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제2형 당뇨병성 신증 진행과정에 따른 혈관내피성장인자 억제제 dRK6의 효과

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Different Effects of anti-VEGF Hexapeptide dRK6 on the Diabetic Nephropathy of db/db Mice According to the Evolution of Diabetes

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We examined the renal effects of hexapeptide dRK6, which blocks the interaction between VEGF-A and the VEGF receptor (VEGFR), in the evolution of type 2 diabetes.

The continuous treatment group in male db/m and db/db mice were treated with dRK6 for 12 wks from 8 wks of age. In db/db mice, the early treatment group was treated for the first 4 weeks and the late treatment group was treated for the last 4 weeks. Diabetes significantly suppressed the VEGF-receptor (VEGFR)-1 and increased VEGFR-2 in the kidneys. Interestingly, dRK6 completely inhibited VEGFR-2, phospho-Akt/eNOS expression, and urinary nitrate/nitrite in the db/db dRK6 early and continuous treatment groups, whereas no effect on VEGFR-1. In the diabetic control, the db/db dRK6 early and continuous treatment groups, albuminuria associated with weak nephrin signaling, glomerulosclerosis and inflammation, and pro-fibrotic growth factors' expressions were more prominent than those of non-diabetic control. They also exhibited increases in the number of apoptotic endothelial cells and strong HIF-1α and 8-hydorxy-deoxyguanosine expressions in the glomerulus. By contrast, dRK6-induced renal changes were not observed in the db/m mice and the db/db dRK6 late treatment group. Only at the high-glucose concentration (30 mmol/L), dRK6 treatment increased the number of apoptotic HUVECs in a dose-dependent manner ($p<0.01$), which was associated with decreases in phospho-Akt/eNOS and NO signals. Taken together, the blockade of VEGF-A/VEGFR-2 using dRK6 provided different renal effects according to the evolution of type 2 diabetes, suggesting that phospho-Akt/eNOS-NO signaling could be a determinant of renal injury.

Key Words : 당뇨병성 신증, 산화질소, 혈관내피성장인자
Diabetic nephropathy, NO, VEGF