Canagliflozin ameliorates renal oxidative stress in Ischemia Reperfusion Syndrome in rats non-diabetics

Ms. Sara Ventura, B.Sc, BR

Ms. Maria de Fatima F. Vattimo, RN, MsC, PhD, BR

Abstract

Recent meta-analyses have shown that sodium-glucose cotransporter 2 (SGLT-2) inhibitors alleviate acute kidney injury (AKI) in diabetic patients. This antidiabetic drug has proven effective in other comorbidities such as heart failure, however, there are no studies that report on its prevention in AKI. Ischemia Reperfusion syndrome (I/R) is one of the leading causes of AKI. The incidence of AKI is increasing, and AKI causes at least 2 million deaths worldwide/year. I/R syndrome is characterized by tissue damage mediated by reactive oxygen species (ROS) generation. Oxidative stress is considered one of the main pathogenic and aggravating factors in kidney disease, in which it contributes to AKI, to the transition from AKI to Chronic Kidney Disease (CKD), and to the progression from CKD to End Stage Renal Disease (ESRD). Thus, the purpose of this study was to investigate the renoprotective of effect of canagliflozin in I/R syndrome in non-diabetic rats. Methods: Wistar rats were randomly divided in: SHAM: surgery simulated control; I/R: ischemic group (30 minutes bilateral renal clamping); CANA: canagliflozin, 30 mg/kg once a day, 5 days; CANA+I/R: as described. Renal hemodynamics as, renal blood flow (RBF) and renal vascular resistance (RVR); renal function (inulin clearance, serum creatinine); oxidative metabolites (urinary peroxides, TBARS, urinary nitrate and thiols in renal tissue) and the activation of the nuclear factor erythroid 2-related factor 2 were analyzed. Results: Compare with Sham group, the I/R group showed significantly decrease renal function and levels of thiol antioxidants, as well as increased oxidative metabolites. Nevertheless, pretreatment with Canagliflozin reversed these changes. In addition, canagliflozin treatment resulted in a marked increase in antioxidant protein expression compared with I/R group. Conclusions: Canagliflozin did not induced hypoglycemia and has significant potential as a therapeutic intervention to ameliorate renal injury after renal I/R and attenuation of oxidative stress.

Image

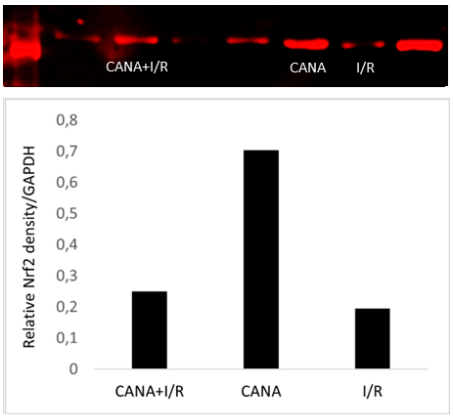


Figure 1: Representative Western blot of Nrf2 in the renal tissue and quantitative analysis of the expressive levels of Nrf2.

Recent Publications

1. Yang S, He W, Zhao L, Mi Y (2022) Association between use of sodium-glucose cotransporter 2 inhibitors, glucagon-like peptide 1 agonists, and dipeptidyl peptidase 4 inhibitors with kidney outcomes in patients with type 2 diabetes: A systematic review and network meta-analysis. PLOS ONE 17(4): e0267025.
2. Bocchi, Edimar Alcides et al. (2021) Emerging Topics in Heart Failure: Sodium-Glucose Cotransporter Inhibitors 2 (iSGLT2) in HF. Brazilian Archives of Cardiology 2021, v. 116, n. 2
3. Naomi Boyer, Jack Eldridge, John R. Prowle, Lui G. Forni (2022) Postoperative AKI. CJASN June 2022, CJN.16541221
4. Sang Jun Han, H. Thomas Lee (2019) Mechanisms and therapeutic targets of ischemic acute kidney injury Kidney Res Clin Pract. 2019;38(4):427-440.
5. Guerrero-Hue M, Rayego-Mateos S, Vázquez-Carballo C, et al. (2020) Protective Role of Nrf2 in Renal Disease. Antioxidants (Basel). 2020;10(1):39.



Biography

The student has ability in exercise search about kidney disease particularly in acute kidney disease. She has the support of her supervisor and the research group of the Animal Model Experimental Laboratory at the University of Sao Paulo's School of Nursing. It seeks to represent nursing in basic research, providing results in evidence-based care.

Email: sara.ventura@usp.br

Notes/Comments: