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고지방식이 유도 비만쥐에서 dipeptidyl peptidase-IV 억제제의 신보호효과 규명

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Renoprotective Effects of Dipeptidyl Peptidase-IV Inhibition in High Fat Diet-induced Obese Mice

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Aims: dipeptidyl petidase-IV (DPP-IV) inhibition is currently being regarded as a promising strategy for diabetes management. However, its direct anti-enzymatic effect on kidney and its consequences are largely unknown. Therefore, in this study, we tested whether DPP-IV inhibition contributes to renoprotection and identified its mechanisms using high fat diet-induced obese mice model.

Methods: normal chow-fed control mice, vehicle-treated high fat diet-induced obese mice, and DPP-IV inhibitor (LC15-0444)-treated high fat diet-induced obese mice were assessed by various metabolic parameters and by the changes in DPP-IV activity of target organs, including kidney.

Results: after 3 months of treatment, the high fat-induced obese mice administered LC15-0444 at the dose of 3 mg/kg via gastric intubation showed no differences in the levels of blood glucose, blood pressure, insulin resistance and oxidative stress parameters, or pro-inflammatory and fibrotic mRNA expressions both in kidney and adipose tissue, compared with vehicle-treated high fat-induced obese mice. However, treatment with LC15-0444 significantly decreased levels of DPP-IV activity measured by fluorophotometric assay in serum, kidney, and liver of the experimental mice. Furthermore, the mice treated with LC15-0444 showed significantly reduced microalbuminuria excretion and the tendency to preserve renal function measured by creatinine clearance. In addition, the mice treated with LC15-0444 also showed significantly decreased left ventricular mass index.

Conclusion: DPP-IV inhibition seems to contribute to target organ protection via modulation of DPP-IV activity, possibly independently of blood glucose control or modulation of metabolic parameters. Further investigations are warranted to elucidate these mechanisms.

Key Words: DPP-IV, 당뇨병성 신증, 비만
DPP-IV, Diabetic nephropathy, Obesity