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Original Article

Familial chylomicronemia syndrome: Bringing to life dietary recommendations throughout the life span

Lauren Williams, MCN, RDN, LD*, Katherine S. Rhodes, PhD, RDN, Wahida Karmally, DrPH, MS, RDN, CDE, CLS, FNLA, Lori A. Welstead, MS, RDN, LDN, Lori Alexander, MSHS, RDN, CCRC, CLS, FNLA, Lindsey Sutton, for the patients and families living with FCS

Risk Evaluation to Achieve Cardiovascular Health (REACH) Clinic, Cook Children's Endocrinology Clinic, Fort Worth, TX, USADr Williams; Cardiovascular Medicine, Michigan Medicine, Ann Arbor, Michigan, USA Dr Rhodes; Irving Institute for Clinical and Translational Research, Columbia University, New York, NY, USA Dr Karmally; Section of Gastroenterology, Hepatology, and Nutrition, University of Chicago Medicine, Chicago, IL, USA Dr Welstead; ENCORE Lipid Center of Excellence, Jacksonville Center for Clinical Research, Jacksonville, FL, USA Dr Alexander; and FCS Foundation, San Diego, CA, USA Dr Sutton

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BACKGROUND: Familial chylomicronemia syndrome (FCS) is a rare autosomal recessive disorder with loss of function mutations of lipoprotein lipase resulting in hypertriglyceridemia and accumulation of chylomicrons in plasma, often leading to acute pancreatitis. The mainstay of treatment is a specialized very-low-fat diet. Even adhering to the diet, some patients may experience high triglycerides and pancreatitis. There currently are no comprehensive dietary guidelines.

OBJECTIVE: To report best practices and develop comprehensive dietary guidelines for nutrition therapy in patients with FCS.

METHODS: Registered dietitian nutritionists (RDNs) convened to develop this report based on experience treating patients with FCS and a review of current literature on the topic. One author provided a patient perspective of living with FCS.

RESULTS: This report provides guidelines and rationales for nutrition therapy associated with FCS across the life span. The top global guidelines are to (1) limit fat to <15 to 20 g per day (<10%–15% of total daily energy intake); (2) meet recommendations for essential fatty acids: α-linolenic acid and linoleic acid; (3) choose complex carbohydrate foods while limiting simple and refined carbohydrate foods; (4) supplement with fat-soluble vitamins, minerals, and medium-chain triglyceride oil, as needed; (5) adjust calories for weight management. Recommended foods include vegetables, whole grains, legumes, lean protein foods, fruits in limited amounts, and fat-free milk products without added sugars. Foods to avoid include alcohol and products high in sugar.

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* Corresponding author. Clinical Dietitian II, Cook Children's Endocrinology Clinic, Cook Children's Medical Center 1500 Cooper St, 2nd floor Fort Worth, TX 76104, USA. Tel.: +1 682 885 6282; fax: +1 682 885 3559.

E-mail address: lauren.williams2@cookchildrens.org

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CONCLUSIONS: These patient-centered nutrition guidelines provide guidance to help patients adhere to the recommended diet and optimize nutritional needs.

Introduction

Familial chylomicronemia syndrome (FCS) is a rare, autosomal recessive genetic disorder that affects 1 to 2 per million people.[1,2] FCS is characterized by severe fasting hypertriglyceridemia (HTG) due to a deficiency in either the enzyme lipoprotein lipase (LPL) or other proteins necessary for proper LPL function. The most common mutations for FCS are found in the following genes: *LPL*, *ApoA5*, *GPIHBP1*, *ApoC2*, *LMF1*, *LPL/LMF1*, *LPL/ApoA5*.[3] Triglyceride (TG) levels in individuals with FCS are often 10-fold to 100-fold or more above normal (<150 mg/dL) and may range from 1500 to 15,000 mg/dL or higher.[4,5]

