P-27

SGLT2 억제제의 허혈재관류 신손상의 보호효과

대전성모병원[1], 충남대학교병원[2]

장윤경[1], 최현수[1], 정진영[2], 정사라[2], 최대은[2], 나기량[2], 이강욱[2]

SGLT2 Inhibitor Attenuates Ischemia Reperfusion Renal Injury

Yoon Kyung Chang[1], Hyun Su Choi[1], Jin Young Jeong[2], Sarah Chung[2]
Dae Eun Choi[2], Ki Ryang Na[2], Kang Wook Lee[2]

Daejeon Saint Mary Hospital[1]
Chungnam National University Hospital[2]

Introduction: SGLT2 inhibitor, dapagliflozin were developed for diabetes control. it wastes the glucose to urine. Although SGLT2 KO mice study showed no reduction of inflammation markers in type 1 DM mice model, some studies showed SGLT2 inhibition have renal protection (reduce hyperfiltration and tubular oxidative stress) in Type1 DM. We evaluate whether SGLT2 inhibitor reduces the renal damage via ischemia reperfusion (IR). Also, we investigate the associating molecular pathway.

Methods: in vitro, IR was simulated by mineral oil in HK-2 cells. Cell survival, apoptosis signal pathway, reactive oxygen species (ROS) generation, HIF1, ERK, AMPK, PGC1 alpha were evaluated in control and IR HK-2 cell with or without SGLT2 inhibitor. In vivo 10 weeks C57BL/6 mice were divided into 4 groups; vehicle (n=5) and dapagliflozin (10 mg/kg PO 4hr and 1hr before operation) treated sham group (n=5), vehicle n=7) and dapagliflozin (n=7) with IR (reperfusion 27 minutes after clamping of both renal artery and vein) renal injury. Kidneys and blood were harvested 24hr after IR injury. We performed real time RT-PCR, western blot and immunohistochemistry for molecular study and H&E stain and PAS stain for histologic examination.

Results: Dapagliflozin treatment significantly increase survival of IR HK-2 cells. Dapagliflozin treatment increase the level of HIF1 in IR HK-2 cells. Also it decrease the Bax/Bcl2 ratio and 8-OH deoxyguanosine generation. in vivo, The levels of BUN and serum creatinine in IR renal injury with dapagliflozin treated mice were significantly lower than that of vehicle with IR renal injured mice ($p<0.05$). In microscopy, dapagliflozin significantly reduced renal tubular epithelial cell necrosis and detachment. Dapagliflozin significantly increased the expression of HIF1 in IR kidney. Dapagliflozin significantly reduced 8-OH deoxyguanosine positive and TUNEL positive cells in IR kidney. Also it significantly decreased the level of Bax/Bcl-2 ratio and phosphorylated caspase -3.

Conclusion: In conclusion, dapagliflozin significantly increases HIF1 in IR injured kidney. Also it attenuates ischemia reperfusion renal injury.

Key Words: SLGT2 억제, 허혈재관류 신손상, HIF1
SGLT2 inhibitor, IR renal injury, HIF1