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# 실험적 당뇨병성 신증에서 사구체 크기에 따른 cyclin dependent kinase inhibitor (CDKi) 및 세포사멸연관 물질의 변화

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# Differential Expression of Cyclin-dependent Kinase Inhibitors (CKIs) and Apoptosis-related Molecules According to Glomerular Size in Experimental Diabetic Nephropathy

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**Background :** Diabetic nephropathy (DN) is characterized pathologically by glomerular hypertrophy and cyclin-dependent kinase inhibitors (CKIs) are known to play an important role in the development of hypertrophy under diabetic conditions. Recent study has demonstrated that nephrin expression is different according to glomerular size in experimental DN, suggesting that gene expression pattern may be different between non- hypertrophied and hypertrophied glomeruli in DN.

**Purpose :** This study was undertaken to elucidate whether there was a difference in CKIs and apoptosis- related molecules according to glomerular size in DN.

**Methods :** Twenty male Sprague- Dawley rats were injected with diluent (C, N=10) or with 65 mg/kg STZ intra-peritoneally (DM, N=10). After 3 months, glomeruli were isolated by sieving technique using sieves with pore size of 250, 200, 150, 125, and 75 μm. Six hundred glomeruli from 125 and 75 μm sieves were counted at 4℃, rinsed and transferred to three tubes (200 glomeruli per tube). For C and DM glomeruli, glomeruli from sieves with pore size of 125 μm (C- and DM- large glomeruli: C- LG, DM- LG) and 75 μm (C- and DM- small: C- SG, DM- SG) were used. Real time- PCR for CKIs (p21, p27, and p57) mRNA expression and Western blot for CKIs and apoptosis- related molecules (Bax, Bcl- 2, and active- caspase- 3) protein expression were performed. Total glomerular cell and podocyte numbers in each group were also determined by laser scanning confocal microscope. Results: The mean volumes of DM- LG ($1.62\pm0.08\times106\mu m^3$) and C- LG ($1.45\pm0.07\times106\mu m^3$) were significantly higher than those of DM- SG ($0.98\pm0.04\times106\ \mu m^3$) and C- SG ($0.93\pm0.04\times106\ \mu m^3$) ($p<0.01$). p27 and p57 mRNA and protein expression were significantly increased in DM- SG compared to DM- LG and C- SG ($p<0.05$), but there was no difference in p27 and p57 expression between DM- LG and C- SG. In contrast, the ratio of Bax/Bcl- 2 protein expression in DM- LG were 2.1- and 2.3- folds higher than those in DM- SG and C- SG, respectively ($p<0.05$). Active caspase- 3 protein expression was also significantly increased in DM- LG relative to DM- SG and C- SG ($p<0.05$). In addition, total glomerular cell and podocyte numbers were significantly decreased in DM- LG ($p<0.05$).

**Conclusion :** The expression of CKIs and apoptosis- related molecules were different according to glomerular size in DN. These findings suggest that non- hypertrophied glomeruli undergo hypertrophy, while hypertrophied glomeruli undergo apoptosis in DN.

**Key Words :** 당뇨병성 신증, 세포사멸, 사구체 비후
Diabetic nephropathy, Glomerular hypertrophy, Apoptosis