deal of bile retention. The stools were large and offensive, and fat-balance studies showed severe steatorrhoea with an average daily excretion of 40 g., while the diet contained 70 g. of long-chain fats per day. After substituting a diet containing 65 g. of medium-chain triglycerides a day the daily excretion of fat fell to 6 g. and the stools became normal in appearance. A diet was therefore devised, with the medium-chain triglyceride milk preparation as the principal source of fat combined with foods having a low content of long-chain fats. This has now been continued for a period of one year.

During the first week after starting the diet she gained weight for the first time in two years; one week later her clinical jaundice disappeared and serum bilirubin fell to 1 mg./100 ml. She has remained free of jaundice since that time and has grown 5.4 cm. and gained 8 kg. in the past 12 months (Fig. 1). She has been attending school full-time for the past eight months, and has energy to spare for sports. Itching has ceased and her skin has returned to normal. Pubertal development has started. Her liver-function

Comparison of Average Daily Intakes and Excretions of Fat (g./day) During Three-day Periods on a Normal Diet and on Medium-chain Triglyceride in 18 Patients with Liver Disease

Case No.	Usual Diet		Medium-chain Triglycerides	
	Intake	Excretion	Intake	Excretion
1	11	6	12	2
2	17	7	30	1
3	45	23	42	6*
4	30	21	32	3
5	18	9	21	4*
6	70	40	65	6*
7	21	13	22	5*
8	8	5	18	1
9	34	15	44	4
10	55	28	60	6*
11	31	18	30	1
12	10	8	20	2
13	13	7	24	1
14	28	12	40	2
15	22	14	24	6*
16	18	13	33	6*
17	18	7	21	2
18	30	9	35	2

* Diet containing both medium-chain and long-chain triglycerides.

tests have improved (serum bilirubin less than 0.5 mg./100 ml., S.G.O.T. 32 units, S.G.P.T. 10 units, cephalic flocculation negative) despite the stopping of prednisolone eight months previously. A needle liver biopsy at that time no longer showed any bile retention; the cellular infiltration had diminished, but the fibrosis remained unchanged.

Discussion

The dramatic improvement in this girl and the absence of any evidence of adverse effects of the medium-chain triglyceride diet on the liver-function tests or in the liver biopsy encouraged us to use the formula as a feeding for infants with liver disease. Initially this preparation replaced the milk feedings of four infants with severe neonatal hepatitis and one with biliary atresia. In each patient there was an improvement in general health, and a gain in weight; the stools became normal in appearance. However, there was no consistent alteration in intensity of the jaundice.

One of the patients with neonatal hepatitis was known to have gross multinodular cirrhosis, and to have developed ascites at the age of 17 months. The use of spironolactone (Aldactone A) controlled this problem, but during the next three months he failed to gain weight. He was lethargic and had not attempted to walk at 20 months. The medium-chain triglyceride diet was begun and three months later he had gained 2 kg., his general condition had improved, and he was walking; the ascites had not recurred, but the diuretic has been continued.

FIG. 1

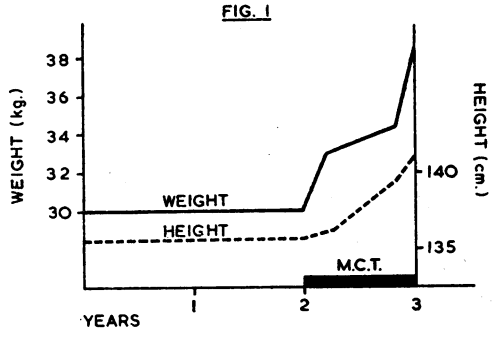

FIG. 2

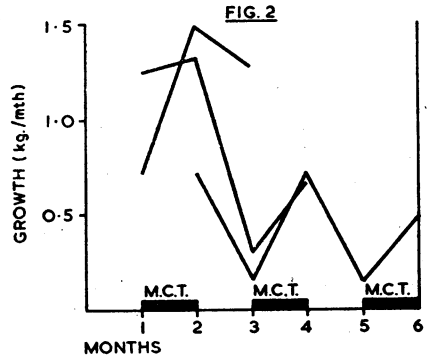

FIG. 1.—Case 1. Growth of patient in relation to the use of the medium-chain triglyceride diet. FIG. 2.—Weight gains (kg./month) of three patients fed a cows'-milk formula and the medium-chain triglyceride preparation alternately. The initial feeding was chosen randomly and changes were made at monthly intervals.

A second baby with neonatal hepatitis also had a cyanotic congenital heart defect, and her early progress was complicated by severe chest infections. Despite the use of the medium-chain triglyceride feeding from birth until the age of 6 months the growth rate was slow. Cows'-milk feedings were then tried, but during the next month she lost weight for the first time. Since reversion to the medium-chain triglyceride preparation her slow but steady growth has resumed.

In these first five babies treated with medium-chain triglyceride feedings the poor initial condition and the improvement found after changing to the medium-chain triglyceride formula made proper documentation of this response by reverting to an ordinary feeding seem unjustified. However, we have since attempted to assess the effects of the medium-chain triglyceride diet in a more controlled fashion by alternating this feeding and cows' milk at monthly intervals in the same infant. All new patients presenting with neonatal hepatitis or biliary atresia are included in the trial, and the feeding used first is chosen randomly. So far we have studied only three babies for periods of more than three months. In each patient the growth rate was greater when the medium-chain triglyceride feeding replaced cows' milk (Fig. 2); in the patient with biliary atresia the growth rate has slowly decreased with time, presumably because of progression of his liver disease. No deleterious effect has been detected clinically or by liver-function tests. Supplements of vitamins A and D have been given to each baby.

Only one patient, an 8-year-old girl with severe chronic liver disease and failure of growth, did not show definite improvement while the medium-chain triglyceride diet was used. Although the daily faecal-fat excretion decreased from 28 to 6 g. when medium-chain triglyceride was fed, the growth rate did not increase. There was some improvement in her general well-being, but because of this equivocal response the diet was used for only three months.

Overall, the results have been encouraging and the study is continuing.

Summary

Our results demonstrate that steatorrhoea is common in babies and children with liver disease. Fat-excretion decreased greatly when a diet containing a high proportion of medium-chain triglycerides was fed. Longer-term trials of this diet in 10 patients were accompanied by improved growth in all except one child.

Susceptibility to infections and delayed wound-healing are major problems in poorly nourished infants with persistent liver disease. The improved nutrition which follows the use of the medium-chain triglyceride diet should therefore decrease morbidity and mortality in this group of infants. This is particularly important in neonatal hepatitis because complete recovery from this condition is possible.

Further studies are in progress to determine the long-term effects of such a diet and its value in managing children with liver disease.

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