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Effect of elevated plasma ketones on cardiac efficiency

Carolina Solis-Herrera MD, Yuejuan Qin MD, Henri Honka MD PhD, Goeffrey Clarke PhD, Curtis Triplitt PharmD, Eugenio Cersosimo MD PhD, Ralph DeFronzo MD

University of Texas Health San Antonio

Abstract

Background: The mechanism(s) responsible for the cardiac benefits of SGLT2 inhibitors remain unknown.
Specific Aim: To examine the effect of increased plasma ketone concentration (with infusion of beta-hydroxybutyrate [BOHB]) on LV function and myocardial glucose uptake.

Methods: Two groups (6 per group) of T2DM with HFrEF (<45%) were studied. Group I (Age=59; BMI=31 kg/m2; A1c = 7.2%; EF=41%) received in random order a 6-hour BOHB infusion (Prime =1.5 mg/kg.min, then 0.75 mg/kg.min) or 6-hour HCO3 infusion with matching volume (control). Group II (Age=56; BMI=34 kg/m2; A1c=7.2%; EF=38%) received a 3-hour BOHB infusion at a higher rate (Prime=4.0 mg/kg.min, then 2.0 mg/kg.min). A cardiac MRI was performed before and after each infusion. Additionally, Group I underwent a PET study with 18F-2-DOG and 15O.

Results: Groups I and II achieved plasma ketone levels of 1.4 and 2.5 mmol/L, respectively. In Group II, BOHB infusion significantly (P<0.01) increased CO and EF, whereas in Group I the increase in CO and EF tend toward significance (p=0.06), suggesting a dose-dependent response to the increase in plasma ketone concentration. NaHCO3 infusion had no effect on any cardiac indices (Fig.1). Myocardial blood flow increased significantly (P<0.01) in both Group I and II. Myocardial glucose uptake was not altered by BOHB infusion.

Conclusion: In patients with T2DM and HFrEF, a physiologic increase in plasma ketone concentration significantly increased LV function and myocardial blood flow without affecting cardiac glucose metabolism. These results suggest that altered myocardial substrate metabolism can be employed therapeutically to improve cardiac function in HFrEF.

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