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Editorial commentary: Dietary management of familial chylomicronemia syndrome

Introduction

Familial chylomicronemia syndrome is an autosomal recessive disorder characterized by severe hypertriglyceridemia (HyperTG), with TG levels generally >1000 mg/dL. Affected individuals are frequently noted to have lipemic plasma and may present with acute abdominal pain secondary to pancreatitis. Physical findings include hepatosplenomegaly, eruptive xanthomas, and lipemia retinalis.[1] The disorder is rare, with an estimated frequency of 1:1,000,000; affecting both males and females. Familial chylomicronemia syndrome is usually caused by lipoprotein lipase (LPL) deficiency; less frequent genetic causes include mutations of apolipoprotein C-II, APO5, glycosylphosphatidlinositol-anchored high-density lipoprotein-binding protein 1 or GPI-HBP1, and lipid maturation factor-1.[1] A familial inhibitor of LPL function has also been described.[2]

The diagnosis of LPL deficiency is based on demonstrating low or absent enzyme activity in plasma after intravenous heparin injection using an assay system containing apoCII but that excludes hepatic triglyceride lipase activity. The enzyme may also be assayed in biopsies of adipose tissue. Demonstration of an LPL gene mutation confirms the diagnosis. However, treatment is not dependent on diagnostic confirmation of the underlying gene mutation.[3]

Acquired conditions, such as diabetes mellitus, medications including estrogens and glucocorticoids, or alcohol use, can also contribute to HyperTG in individuals with common familial forms of HyperTG or in heterozygous carriers of an LPL mutation.[4]

Management

Because the severe HyperTG in familial chylomicronemia syndrome is the result of dietary-derived chylomicrons, standard lipid-lowering therapies, such as omega-3-fatty acids, niacin, and fibrates, are generally ineffective. Triglycerides may be substantially lowered, however, by restricting dietary fat to <15% of the total daily caloric intake.[5] If triglycerides are not lowered to goal, further dietary fat restriction may be necessary while ensuring essential fatty acid (EFA) needs are met (2-4% of total calories as linoleic acid).[6] As tolerated, the fat-restricted diet may include 10%–15% calories from long- and short-chain fat, 60% calories from complex carbohydrates, and 25%–30% calories from protein, while avoiding concentrated carbohydrates.

It is important to closely monitor those on very low fat diets to ensure the diet provides adequate macronutrient and micronutrient intake for proper growth and development. A registered dietitian is critical in formulating and ensuring adequacy of the fat-restricted diet, educating the family on proper dietary choices, providing helpful feeding tips, and adjusting the diet as needed with advancing age and growth.

If dietary fat is limited to essential fatty acids, supplemental medium-chain triglycerides (MCT), containing fatty acids of 8 to 12 carbon atoms in length, should be considered to improve macronutrient balance, while providing additional fat and calories.[7] MCTs are absorbed directly into the portal circulation without chylomicron formation, therefore avoiding further increase in blood TG levels. Diets should be composed of adequate long-chain fats to meet EFA requirements, with addition of MCT, as tolerated, to increase total fat intake to 10%–15% daily calories. It is best to introduce MCT oil slowly, to avoid adverse effects such as diarrhea or abdominal pain. The effects of long-term MCT supplementation are unknown and require further research.

Adequate intake of fat-soluble vitamins (A, D, E, and K) should be monitored. Recommended daily intake of each may be viewed in Table 1. Supplementation may be required when test results or physical symptoms suggest fat-soluble vitamin deficiency.

Normalization of the fasting TG level has been reported in a small subset of children treated with omega-3-fatty acids, as they may decrease very low density lipoprotein (VLDL). However, omega-3 supplementation is often

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Table 1 Micronutrient dietary reference intakes (DRIs): recommended dietary allowances and adequate intakes, fat-soluble vitamins, and calcium

Age	Vitamin A (mcg/d)	Vitamin D (mcg/d)	Vitamin E (mg/d)	Vitamin K (mcg/d)	Calcium (mg/d)
Infants					
0–6 mo	400*	10	4*	2.0*	200*
7–12 mo	500*	10	5*	2.5*	260*
Children					
1–3 y	**300**	15	**6**	30*	700*
4–8 y	**400**	15	**7**	55*	1000*
Males					
9–13 y	**600**	15	**11**	60*	1300*
14–18 y	**900**	15	**15**	75*	1300*
Females					
9–13 y	**600**	15	**11**	60*	1300*
14–18 y	**700**	15	**15**	75*	1300*
Pregnancy					
14–18 y	**750**	15	**15**	75*	1300*

Table depicts recommended dietary allowances (RDAs) in bold and adequate intakes (AIs) followed by an asterisk (*).
Table modified from Texas Children's Hospital Pediatric Nutrition Reference Guide.[14]

ineffective in individuals with FCS, as elevated TG is secondary to an inability to hydrolyze plasma TG rather than hepatic overproduction.[8]

Age appropriate nutritional management

Infants

During infancy, adequate intake of long-chain fats is important to prevent essential fatty acid deficiency, fat-soluble vitamin deficiency, as well as contribute to normal neurological development. Breast milk and standard infant formulas may contribute to elevated TG in familial chylomicronemia syndrome due to their high-fat content. To normalize TG levels in affected infants, a low fat, high MCT formula complete in micronutrients may be beneficial. Efficacy of skimmed, fortified breast milk instead of high MCT formula is unknown and requires further research. Table 2 is a comparison of infant formulas and human breast milk. While use of other commercial formulas may be appropriate, the content of each and need for supplementation to assure all nutritional needs are being met should be carefully reviewed before use.

When advancing to solid foods, items such as vegetables, lean meats, and complex carbohydrates may be offered. As the child is weaned from low fat, modified formula feedings, a diet analysis is recommended to determine current caloric intake and macronutrient distribution. When the child is no longer receiving formula, MCT supplementation may be initiated in small doses. A selection of MCT supplements currently available are included in Table 3.

Children and adolescents

Continuing a very low fat diet with MCT supplementation may become more difficult with age. Challenges may include "picky eating" in children and decreased diet compliance in adolescence. Dietary fat intake and MCT supplementation, as well as overall caloric intake, should be adjusted for age and growth. Orlistat, a lipase inhibitor, which limits absorption of dietary fat, may lead to increased compliance and decreased TG. Disadvantages in using Orlistat include decreased long-chain fat absorption, possible decreased fat-soluble vitamin levels, and side effects such as oily stools.[8]

Conclusions

Although standard lipid-lowering therapies are generally ineffective in patients with familial chylomicronemia syndrome, TG may be significantly lowered through strict adherence to a very low fat diet. MCT supplementation may be useful in balancing the macronutrient composition of the diet, as well as meeting caloric needs. Each patient's diet should be closely monitored by a registered dietitian to prevent essential fatty acid and fat-soluble vitamin deficiency. Further supplementation of fat-soluble vitamins and diet modification should be provided based on age, growth trends, and laboratory data.

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