F-D9

2형 당뇨 쥐에서 DPPIV 억제제 단독치료 및 ARB와의 병합 치료가 신기능에 미치는 효과

고려대학교 안산병원 내과[1], 안양 샘병원[2], 원광대학교 산본병원 내과[3], 인하대학교 병리과[4]

민혜숙[1], 김성진[2], 김기태[1], 차진주[1], 김정은[1], 기정연[1], 이지은[3], 김현욱[3], 한지영[4], 강영선[1], 차대룡[1]

Effects of DPPIV Inhibitor Versus Combined Treatment with DPPIV Inhibitor and ARB on Renal Function in Type 2 Diabetic Mice

Hye Sook Min[1], Sung Jin Kim[2], Ki Tae Kim[1], Jin Joo Cha[1], Jung Eun Kim[1], Jung Yeon Ghee[1]
Ji Eun Lee[3], Hyun Wook Kim[3], Jee Young Han[4], Young Sun Kang[1], Dae Ryong Cha[1]

Department of Internal Medicine[1] Korea University Ansan Hospital
Sam Hospital in Anyang[2]
Department of Internal Medicine[3] Wonkwang University Sanbon Hospital
Department of Pathology[4] Inha University

Background: Recent evidence has shown that DPPIV is involved in all steps leading to renal fibrosis, such as inflammatory response, cell apoptosis and fibrosis. The aim of the present study is to investigate the mechanism and effects of DPPIV inhibitor (DA1229) alone and combined treatment with DPPIV inhibitor and ARB (LC158809) on renal injury in db/db mice.

Methods: The mice were divided into five groups as follows: non-diabetic db/m mice (control) (n=7), untreated db/db mice (n=8), db/db mice treated with DA1229 (300 mg/kg/d) (n=8), db/db mice treated with LC158809 (1.5 mg/kg/d) (n=8) and db/db mice combined treatment with DA1229 and LC158809 (n=8) for 12 weeks.

Results: HbA1c was significantly decreased in combined treatment with DA1229 and LC158809 at 12 weeks. Plasma and urine isoprostane were markedly increased in db/db mice. However, it did not shown significant difference in db/db mice after treatment because of differences among individual mice. DPPIV was expressed on the podocyte membrane and activated by angiotensin-II. Interestingly, expression of the nephrin in cultured podocyte was suppressed by high glucose and angiotensin-II and recovered by DA1229. However, other DPPIV inhibitors were not able to observe the recovery of nephrin. Activity of DPPIV in serum was significantly increased in db/db mice and decreased in treated with DA1229. Albuminuria was continuously decreased from after 2 months of treated with LC158809 and significantly decreased from after 3 months of treated with DA1229. However, additional decrease of proteinuria was not observed in combined treatment with DA1229 and LC158809. Administration of DA1229 and LC158809 were significant decreased in accumulation of ECM protein, TLR4 and NOX4 in glomerular. However, additional decrease of those was not observed in combined treatment with DA1229 and LC158809. Urinary excretion of nephrin was significantly increased in db/db mice and significantly decreased in combined treatment with DA1229 and LC158809.

Conclusion: In our study, additional decrease of proteinuria was not observed in combined treatment with DA1229 and LC158809. Among DPPIV inhibitors, the recovery of nephrin were observed only in DA1229. Our data suggest that renoprotective effects of DA1229 in db/db mice may be associated with protective effect of podocyte injury. DA1229 may be used as potential therapeutic agents in a variety of glomerular diseases inducing proteinuria.

Key Words: DPPIV, 당뇨병성 신증, 족세포
DPPIV, Diabetic nephropathy, Podocyte