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고포도당하에서 사구체 내피세포의 알부민 투과도에 대한 활성화된 국소 레닌-안지오텐신 시스템의 역할

연세대학교 의과대학 내과학교실

팽지선, 남보영, 이순하, 강혜영, 김성훈, 이미정, 김찬호
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Activated Local Renin-Angiotensin System Plays a Role in Albumin Permeability in Glomerular Endothelial Cells under High Glucose Condition

Ji Sun Paeng, Bo Young Nam, Soon Ha Lee, He Young Kang, Sung Hoon Kim
Mi Jung Lee, Chan Ho Kim, Fa Mee Doh, Hyang Mo Koo, Hyung Jung Oh
Jung Tak Park, Seung Hyeok Han, Tae-Hyun Yoo, Shin-Wook Kang

Yonsei University College of Medicine Department of Internal Medicine

Background: Local renin-angiotensin system (RAS) is present in mesangial cells and podocytes, and their activation has been demonstrated to play an important role in the pathogenesis of diabetic nephropathy. However, little is known on local RAS within glomerular endothelial cells (GEC). This study was undertaken to investigate the existence of RAS components in GEC, their changes under high glucose conditions, and the role of local RAS in morphological and functional changes in high glucose-stimulated GEC.

Methods: GEC were exposed to 5.6 mM glucose (NG) or 30 mM glucose (HG) with or without 10-7 M losartan for 24 hours. Real-time PCR and Western blot analysis were performed for all components of RAS. Angiotensin I (AI) and AII concentrations in conditioned media were measured by ELISA. Renin activities were defined as the formation of AI in the presence of porcine angiotensinogen (AGT). Morphological changes were examined by scanning electron microscopy (SEM) and a Transwell assay was performed to determine FITC-tagged albumin permeability.

Results: AGT mRNA and protein expression were significantly increased in HG-stimulated GEC compared to NG cells. AI and AII concentrations were also significantly higher in HG-conditioned media. In contrast, there were no differences in renin activities, and angiotensin converting enzyme and AII type 1 and type 2 receptor expressions among the groups. On SEM examination, the diameter of fenestrae in HG-stimulated GEC was significantly greater compared to NG cells. The number of fenestrae tended to be increased in GEC exposed to HG, but did not reach statistical significance. A Transwell assay revealed that FITC uptakes in filtered media through HG-stimulated GEC were 3.3-fold higher compared to NG cells ($p<0.05$). The increase in fenestrae diameter and enhanced albumin permeability through GEC under HG conditions were significantly abrogated by losartan pretreatment.

Conclusions: These findings suggest that local RAS is activated in GEC under HG conditions and this activated RAS may play an important role in the development of albuminuria in diabetic nephropathy.

Key Words: 레닌-안지오텐신 시스템, 사구체 내피세포, 당뇨병성 신증
RAS, Glomerular endothelial cell, Diabetic nephropathy