

고포도당이 족세포내 국소 알도스테론계에 미치는 영향

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Local Activation of Aldosterone System within Podocytes in Diabetes

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Background : Recently, accumulating evidence has suggested that aldosterone plays an important role in the pathogenesis of diabetic nephropathy via inducing fibrosis and inflammation. Since local renin-angiotensin system (RAS) and angiotensin II type I receptor (AT1R) have been demonstrated in podocytes, there is a possibility that a local aldosterone system also exists in podocytes. However, aldosterone biosynthesis and the expression of aldosterone synthase (CYP11B2), a key enzyme in aldosterone biosynthesis, have not yet been investigated in podocytes.

Purpose : This study was performed to investigate whether a local aldosterone system was present in podocytes and whether aldosterone production and the expression of CYP11B2 and mineralocorticoid receptor (MR) were changed in podocytes under diabetic conditions.

Methods : In vivo, 32 Sprague-Dawley rats were injected either with diluent (n=16, C) or with STZ intraperitoneally (n=16, DM). In vitro, immortalized mouse podocytes were exposed to media containing 5.6 mM glucose (NG), NG+24.4 mM mannitol (NG+M), NG+10-7M angiotensin II (NG+AII), 30 mM glucose (HG), or HG+10-7 M L158.809 (AT1R blocker, ARB) for 24 hours. At 12 weeks after DM induction, 24-hour urinary albumin excretion (UAE) was determined by ELISA. Real-time PCR and Western blot were performed for CYP11B2 and MR mRNA and protein expression, respectively, with sieved glomeruli and cell lysates. Aldosterone levels in cell lysates were measured by radioimmunoassay. CYP11B2 and MR protein expression in renal tissue were also determined by immunohistochemical (IHC) staining.

Results : Glomerular CYP11B2 and MR mRNA and protein expression were significantly increased in DM compared to C rats. IHC staining scores for CYP11B2 and MR protein were also significantly higher in DM relative to C glomeruli by 181.3% and 161.5%, respectively (p<0.05). Aldosterone levels were significantly increased in HG-stimulated or AII-treated podocytes compared to NG cells by 196.5% and 213.2%, respectively (p<0.05). CYP11B2 and MR mRNA and protein expression were significantly increased in HG and NG+AII groups relative to NG cells (p<0.05), and these HG-induced increases in CYP11B2 and MR expression were ameliorated by the administration of ARB. **Conclusions:** Local aldosterone system exists within podocytes and is activated under diabetic conditions, which seems to be mediated by locally activated RAS.

Key Words : 국소 알도스테론계, Aldosterone synthase
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