

제2형 당뇨병 모델에서 당뇨병성 혈관질환에 대한 레닌 차단제의 효과

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Effect of Direct Renin Inhibition on the Progression of Diabetic Vascular Complication in Type 2 Diabetic Mice

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Aliskiren, a highly potent inhibitor of renin, is a new orally available, highly specific, and effective inhibitor of RAAS (renin-angiotensin-aldosterone system) activity. Clinical studies have provided convincing evidences of both blockade of RAAS and blood pressure lowering effect of direct renin inhibitor. However, there is a little in vivo evidence which show the organ protective effect of direct rennin inhibitor in type 2 diabetic animals. We investigated the effects of Aliskiren on diabetic vascular complications in db/db mice. Experimental animals were treated with or without aliskiren at a dose of 25 mg/kg/day via osmotic minipump for three months, and observed various biochemical parameters at the end of study period. Aliskiren treatment did not induce significant changes in blood glucose levels and blood pressure. However, aliskiren treatment induced an improvement in insulin resistance state including HOMA-IR and plasma insulin levels and improved lipid abnormalities. Aliskiren treatment also markedly improved urinary albumin excretion and cardiac functions including systolic and diastolic functions and LVH (left ventricular hypertrophy). There were no significant changes in serum creatinine, sodium and potassium levels between diabetic controls and aliskiren treated diabetic groups. Although there was no statistical difference, aliskiren treatment reduced a plasma renin activity (PRA) and plasma aldosterone levels. In accordance with these biochemical changes, aliskiren treatment suppressed mRNA expressions for MCP-1 (monocyte chemoattractant protein-1), TGF- β 1 (transforming growth factor- β 1), PAI-1 (plasminogen activator inhibitor-1) and type IV collagen in both kidney and heart, which were remarkably up-regulated in type 2 diabetic mice. Interestingly, urinary excretion of VEGF was also dramatically decreased after aliskiren treatment. Taken together, these data suggest that aliskiren treatment provided organ protective effect through both improvement in metabolic alteration and molecular alteration in type 2 diabetic animals.

Key Words : 레닌 차단제, 당뇨병성 신증

Aliskiren, Renin inhibitor, Diabetic complication