

Resveratrol의 당뇨병성 신병증에서 AMPK-SIRT1-PGC-1 α 와 PPAR- α -ERR1 α 신호전달 체계를 통한 lipotoxicity에 대한 보호효과

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Resveratrol Prevents Renal Lipotoxicity by Activating the AMPK-SIRT1-PGC-1 α Pathway and Its Downstream PPAR- α -ERR-1 α in db/db Mice

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Aim/hypothesis: AMPK and SIRT1 play key roles in the regulation of lipid and glucose homeostasis and in the control of oxidative stress. Many of the effects of resveratrol are consistent with the activation of SIRT1-AMPK-PGC-1 α and the modulation of their targets.

Methods: Four groups of male C57BLKS/J db/m and db/db mice were used in this study. Resveratrol was oral gavaged to diabetic mice and nondiabetic mice (db/m Res, n=8) starting at 8 weeks of age for 12 weeks.

Results: Presently, db/db mice treated with resveratrol displayed decreased albuminuria. Resveratrol ameliorated glomerular matrix expansion, inflammatory cell infiltration and the free fatty acid and triglycerides contents associated with increased phospho-Thr172 AMPK-SIRT1-PGC-1 α signaling, and one of the key downstream effecters the PPAR α -ERR-1 α expressions compared to the control db/db mice. Furthermore, resveratrol decreased the activity of PI3K-Akt phosphorylation and FoxO3a phosphorylation, which resulted in a decrease of Bax and increases in Bcl-2 and SOD1 and SOD2 expressions. Consequently, resveratrol reversed the increased renal apoptotic cells and oxidative stress, as reflected by the serum 8-OH-dG and the urinary 8-OH-dG and isoprostan levels. In cultured mesangial cells, resveratrol prevented high glucose-induced oxidative stress and apoptosis, which were related to the inactivation of phospho-Thr172 AMPK-SIRT1-PGC-1 α signaling and their downstream effecters the PPAR α -ERR-1.

Conclusions: interpretations The collective results suggest that resveratrol prevents diabetic nephropathy in db/db mice by activation of AMPK-SIRT1-PGC-1 α signaling, which results in prevention of lipotoxicity, apoptosis and oxidative stress in the kidney.

Key Words: 당뇨병성 신병증, 지방독성, 보호효과

Diabetic nephropathy, Resveratrol, Prevention