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당뇨병성신증 진행에 있어 ACE와 ACE2의 역할

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The Role of Renal ACE and ACE2 in the Progression of Nephropathy in Diabetic Rats

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Purpose : The angiotensin converting enzyme-related carboxypeptidase 2 (ACE2) has a high affinity for angiotensin II, resulting in its degradation to the vasodilator, angiotensin 1-n it may counterbalance the angiotensin II forming activity of ACE. The renin-angiotensin system (RAS) has been implicated in the pathogenesis of diabetic nephropathy, however, the role of ACE2 in the regulation of RAS is not well known. The present study was conducted to investigate the changes of ACE and ACE2 expression in the kidney under the hypothetic basis that the reduction of ACE2 is associated with the development and progression of diabetic nephropathy.

Methods : Streptozotocin induced diabetic rats were examined at two and eight weeks. Levels of the angiotensin I and angiotensin II were measured in plasma, urine, and tissue from the renal cortex. ACE and ACE2 from the renal cortex were assessed by reverse transcription-polymerase chain reaction, Western blot, and immunohistochemistry.

Results : Urinary albumin excretion was markedly increased in the eight week diabetic rats. The plasma level of angiotensin II was increased with hyperglycemia but the urinary level of angiotensin II excretion was increased according to the development of proteinuria. For renal cortical tissue, the increment of increased angiotensin II levels was more intensified in the eight week diabetic rats than in the two week diabetic rats. With the onset of proteinuria, ACE expression was higher at both the mRNA and protein levels; the presence of ACE2 protein demonstrated a 2.2 fold higher level with no significant difference at the mRNA level when compared to the other rats. Tubular immunohistochemical staining of ACE and ACE2 had a similar pattern to that of the protein expression. Immunohistochemical staining of glomerular ACE was increased in the eight week diabetes rats while ACE2 was decreased.

Conclusion : In the early diabetic rats with nephropathy, the development of proteinuria was related to glomerular decrease of ACE2 and increase of ACE; these events may lead to activation of tubular RAS. These findings suggest an association between increased levels of intrarenal angiotensin II and the progression of diabetic nephropathy. This study also proposes the different pattern of ACE2 activity in the glomeruli and tubules in the development of diabetic nephropathy.