KSN 2019
Seoul, Korea · May 23 - 26

Abstract Type : Oral
Abstract Submission No. : OR-1309

Empagliflozin attenuates diabetic tubulopathy by improving mitochondrial fragmentation and autophagy

Yu Ho Lee[1], Jun Mo Kang[1], Dong-Jin Kim[2], Seon Hwa Park[2], Minji Sung[1], Jaehee Kim[1], Dong Ho Yang[1], Sang Ho Lee[2], **So-Young Lee[1]**
[1]Department of Internal Medicine-Nephrology, CHA University, Korea, Republic of
[2]Department of Internal Medicine-Nephrology, Kyung Hee University Hospital at Gangdong, Korea, Republic of

Objectives: We examined the effects of empagliflozin, a selective inhibitor of sodium glucose cotransporter-2 (SGLT-2) on mitochondrial quality control and autophagy in renal tubular cells in a diabetic environment in vivo and in vitro.

Methods: Human renal proximal epithelial cells (hRPTCs) were incubated in high-glucose conditions. Diabetes was induced with streptozotocin in male C57/BL6J mice.

Results: Improvements in mitochondrial biogenesis and balanced fusion/fission protein expression were noted in hRPTCs after treatment with empagliflozin in high-glucose media. Empagliflozin also increased autophagic activities in renal tubular cells under high glucose environment which was accompanied with mTOR inhibition. Moreover, reduced mitochondrial ROS production and decreased apoptotic and fibrotic protein expression were observed in hRPTCs after treatment with empagliflozin, even in hyperglycemic circumstance. Importantly, empagliflozin restored AMPKα phosphorylation and normalized the levels of AMP/ATP ratios in human renal tubular cells subject to a high-glucose environment which suggested the way of empagliflozin to involve in mitochondrial quality control. Empagliflozin effectively suppressed SGLT2 expression and ameliorated renal morphologic changes in the kidneys of STZ-induced diabetic mice. Electron microscopy analysis showed that mitochondrial fragmentation was decreased, and 8-OHdG content was low in the renal tubular cells of the empagliflozin treatment groups compared with those of the diabetic control group.

Conclusions: We suggest one mechanism related to the renoprotective actions of empagliflozin, which reverse mitochondrial dynamics and autophagy.