Journal of Cystic Fibrosis 13 (2014) 572–578

www.elsevier.com/locate/jcf

Original Article

Effect of a dietary intervention on growth and energy expenditure in children with cystic fibrosis☆,☆☆,★

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Received 19 July 2013; received in revised form 1 December 2013; accepted 17 January 2014
Available online 8 February 2014

Abstract

Background: The study aim was to determine the effect of a dietary intervention on growth, body composition and resting energy expenditure (REE) in children with cystic fibrosis (CF) and pancreatic insufficiency (PI) in a randomized, double blind, placebo-controlled trial.
Methods: Subjects (5 to 17 yrs) participated in a 12-month trial of the organized lipid matrix LYM-X-SORB™ (LXS) vs. placebo dietary supplements with similar calories, total fat and fatty acids. Dietary intake was assessed using 3-day weighed food records. Height (HAZ), weight (WAZ), BMI (BMIZ), mid-upper arm muscle (UAMAZ) and fat area (UAFAZ) Z-scores were calculated. Fat mass (FM) and fat-free mass (FFM) were obtained by whole body DXA. REE (kcal/d) was evaluated by indirect calorimetry at baseline, 3 and 12 months and %REE calculated using Schofield equations. No growth or REE differences were observed between LXS and placebo groups so data were pooled for analysis.
Results: 63 children (57% males, age 10.6 ± 2.9 yr, 43% receiving LXS) completed REE measurements. Caloric intake increased from a median of 2502 [1478, 4909] to 2616 [1660, 4125] kcal/d at 12 months. HAZ, WAZ and UAMAZ increased ($p < 0.05$) over 12 months. Mean REE was 109 ± 8% predicted at baseline and 107 ± 9% at 12 months ($p < 0.05$). REE (kcal/d) adjusted for FFM and FM decreased over 12 months ([mean ± SE] −31 ± 12 kcals, $p < 0.01$), significant only in males (−49 ± 16 kcals, $p < 0.01$).
Conclusions: Over a 12 month nutrition intervention with either LXS or placebo, the growth status, muscle stores and REE improved. Sustained increased energy intake improved energy metabolism, growth and nutritional status in school age children with CF, PI and mild lung disease.

Keywords: Resting energy expenditure; Cystic fibrosis; Children; Dietary intervention

1. Introduction

Cystic fibrosis (CF) is one of the most common chronic, multi-system inheritable diseases. Most children with CF, in addition to pulmonary disease, suffer from pancreatic insufficiency (PI) and the nutritional consequences of lifelong malabsorption [1]. Chronic fat malabsorption may result in malnutrition, growth failure, and fat-soluble vitamin, essential fatty acid and choline deficiencies [2–4]. The treatment of fat malabsorption remains a challenge for the CF care team. Considering recent CF Foundation and Registry data from the

☆ Data presented on October 11, 2012 at the 26th Annual North American Cystic Fibrosis Conference, Orlando.
☆☆ Clinical Trial Registration: Study of LYM-X-SORB™ to improve fatty acid and choline status in children with cystic fibrosis and pancreatic insufficiency, NCT00406536.
★ Groleau V et al. (abstract #504) Pediatric Pulmonology supp. 35: 408, 2012.
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1569-1993/$ -see front matter
http://dx.doi.org/10.1016/j.jcf.2014.01.009

US, nutrition-related growth failure is still at an unacceptably high rate [1]. Malnutrition and poor growth in clinically stable children with CF and PI result from chronic negative energy balance due to insufficient caloric intake to overcome modestly higher energy requirements, related to the variable degree of energy loss from malabsorption and the mildly increased resting energy expenditure (REE) [5–13].

These data were collected as part of a randomized, placebo controlled trial of LYM-X-SORB™ (LXS, Avanti Polar Lipids, Alabaster, AL) to evaluate choline status in children with CF and PI. LXS is a choline-rich structured lipid matrix that has previously been shown to be absorbable without pancreatic enzyme therapy and to improve nutritional status and clinical outcomes for children with CF and PI [14]. The second generation LXS used in the present protocol had improved palatability and solubility characteristics, and was designed to be mixed with a variety of foods and beverages. The aim of this report was to evaluate the changes in dietary intake, growth, body composition and REE occurring over 12 months of daily supplementation with either LXS or the isocaloric placebo.