In FCS, HTG results from the inability to metabolize TGs and other fats. Fats are absorbed through the small intestine, where chylomicrons are formed. When LPL is functioning, it helps metabolize TGs into free fatty acids through the LPL-dependent pathway.[5] Although TGs are also metabolized via the LPL-independent pathway, this pathway cannot compensate for the loss of LPL function. In FCS, chylomicrons, chylomicron remnants, and TG-rich lipoproteins cannot be metabolized and accumulate in the plasma. Accumulating TGs may impair pancreatic blood flow and activate inflammatory processes, resulting in acute pancreatitis.[6–8] It is estimated that severe HTG is the cause of 10% of all cases of acute pancreatitis.[7] Patients with HTG-induced acute pancreatitis may have a more severe course, leading to longer median hospital stays, increased need for intensive care, a higher rate of pancreatic necrosis, more frequent persistent organ failure, and higher rates of mortality.[9]

Acute pancreatitis is one of the severe, debilitating symptoms of FCS. Acute pancreatitis can lead to chronic pancreatitis,[10,11] signs of exocrine or endocrine pancreatic insufficiency, including pancreatic (type 3c) diabetes,[12] and can be fatal. Acute pancreatitis was reported by 42% of patients with FCS, making it the most common and potentially severe comorbidity.[13] Other symptoms of FCS are recurrent pancreatitis, severe abdominal pain ranging from mild to incapacitating (with or without pancreatitis), hepatosplenomegaly, lipemic plasma, eruptive xanthomas, lipemia retinalis,[1,14,15] and decreased quality of life.[13]

Because patients with FCS cannot metabolize TGs and fats, current medical nutrition therapy is a very-low-fat diet consisting of total fat intake <10% to 15% daily calories (ie, <15–20 g of fat per day) with limited simple, refined carbohydrates and avoidance of alcohol. In addition to a restricted diet, patients with FCS need to avoid drugs known to increase TG levels, including diuretics, systemic steroids, oral estrogens, antihypertensive drugs, retinoids, isotretinoin, bile acid sequestrants, protease inhibitors, immunosuppressants, antidepressants (sertraline), and beta-adrenergic blocking agents.[1] Effectiveness of omega-3 fatty acids, routinely used in pharmacologic doses for treatment of severe HTG, has been inconsistent in patients with FCS.[3,16–18,20] At the present time, there are no Food and Drug Administration–approved treatments for FCS.

Strict dietary adherence is critical for patients with FCS, but is difficult to maintain long term. Short-term ingestion of dietary fat, and even limited alcohol consumption, can result in highly exaggerated TG elevations that place patients at high risk for acute pancreatitis, despite otherwise good adherence with the diet. Even when patients adhere to the very-low-fat diet and are monitored by a registered dietitian nutritionist (RDN), TG levels may remain dangerously high.[3,20,21] FCS patients of all ages must be monitored regularly to ensure proper nutritional intake of macronutrients and micronutrients, particularly fat-soluble vitamins.

For patients with FCS to receive proper care, a diagnosis of FCS must be made. FCS is diagnosed as severe, refractory HTG in people with a history of acute pancreatitis or recurrent abdominal pain and the absence of other causes (alcoholism, gallstones, uncontrolled diabetes, medications, or medical conditions known to cause HTG). The most distinctive clinical feature of FCS is fasting hyperchylomicronemia, which results in lipemic, milky-appearing plasma samples. A lack of familiarity with FCS among health care providers may be one reason patients with FCS report visiting at least 5 physicians (range 1–30) before receiving a diagnosis of FCS.[13] A delay in diagnosis may place patients at an increased risk for acute pancreatitis.[11] This risk may be lowered by treatment with a health care team that includes a lipidologist, pancreatologist, gastroenterologist, primary care physician, RDN, psychologist, and/or social worker.

For patients with FCS to receive proper health care, dietary guidelines across the life span are critical. Currently, the only published guidelines for managing diet restrictions in patients with FCS are for infants, children, and adolescents.[22] No comprehensive best practice dietary guidelines across the life span exist. There are also no randomized controlled trials or meta-analyses, in part due to rareness of the condition.

To address this need, a panel of RDNs convened to identify gaps of medical nutrition therapy guidelines for treating FCS, and put forth best practice guidelines based on personal experiences treating patients with FCS, and the current clinical and scientific literature. The patient