F-D7

제2형 당뇨모델인 db/db mice에서 AdipoRon에 의한 당뇨병성 콩팥병 보호 효과

가톨릭대학교 의과대학 내과학교실 신장내과

김예니, 임지희, 김민영, 홍유아, 최선령, 박훈석
정성진, 신석준, 김형욱, 최범순, 김용수, 장윤식, 박철휘

AdipoRon Ameliorates Diabetic Nephropathy in db/db Mice

Yaeni Kim, Ji Hee Lim, Min Young Kim, You Ah Hong, Sun Ryoung Choi
Hoon Suk Park, Sungjin Chung, Seok Joon Shin, Hyung Wook Kim
Beom Soon Choi, Yong-Soo Kim, Yoon Sik Chang, Cheol Whee Park

The Catholic University of Korea, College of Medicine, Department of Internal Medicine, Division of Nephrology

Adiponectin is one of the numerous bioactive substances known as adipokines produced by adipose tissue. Adiponectin is considered to interplay with other adipokines to exert the milieu of metabolic syndrome. It binds to adiponectin receptors (AdipoR), AdipoR1 and AdipoR2 and exhibits antidiabetic effects via activation of AMPK and PPAR-α pathways. Orally active synthetic small-molecule AdipoR agonist, AdipoRon binds to both AdipoR1 and AdipoR2 in vitro and ameliorates obesity-related disease such as type 2 diabetes. Besides, it has been suggested that adiponectin confers renoprotective effects in diabetes. Therefore, we investigated the possible role of AdipoRon in renal physiology in the view of prevention and development of diabetic nephropathy in diabetic mouse model. Male db/db mice and db/m controls were fed either a regular diet chow or a diet containing AdipoRon (30 mg/kg/day p.o. for 4 weeks from 17 to 20 weeks of age). Serum, urine and renal tissue specimen were obtained to analyze for changes in metabolic parameters, relevant molecular levels and their association with regard to structural influence. AdipoRon fed db/db mice showed decreased amount of albuminuria with no significant changes in the levels of serum adiponectin, glucose and creatinine and it seems to be weight neutral. In the molecular level, increased expressions of AdipoR1 and AdipoR2 in the renal cortex, more preferentially AdipoR1, were observed in db/db mice with AdipoRon administration. Consistent up-regulations of phophorylated AMPK and PPAR-α level were associated within the same group. With respect to ultrastructure, AdipoRon treatment showed favorable effects on diabetes-induced GBM thickening, foot process widening and slit diaphragm space narrowing, further decreasing glomerular matrix expansions and inflammation. Increased expressions of renal AdipoR1and AdipoR2 levels indicate that renal injury may cause a compensatory up-regulation of relevant receptors in kidneys to mitigate further renal injury. AdipoRon may control oxidative stress in glomerulus through AMPK and PPAR-α activated pathways and further contribute to prevent deterioration of renal function. The protective role of AdipoRon against the development of albuminuria seems to occur through a direct action on podocytes independently of systemic effects of adiponectin. Its reduction of oxidative stress provides protection against albuminuria and podocyte damage thereby ameliorating endothelial dysfunction.

Key Words: 당뇨병성 콩팥병, 아디포론
Diabetic nephropathy, AdipoRon