Canagliflozin Therapy Affects Osmolyte Homeostasis in the Normotensive Rat by Increasing Total Urinary Betaine Excretion

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Abstract

Purpose / Objectives: Osmolytes stabilize proteins under high osmotic pressure. Betaine, one such osmolyte, has beneficial effects on the cardiovascular system. We investigated the effect of canagliflozin on betaine in rat tissues. Canagliflozin, an SGLT-2 inhibitor, is widely used in heart failure treatment, yet its mechanism of action remains unclear.

Materials / Methods: An in vivo study was conducted on 21 male Sprague-Dawley rats. They received canagliflozin for 28 days at doses of 10 mg/kg/d (LD) and 30 mg/kg/d (HD). The control group received water. Betaine and osmolyte concentrations were measured in blood, urine, and tissues. The mRNA expression of betaine transporters (scl6a12, scl6a20) was analyzed in the kidney.

Results: We have shown that canagliflozin consumption at both low and high doses increases total fluid intake and urine excretion. Canagliflozin also increased total urinary betaine excretion. In addition, the ratio of excreted betaine to creatinine is increased. There were no differences between groups in mRNA expression levels for both the scl6a12 and scl6a20 transporters.

Conclusions: Canagliflozin enhances urinary betaine excretion without affecting its retention, reducing the risk of hypertonic dehydration and promoting osmotic diuresis. These effects may support the primary mechanisms of SGLT-2 inhibitors in heart failure treatment.