

당뇨쥐에서 안지오텐신 II 수용체 억제제가 사구체 족세포에 미치는 영향 : Vascular Endothelial Growth Factor 과발현의 차단을 통한 신보호 효과

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Vascular endothelial growth factor (VEGF) is a potent cytokine that markedly increases vascular permeability to macromolecules and is abundantly expressed in glomerular podocytes. Angiotensin II can stimulate the release of VEGF, and the protective effects of angiotensin II antagonist against diabetic glomerular injury suggest that the angiotensin II-induced VEGF is an important pathogenetic mechanism in the development of proteinuria during diabetic nephropathy. However, this mechanism is not fully understood, so we studied the changes of VEGF expression in experimental diabetic nephropathy to determine whether these changes were modified by renoprotective intervention by blockers of angiotensin II receptors. We observed streptozotocin-induced diabetic rats without and with L-158,809, a blocker of angiotensin II receptors, for 12 weeks. Age-matched rats without and with L-158,809 served as controls.

Semiquantitative reverse transcription-polymerase chain reaction and immunohistochemistry were used to assess and quantify gene and protein expression of VEGF. A progressive increase in urinary protein excretion was observed in diabetic rats. Glomerular VEGF expression was significantly higher in diabetic rats than in the control groups, with a significant reduction in glomerular VEGF expression and proteinuria in L-158,809-treated diabetic rats. VEGF mRNA was also significantly higher in diabetic kidneys than in the control groups, with a significant reduction in VEGF mRNA in L-158,809-treated diabetic kidneys. This study demonstrates that VEGF expression is significantly increased in diabetic podocytes, and angiotensin II receptor antagonist attenuated these changes in VEGF expression and prevented the development of proteinuria in vivo. Attenuation of increased VEGF expression in podocytes could contribute to the renoprotective effects of angiotensin II receptor antagonists in diabetic nephropathy.

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