
Metabolic and Pharmacokinetic Profiling of a Ketone Ester by Background SGLT2 Inhibitor Therapy in HFrEF

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Why We Did This Study

Heart failure with reduced ejection fraction (HFrEF) is a serious heart condition affecting millions of Americans. Researchers think ketones — a natural fuel the body can make — may help the failing heart work better. A type of heart failure drug called SGLT2 inhibitors also raises ketone levels. This study tested whether a ketone drink was safe and how the body processed it in people with HFrEF, both with and without an SGLT2 inhibitor. Researchers also wanted to know how the dose of the ketone drink affected results.

Who Participated in This Study?

Twenty adults with HFrEF were enrolled at Duke University Health System between March 2023 and January 2024. Participants were at least 18 years old, had a weakened heart (ejection fraction of 45% or less), and had a systolic blood pressure of at least 90 mmHg. The average age was 64 years; 45% were women. Most were White/non-Hispanic (70%), and 20% were Black/non-Hispanic. Half had previously been hospitalized for heart failure. Ten participants were on an SGLT2 inhibitor and ten were not.



What Were the Results?



After drinking the ketone drink, blood ketone levels rose quickly — peaking within 1 to 1.5 hours — then came back down. Insulin levels went up and fatty acid levels fell. Most other blood markers also decreased. Blood pressure dropped slightly and heart rate rose slightly, but both returned to normal by the end of the visit.

Blood acidity (pH) dropped briefly but also recovered. Higher doses raised ketone levels more and caused more temporary acidity. Side effects were rare: only two participants had mild headaches. No serious side effects were reported.

What Do These Results Mean?

This study suggests the ketone drink is safe for people with HFrEF, even when taken with an SGLT2 inhibitor — a drug that also raises ketone levels. The body processes the drink quickly, which can help doctors decide on the right dose and how often to give it. Changes in blood pressure, heart rate, and blood acidity were mild and short-lived. Higher doses appear to activate more beneficial metabolic pathways but also cause more temporary acidity. These findings lay the groundwork for larger studies of ketone therapy in heart failure.