2. Methods

Study participants ages 5.0 to 17.9 years with CF and PI from ten CF Centers were evaluated from March 2007 to May 2011. This study was approved by the Institutional Review Board of the Children's Hospital of Philadelphia (CHOP) and at each CF Center. Verbal assent was obtained from the subjects <18 yrs of age with written consent from their parents/guardians. Exclusion criteria were FEV_1 <40% predicted, residual pancreatic lipase activity (fecal elastase >15 μg/g stool), liver disease as defined as a serum GGT >3× reference range or other chronic health conditions that may affect gastrointestinal absorption or growth. After enrollment, subjects were randomized to receive daily supplementation with either LXS or placebo powder. The random allocation sequence was generated by the CHOP Research Pharmacy who assigned participants to their groups with stratification for age and sex. LXS was composed of lysophosphatidylcholine, triglycerides and essential fatty acids. The placebo had similar calories, total fat and fatty acids with similar macronutrient distribution (kcal protein 6%, carbohydrate 58% and lipid 34%). LXS contained more choline than placebo (295 vs 39 mg/packet). Both powder supplements were mixed with wheat flour and sugar, provided in sealed packets (32 g/packet) with identical appearance, and mixed with a variety of food and beverage. All subjects and study team were blinded to group assignment. Subjects between the ages of 5.0 and 11.9 years consumed two packets per day (64 g/d of powder with 304 kcal/d), and ages 12.0 to 18.9 years consumed three packets per day (96 g/d with 456 kcal/d). LXS and placebo were produced by Avanti Polar Lipids, Inc. (Alabaster, AL) and the calorie, macronutrient and micronutrient content was verified in an independent laboratory (Eurofins Inc., Des Moines, IA) using standard methods.

Subjects completed study visits at CHOP following an overnight admission in the Clinical and Translational Research Center (CTRC) at baseline and after 3 and 12 months of supplementation. Dietary intake was assessed at each time point using 3-day weighed food records. Subjects and parents/guardians were provided with measuring cups, spoons, a digital food scale and detailed verbal and written instructions to weigh and record each food/beverage consumed. Completed diet records were reviewed and analyzed by the CTRC research nutritionist using Nutrition Data System for Research software (National Coordinating Center, University of Minnesota, Minneapolis, MN). Energy intake was assessed using the Dietary Reference Intakes [15], and expressed as percent Estimated Energy Requirement (%EER) for active children. The "active" physical activity level for the calculation of %EER has been found to best approximate the total energy requirements in children with CF and PI [16]. Families were contacted by telephone every 28 days to report adherence based on number of packets consumed over the previous 28 days. These data were used to calculate an average percent adherence as a measure of overall adherence for the two intervals (cumulative adherence estimates: baseline until 3 months and baseline until 12 months. However, when adjusting LXS and placebo nutrient intake at the 3 and 12 month dietary assessments, we used an adherence estimate close (within one month) to the dietary assessment (proximate adherence estimate).

Growth, body composition and REE were assessed at baseline, 3 and 12 months. Weight was measured to the nearest 0.1 kg using an electronic scale (Scaletronix, White Plains, NY) and height to the nearest 0.1 cm using a stadiometer (Holtain, Crymych, UK). Age- and sex-specific standard deviation scores (Z-scores) for weight (WAZ), height (HAZ) and body mass index (BMIZ) were calculated [17]. Mid-upper arm circumference was measured using a linen tape measure (McCoy, Maryland Heights, MO). A skinfold caliper (Holtain, Crymych, UK) was used to measure tricep skinfold thickness on the right side. Upper arm muscle and fat areas were derived, and z scores for upper arm muscle area (UAMAZ) and upper arm fat area (UAFAZ) were computed [18]. Total fat-free mass (FFM), fat mass (FM) and percent body fat were obtained by whole body dual energy X-ray absorptiometry (DXA, Delphi A, Hologic, Inc., Bedford, MA). Pubertal status was determined using Tanner stages with a validated self-assessment questionnaire [19].

REE was measured by open circuit indirect calorimetry using a computerized metabolic cart (SensorMedics Spectra, Yorba Linda, CA). In preparation for the REE, each subject received a standardized evening meal followed by a 12-hour fast. The subject was awakened on the day of study and restricted to minimal physical activity. A 60-minute REE assessment was performed between 7 and 10 AM. Data from the first 10 min and from periods of documented physical movement or coughing were omitted and the remaining data averaged. REE was calculated from the modified Weir equation [20]. REE was compared to predicted values derived from the Schofield equations that adjust for age, sex, weight and height [21]. Pulmonary function was evaluated by standard methods for spirometry [22] using a MedGraphics spirometer (Medical Graphics Corporation, Minneapolis, MN). FEV_1% predicted was calculated using Wang et al. [23] and Hankinson et al. [24] equations. Adverse events from patient report every 28 days, and from medical record review were collected.