KSN 2021
FULLY VIRTUAL MEETING
September 02 (Thu) - 05 (Sun)

Oral Communication Abstract
Presentation No. OC2-06 (Abstract Submission No. 2320)

Oral Communications 2 Sep. 2 (Thu), 13:40-15:40

Canagliflozin attenuates Renal Tubulointerstitial Fibrosis of Hyperuricemic Nephropathy in Rats

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Objectives: Hyperuricemic nephropathy is a disease in which purine metabolism is disturbed and urate crystal deposition causes damage to renal tubular epithelial cells and interstitial tissue, leading to tubular atrophy and interstitial fibrosis. The SGLT2 inhibitor canagliflozin is a novel hypoglycemic drug that can protect the kidney by reducing urinary protein, inflammatory response, oxidative stress and other pathways.The purpose of this study was to investigate whether Cagliazin is involved in the progression of renal interstitial fibrosis in hyperuricemia kidney disease and its possible mechanism of action, so as to provide experimental basis for clinical search for new therapeutic targets to improve interstitial fibrosis in hyperuricemia kidney disease.

Methods: 24 male Sprague-Dawley (SD) rats (6-8weeks old) that weighed 200-220g. They were randomly divided into 5 groups: (1) sham (2) HN (3) HN + canagliflozin (10mg/kg) (4) HN + canagliflozin (25mg/kg) (5) HN + benazepril (10mg/kg). The HN rats model was established by feeding the mixture of adenine (0.1g/kg) and potassium oxonate (1.5g/kg) every day. All of the rats were killed after 21 days and subsequent kidneys were collected. SGLT2、COL1、FN、E-cad、α-SMA were analyzed by western blot. MCP-1、IL-1β、TNF-α、NF-κB、Smad-3 were examined by ELASA.

Results: 1. Canagliflozin alleviates renal SGLT2 expression and fibrogenesis in HN rats;
2. Canagliflozin alleviates EMT in HN rats;
3. Canagliflozin reduces the expression of proinflammatory cytokines in HN rats;
4. Pharmacologic blockade of SGLT2 abrogates NF-κB (p65) phosphorylation and suppresses TGF-β1/Smad3 signaling in the HN rats.

Conclusions: our study revealed that canagliflozin prevents TIF in HN rats. Mechanistically, the reno-protective effect of cagagliflozin are mediated by the inactivation of TGF-β/Smad3 signaling pathway, suppression of pre-inflammatory cytokines, blockade of EMT and ECM. Therefore, SGLT2 inhibitor canagliflozin could be a useful therapeutic strategy to prevent the onset and progression of renal TIF in HN.

Figure 1. Canagliflozin alleviates EMT in HN rats.

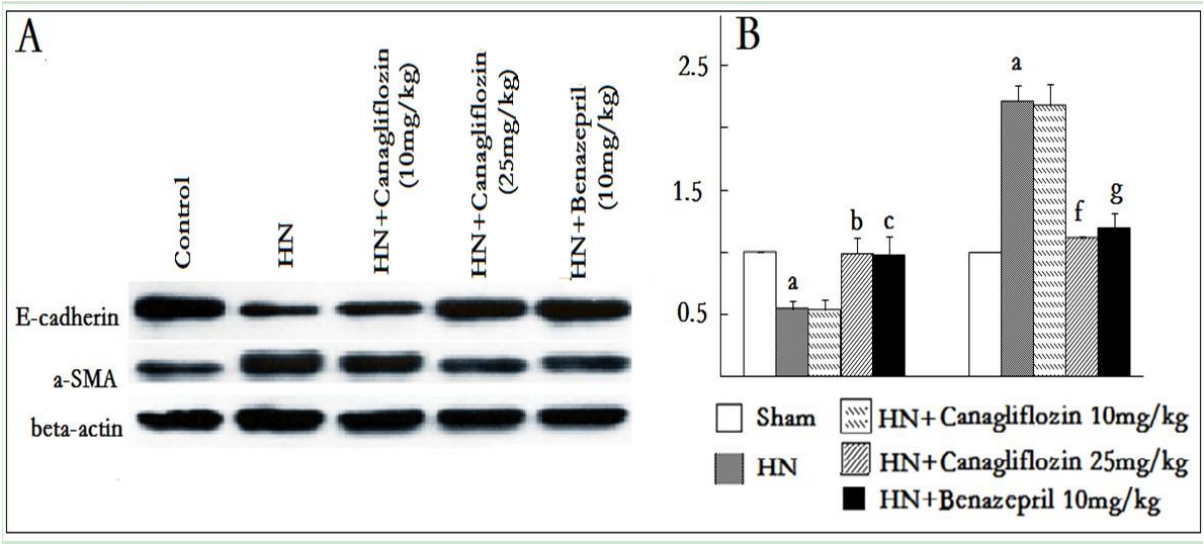

Figure 2. Canagliflozin reduces the expression of MCP-1, IL-1β, and TNF-α in the kidney of hyperuricemic rats.