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자연발생 고혈압 쥐에서 고지방식이로 유발된 신장 지방독성에 대한 fenofibrate의 효과

가톨릭대학교 의과대학 내과학교실

정성진 · 신석준 · 임지희 · 김민영 · 정현화 · 김형욱 · 김용수 · 장윤식 · 박철휘

Peroxisome Proliferator-Activated Receptor Alpha Activator Fenofibrate Prevents High-fat Diet Induced Renal lipotoxicity in Spontaneously Hypertensive Rats

Sungjin Chung, Seok Joon Shin, Ji Hee Lim, Min-Young Kim, Hyun Wha Chung
Hyung Wook Kim, Yong Soo Kim, Yoon Sik Chang, Cheol Whee Park

Department of Internal Medicine College of Medicine The Catholic University of Korea

Background : We investigated the effects of high-fat diet and PPARα activation on the intrarenal lipotoxicity associated with renin-angiotensin system (RAS) and oxidative stress, using spontaneously hypertensive rats (SHR).

Methods : Male SHR and Wistar-Kyoto rats (WKY) at eight weeks of age were fed either a normal-fat diet or a high-fat diet without or with fenofibrate treatment for 12 weeks.

Results : Severe intrarenal lipid accumulation was noted in the SHR fed with high-fat diet compared to the WYK fed with high-fat diet ($p<0.05$), this was related to decrease in the renal PPARα expression in the SHR by 70%, whereas a high-fat diet increased the expression of PPARα in the WKY by 3 fold. A high-fat diet also activated intrarenal RAS, not the systemic, and induced oxidative stress in the kidney. By contrast, fenofibrate attenuated the weight gain, the fat mass, and insulin resistance. Fenofibrate recovered high-fat diet-induced decreases in intrarenal PPARα expression and fat accumulation and abolished intrarenal RAS activation and oxidative stress in the SHR-HF animals ($p<0.01$), which conferred protection against the increased BP, glomerulosclerosis and renal inflammation. Intrarenal free fatty acid and triglycerides concentrations correlated positively with AT II ($\gamma=0.63$, $\gamma=0.36$), 24 hr urinary 8-OH-dG ($\gamma=0.36$, $\gamma=0.39$ and negatively with PPARα contents ($\gamma=-0.47$, $\gamma=-0.44$; $p<0.05$).

Conclusion : A high-fat diet induced lipotoxicity by depletion of intrarenal PPARα, which aggravated BP and renal inflammation as a result of intrarenal RAS activation and oxidative stress. Therefore, intervention with the PPARα activators can effectively prevent diet-induced renal lipotoxicity in the hypertensive rats.

Key Words : 고혈압, 비만, PPARα
Hypertension, Obesity, PPARα