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Cystic Fibrosis Research News

Title:
Changes in fecal microbiota with CFTR modulator therapy: A pilot study

Lay Title:
Pilot study suggests that the gut bacteria in people with CF change with CFTR modulator therapy

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What was your research question?
Studies have shown that people with cystic fibrosis (CF) have different bacterial communities-microbiomes- in their guts compared with people without CF. We wanted to see whether and how the gut microbiomes of people with CF would change when they begin treatment with two different CFTR modulator treatments—ivacaftor and lumacaftor/ivacaftor—both of which treat the underlying cause of CF for people with different CFTR mutations.

Why is this important?
The gut microbiome normally plays several important roles in health and development. For example, gut bacteria extract nutrients and energy from otherwise undigested food, help the body to absorb these nutrients, and regulate the immune system's activities in the digestive system and in other organs, including the lungs. Recent evidence suggests that people with CF have different combinations of bacteria in their guts compared with other people, and that this "CF dysbiosis" could play a part in many problems common in CF, including difficulties gaining weight or height, problems absorbing vitamins and fats in the intestine, development of diabetes and liver disease, and even lung disease.

What did you do?
We identified the bacteria in stool samples from two groups of people with CF before and after they started treatment with either ivacaftor or lumacaftor/ivacaftor. The people in the two groups had different degrees of gastrointestinal disease, especially in terms of their

abilities to absorb nutrients: Those taking lumacaftor/ivacaftor generally had normal absorption. Two weeks after starting to take lumacaftor/ivacaftor, that group also started taking antibiotics, allowing us to compare the effects of the modulator treatment, which has not yet been studied well, and of antibiotics, which we known can change microbiomes and provided a useful comparison.

What did you find?

Many people did not have an obvious change in either their nutrient absorption or the in their stool bacteria with either CFTR modulator treatment. However, most people taking antibiotics had a noticeable change in bacteria, showing that CFTR modulators do not always change how well the intestines work or their gut bacteria. However, those with problems absorbing nutrients had an obvious change in how well fat was absorbed after starting ivacaftor, and we saw parallel trends of changes in their stool bacteria. In fact, with ivacaftor treatment, this group's stool bacteria looked more like those of people with mild or no digestive problems.

What does this mean and reasons for caution?

Our findings suggest that ivacaftor allows nutrients to be better absorbed in some people with CF and may alter the bacteria in their intestines to become more like the combinations seen in people with less severe digestive problems. This is important because firstly, restoring the function of CFTR, which is defective in CF, may improve nutrient absorption and availability. Secondly, the parallel changes we found in gut bacteria and nutrient absorption with ivacaftor treatment suggests that the different gut bacteria people with CF tend to carry may hamper their nutrition. This finding opens the door to new potential treatments for malnutrition; however, these early results need further study and confirmation.

What's next?

These results must be checked in a larger study of more people with CF. In addition, the people who took part in this study were less likely to have dramatic improvements in their nutrient absorption than those who are taking the newest generation of CFTR modulators, such as elexacaftor/tezacaftor/ivacaftor, who should also be studied.

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