Cystic Fibrosis Research News

Title:
Alterations in lipids after initiation of highly effective modulators in people with cystic fibrosis

Lay Title:
Changes in cholesterol levels in people with cystic fibrosis after starting highly effective modulators

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What was your research question?
We were interested to learn if blood cholesterol levels changed in people with cystic fibrosis (CF) after starting on highly effective modulator therapy (HEMT) like ivacaftor and elexacaftor/tezacaftor/ivacaftor. We predicted that HEMT would negatively impact cholesterol levels (total cholesterol [TC], low-density lipoprotein [LDL], high-density lipoprotein [HDL], and TC/HDL ratio).

Why is this important?
There have been many changes in health and life expectancy for people with CF due to HEMT. Although cardiovascular disease (CVD) has been rare in people with CF, some of the risk factors such as being overweight or obese, development of diabetes, and aging are increasing in the CF population. High cholesterol is another important risk factor for CVD. People with CF previously had low levels of cholesterol before widespread availability of HEMT. We do not know how cholesterol levels may be changing in CF now that there are more patients starting on HEMT.

What did you do?
From review of prior medical records, we identified 41 patients at our CF center that had their cholesterol levels checked at some time before starting HEMT, and at some point after starting HEMT. We did not include patients who had had a solid organ transplant. Patients' records were also evaluated for other risk factors for CVD, such as high blood pressure, tobacco smoking, and family history of CVD.

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What did you find?

We found large increases in the levels of TC and LDL ("bad" cholesterol associated with increased risk of CVD), and in the TC/HDL ratio after starting HEMT, but levels of HDL ("good" cholesterol associated with lower risk of CVD) did not change. Body mass index (BMI) also increased considerably after starting HEMT. We found that patients who had a family history of CVD risk factors had a larger increase in their TC and LDL levels over time. Patients who had a history of CF liver disease did not have as large of a change in TC and LDL.

What does this mean and reasons for caution?

Based on this study's results, we recommend careful consideration of cholesterol screening in people with CF, especially those using HEMT with other CVD risk factors like family history. Our study has limitations. Cholesterol levels were not always collected when patients were fasting and different testing locations may have led to variations in results. Our population may also be a higher risk group for CVD: they were older (average age: 44 years old), with higher rates of high blood pressure, CF related diabetes, and obesity than reported in the US CF registry, and so these results may not reflect changes in the broader CF population.

What's next?

Repeating this study in a lower risk group of CF patients will help confirm our study's findings. More studies are needed to understand the ways in which HEMT may be impacting cholesterol levels, and if people with CF go on to develop CVD as a result of cholesterol changes.

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