

中文題目:鈉-葡萄糖共同運輸蛋白-2 抑制劑恢復糖尿病腎臟之RBP4 接受器訊息及腎臟的傷害

英文題目:Sodium-glucose cotransporter 2 inhibitor retrieves disruption of RBP4 receptor signals and renal damage in kidney of diabetes

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Background: Sodium-glucose cotransporter 2 inhibitors (SGLT2 inhibitors) have been demonstrated to capably lower CV events, mortality and albuminuria in type 2 diabetes. However, the mechanisms of these benefits from SGLT2 inhibitors are still speculative. In the kidneys and artery of dyslipidemia, we found that the perturbation of retinol-binding protein 4 receptor (RBP4R) signals can cause dyslipidemia-related renal and vascular disease. In this study, SGLT2 inhibitor was investigate to attenuate renal damage and reverse the perturbation of RBP4 receptor signals in high glucose-cultured HEK cells and in the kidney of *db/db* diabetic mice.

Methods: 23 week-old mice were subdivided into: (1) control (n=3); (2) control + empagliflozin (10 mg/kg/day) for 2 weeks (n=3); (3) *db/db* + insulin (lantus 0.5 U/day) (n=3); (4) *db/db* + insulin (lantus 0.5 U/day) + empagliflozin (10 mg/kg/day) for 2 weeks (n=4). Blood glucose values of 4 groups were 60.3±16.7, 63.0 ± 6.6, 313.3 ±49.2, 234.3 ±19.4 mg/dL at the end of study, respectively. The expression of SGLT2, p-JNK1, p-Smad2, TGF β, collagen 1, coallagen 3, RARα, CRBP1, LRAT and CRABP were measured by Western blot. Retinol, retinal and retinoic acid were measured by enzyme assay. SGLT2, TUNEL and trichrome stain were performed by immunohistochemistry.

Results: Empagliflozin can reduce the increase of albumin/creatinine ratio and reverse the increase of SGLT2, p-JNK1, p-Smad2, TGF β, collagen 1, collagen 3, TUNEL and trichrome stain in the kidney of *db/db* mice while empagliflozin can retrieve the disruption of RBP4 receptor and retinol signals, including retinol, retinal, retinoic acid, RARα, CRBP1, LRAT and CRABP. In high glucose-cultured HEK cells, SGLT2 inhibitor reversed the increase of SGLT2, STRA6, collagen 1, and apoptotic cell, and retrieved the suppression of retinol signals caused by high glucose.

Conclusion: SGLT2 inhibitors can attenuate renal damage and rescued the perturbation of RBP4 receptor/retinol signals in kidney of diabetes.