S-C5

Gemigliptin은 혈당조절의 독립적인 당뇨병 성 신증을 향상시킨다

경희대학교 의과대학 신장내과[1], 경희대학교 의과대 병리과[2]

서정우[1], 이유호[1], 김세연[1], 김양균[1], 정경환[1], 이상호[1], 이태원[1], 임천규[1], 임성직[2], 문주영[1]

Gemigliptin Improve Diabetic Nephropathy Independent of Glucose Control in db/db

Jung-Woo Seo[1], Yu-Ho Lee[1], Se-Yun Kim[1], Yang-Gyun Kim[1], Kyung-Hwan Jeong[1]
Sang-Ho Lee[1], Tae-Won Lee[1], Chun-Gyoo Ihm[1], Sung-Jig Ihm[2], Ju-Young Moon[1]

Division of Nephrology, Department of Internal Medicine[1], Department of Pathology[2],
College of Medicine, Kyung Hee University, Seoul, Korea

Background: Recent studies have reported that dipeptidyl peptidase (DPP) IV inhibitors reduced reactive oxygen species (ROS), podocyte apoptosis, and renal fibrosis in diabetes. However, the mechanism of DPP IV inhibitor in the development and progression of diabetic nephropathy remains not clear. In this study, we examined whether DPPIV inhibitor, gemigliptin, could attenuate diabetic nephropathy in a manner associated with regulation of Akt pathway in db/db mice.

Methods: We designed four animal groups as following; 1) db/m; 2) db/db; 3) 0.04% gemigliptin- treated db/db (db/db+0.04% GG); 4) 0.4% gemigliptin-treated db/db (db/db+0.4% GG) from 8 to 20 weeks.

Results: Dose-dependent gemigliptin treatment reduced kidney to body weight ratio, urinary albumin excretion, and mesangial expansion in db/db mice. Interestingly, db/db+0.04% GG showed similar physical and biochemical characteristics to that of db/db+0.4%, although HbA1c level remain unchanged in db/db+0.04% GG. Phosphorylated-Akt (p-Akt) was increased in db/db mice, however, 0.4% gemigliptin reduced p-Akt and modulated phosphorylated-FoxO3a (p-FoxO3a). 0.4% gemigliptin significantly attenuated the ratio of Bax/Bcl2 in db/db kidney. In addition, gemigliptin regulated iNOS and NAD(P)H oxidase (Nox4, p67-phox, p47-phox and p22-phox) in db/db kidney, resulting in the reduction of 8-OHdG production.

Condusion: Our study results indicated that gemigliptin modulate Akt/FoxO3a pathway in db/db kidney. It is resulted in decrease of microalbuminuria and glomerular injury without reduction of HbA1c. In addition, oxidative stress and apoptotic injury in diabetic kidney was attenuated by gemiglipin in a dose dependent manner. As taken together these results suggest that gemigliptin improve the tyep 2 diabetic nephropathy indepnednet of glucose control.

Key Words: 당뇨병성 신증, DPP-4 억제제, Akt pathway
Diabetic nephropathy, DPP-4 inhibitor, Akt pathway