

Cystic Fibrosis Research News

Title:

Improvement of lipid and lipoprotein profiles in children and adolescents with cystic fibrosis on CFTR modulator therapy

Lay Title:

CFTR modulator therapy may improve lipid levels in children and adolescents with cystic fibrosis.

Authors:

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What was your research question?

The main goal of this study was to investigate the effect of CFTR modulator therapies on the levels of various lipids and lipoproteins in children and adolescents with cystic fibrosis (CF).

Why is this important?

Over several decades, to offset malabsorption and underweight, many people with CF (pwCF) consumed unrestrictive high fat /high calorie diets. These diets are often associated with obesity, hyperlipidemia, hypertension, cardiovascular disease (CVD) risk, and type 2 diabetes in the general population. Previous research determined that people with CF have lower total cholesterol and lower high-density lipoprotein (HDL) cholesterol compared to people without CF. At the same time research showed higher triglycerides (type of fat found in your blood) levels in pwCF, suggesting higher CVD risk.

As life span expectations for pwCF increase, so has concern for the impact of high fat/high calorie diets on acquiring diet-related chronic disease.

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What did you do?

Blood samples were obtained from 153 children and adolescents with CF (subjects) and 60 people without CF (controls) with the same age. Seventy percent of these samples were from pwCF on the CFTR modulator therapy for greater than one month. Dietary recalls were collected for the 24-hour period prior to the blood draw. At least one copy of the most common CF-causing gene (F508del) was present in 97% of subjects. Overall, CF subjects were clinically stable with good lung function and generally well nourished. Most pwCF (91%) were pancreatic insufficient, and 14% had glucose intolerance or CF-related diabetes.

What did you find?

Dietary recalls from CF subjects revealed $36 \pm 8\%$ of total calories were derived from fat, higher than the recommended 25-30% for the general population. Total cholesterol and low-density lipoprotein (LDL) cholesterol levels were significantly lower in pwCF compared to controls. However, only pwCF not receiving CFTR modulators had also significantly lower anti-atherogenic HDL cholesterol and HDL particle number than controls. Individuals on modulator therapy had higher concentrations of HDL cholesterol and HDL particles with lower levels of atherogenic lipids compared to pwCF without CFTR modulator therapy.

What does this mean and reasons for caution?

CFTR modulator therapy seems to have a beneficial effect on lipid profiles in CF. Modulator use was associated with higher levels of “good” HDL cholesterol and HDL particle number, while measures associated with greater CVD risk such as large VLDL particles, small LDL particles and triglycerides were lower in participants on modulators compared to pwCF without modulators. It remains to be seen if these positive changes translate into decreased CVD risk later in life given the increasing life expectancy in CF.

What's next?

Shifting away from a high fat/high calorie dietary intake to a more moderate, individualized, and healthier diet has potential to further impact lipid levels. A focus on high quality and nutrient dense food with healthy fats should be encouraged. Routine lipid monitoring could inform and improve dietary recommendations.

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