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2형 당뇨 쥐에서 DPPIV 차단이 신기능에 미치는 효과

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Effects of Dipeptidyl Peptidase IV Inhibition on Renal Function in Type 2 Diabetic Mice

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Purpose: The aim of the present study is to investigate the mechanism and effect of dipeptidyl peptidase (DPP) IV inhibition on renal injury in db/db mice.
Methods: The mice were divided into three groups as follows: non-diabetic db/m mice, untreated db/db mice, and db/db mice treated with DA-1229 (300mg/kg/d) for 12 weeks.
Results: There were no difference in liver, fat and heart DPP4 activities and active GLP-1 levels between db/m mice and db/db mice, and these activities were suppressed by DA-1229 in db/db mice. Although plasma DPPIV activity did not show significant differences among groups, DPPIV activity in kidney was significantly higher in diabetic mice compared with control db/m mice, which was abolished by DPPIV inhibition. DPPIV treatment induced significant improvement in lipid abnormality and hepatic steatosis. However, there was no significant change in HbA1c and HOMA-IR after DPPIV inhibition. Treatment with DA-1229 for 12 weeks showed a little effect on body weight, systolic blood pressure and insulin resistance. DA-1229 treatment improved renal lipid metabolism, renal hypertrophy and significantly decreased urinary albumin excretion and fibrotic process in the kidney. Moreover, treatment with DA-1229 induced a significant reduction in serum creatinine and improvement in creatinine clearance in db/db mice. Interestingly, DA-1229 treatment significantly decreased urinary excretion of nephrin, and high glucose and angiotensin II stimulation significantly increased DPPIV activity in cultured podocytes.
Conclusion: A novel DPPIV inhibitor, DA-1229 improved lipid abnormality and ameliorated renal injury in db/db mice independent of glucose lowering effect. Our data suggest that renoprotective effects of DA-1229 in db/db mice may be associated with suppression of kidney DPPIV activity irrespective of insulin resistance and possibly mediated by improvement of podocyte injury.

Key Words: DPPIV, 당뇨병성신증, 족세포
DPPIV, Diabetic nephropathy, Podocyte