Cystic Fibrosis Research News

Title:
The effect of elexacaftor/tezacaftor/ivacaftor (ETI) on glycemia in adults with cystic fibrosis

Lay Title:
The effect of ETI (Trikafta™) on blood sugars in adults with cystic fibrosis

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What was your research question?
Elexacaftor-tezacaftor-ivacaftor (ETI) was approved for use in 2019. ETI improves lung function in individuals with the most common CF mutation, F508del. But what is the impact of this medication on blood glucose (sugar)? Our goal was to investigate the effect of starting ETI on blood sugar levels in adults with CF.

Why is this important?
As care improves and individuals with CF live longer, they are at risk for other problems associated the disease outside of the lungs, particularly cystic fibrosis related diabetes (CFRD), which causes high blood glucose levels. CFRD has been associated with worse lung function, poor nutritional status, and earlier death. Prior studies looking at how older versions of CFTR modulators (ivacaftor and invacaftor/lumacaftor) impact glucose showed mixed results. If ETI does improve glucose, this may help us better understand how CFRD develops, slow or lessen progression to CFRD, and guide future studies developing new treatments for CFRD.

What did you do?

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We utilized a new type of diabetes technology called continuous glucose monitoring (CGM), which uses a sensor worn just under the skin to continuously measure glucose levels (instead of using finger pricks). We enrolled 34 adults with CF before they started treatment with ETI. Half of these individuals had a history of CFRD, and half did not. Each adult wore a CGM sensor for 14 days before starting ETI, then again 3-12 months after starting ETI. We also asked participants to tell us about symptoms of low blood glucose, and recorded recent height, weight and lung function data from their medical records.

What did you find?

When we compared CGM results from before and after starting ETI, participants had significant improvements in several important measures, incuding average glucose, standard deviation (how much glucose levels fluctuated), the percentage of time glucose was in the high range (above 200 mg/dL), and the percentage of time that glucose was in the goal range (70-180 mg/dL). Participants also did not have any increase in the frequency of low glucose, either measured by CGM or reported with symptoms. Improvements were more notable in individuals with CFRD, but were also seen in individuals without CFRD.

What does this mean and reasons for caution?

This is the first prospective study looking at the impact of ETI on glucose in adults with CF. Our results will help patients and providers anticipate glucose changes when starting ETI. These results also raise the promising possibility that ETI could improve glucose abnormalities and potentially delay the development of CFRD, particularly as ETI is approved for use in younger children.

Due to the impact of COVID-19 on in-person visits, only 23 participants completed the study. The study was relatively small and from a single geographic area. If participants had worn CGMs throughout the entire study period, we would have collected much more data for our analysis.

What's next?

Further studies are needed to better understand the reason why ETI improves glucose, and if these changes have any long-term effects on the development or severity of diabetes in individuals with CF.

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