



Cystic Fibrosis Research News

Title:

Glucose ingestion in cystic fibrosis induces severe redox imbalance: a potential role in diabetes

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What was your research question?

Redox is a chemical reaction that involves electrons moving from one molecule (called a reducing agent) to another molecule (called an oxidizing agent). In the body, redox balance refers to the proportion of a reducing agent to an oxidizing agent and this can vary according to different sites in the body. We wanted to see if having CF would make you more likely to have a **redox imbalance** after eating simple sugars.

Why is this important?

Diabetes associated with CF is common. Diabetes in CF can make a person's lung disease worse, but we are not sure why. There is evidence that having CF may make a person more likely to have a redox imbalance (where they have too many oxidized agents in their body). Diabetes may make this worse, which may cause more inflammation. This could further damage a person's cells including in their lungs and their pancreas. If we see that development of a redox imbalance is one of the reasons diabetes makes CF worse, we may be able to develop new therapies if we better understand this process.

What did you do?

People with CF were recruited and divided into groups based on whether or not they had diabetes. People without CF or diabetes were also included in the study as "healthy controls." Participants took an oral glucose tolerance test (a test to diagnose diabetes). Basically, after not eating anything overnight, participants were given a sugary drink with a specific amount of glucose (sugar) in it. We then measured markers of inflammation, their redox status and insulin production in their blood, both before and for two hours after, they drank the drink.

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What did you find?

Interestingly, there were no significant differences between groups in their fasting blood sugars or levels of inflammation. However, having CF made their redox imbalance worse, and the imbalance was even greater (more oxidized) if they had CF and diabetes. After drinking a sugar drink, healthy controls were able to keep their blood redox mostly balanced. However, for people with CF, they had a significant worsening of their redox imbalance after a sugar drink. Finally, the more imbalanced their blood redox levels (more oxidized), the less insulin they were able to secrete to manage their blood sugars.

What does this mean and reasons for caution?

We speculate that repeated exposures to redox imbalance in CF and CF diabetes can cause a chronic imbalance and lower insulin release. In turn, this may cause poorer blood sugar control and lead to cell damage.

This is a small study and so the findings may not apply to everyone. All of these participants were stable and not experiencing a pulmonary flare-up. We do not know how their redox balance may behave if they were acutely sick. Also, most of these participants were not on the new CFTR modulators. We do not yet know how CFTR modulators (eg: Trikafta) may affect redox balance and blood sugar control.

What's next?

Future studies will need to look at CF redox balance during different states of health. We also need to see if the redox imbalance is all over the body, or just in certain areas. We need to find out whether this sugar-induced imbalance is present in CF toddlers as we now believe that the steps leading to CF diabetes begins in young children. Finally, we want to see if health outcomes are better if we can fix the redox imbalance that we see here.

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