

당뇨병성 신병증에서 사구체 비후 정도에 따른 Cyclin-Dependent Kinase Inhibitors (CKIs)와 세포사멸-연관 단백질의 발현 차이

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Differential Expression of Cyclin-Dependent Kinase Inhibitors (CKIs) and Apoptosis-Related Molecules in Diabetic Kidney Disease

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Background : Kidney size is increased in diabetes due to glomerular and tubular hypertrophy, which is principally mediated by CKIs. Several evidences have shown that CKIs also play an important part in the development of apoptosis, which has been considered one of characteristic findings in diabetic nephropathy (DN). We have previously shown that nephrin expression was different between relatively small and large glomeruli isolated from early diabetic rats. Moreover, prior studies have suggested that glomerular hypertrophy in diabetes does not develop in all glomeruli concurrently. Based on these findings, it is supposed that apoptosis may also occur differentially in diabetic glomeruli. In this study, we hypothesized that more hypertrophied glomeruli rather than less hypertrophied glomeruli may undergo apoptosis.

Methods : Thirty male Sprague-Dawley rats were used for the study. Fifteen rats were injected with diluent (C) and 15 with 65 mg/kg streptozotocin intraperitoneally (DM). After 3 months, glomeruli were isolated by a sieving technique using sieves with pore sizes of 250 μm , 150 μm , 125 μm , and 75 μm , and then classified into large glomeruli (on the 125 μm sieve, LG) and small glomeruli (on the 75 μm sieve, SG) groups. Western blot for apoptosis-related molecules (Bax, Bcl-2, and active caspase-3), and CKIs (p21, p27, and p57) protein expression and real time-PCR for CKIs mRNA expression were performed. The number of total cells in isolated glomeruli was determined by transmission electron microscopy.

Results : The ratio of Bax/Bcl-2 protein expression and active caspase-3 protein expression were significantly increased in DM-LG compared to DM-SG and C-SG. In contrast, Akt activity was significantly increased in DM-SG, while it was significantly decreased in DM-LG. p27 and p21 mRNA and protein expression were significantly increased in DM-SG compared to DM-LG and C-SG, but there was no difference in p27 and p21 expression between DM-LG and C-SG. The numbers of total glomerular cells in DM-SG and C-LG were significantly higher than that in C-SG. In contrast, there were significantly less total glomerular cells in DM-LG compared to the other groups.

Conclusion : Apoptosis-related molecules and CKIs were differentially expressed according to glomerular size in DN, suggesting that hypertrophic process is ongoing only in less hypertrophied glomeruli and once they become large enough, the hypertrophic mechanism seems to be replaced by apoptosis.

Key Words : 당뇨병성 신병증, 세포비후, 세포사멸

Diabetic nephropathy, Hypertrophy, Apoptosis