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안지오텐신 II 합성과 관련있는 유전자 다형성이 IgA 신장병 진행에 미치는 영향

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Impact of Polymorphisms of Genes Related with the Synthesis of Angiotensin II on the Progression of IgA Nephropathy

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Background : Angiotensin II (AngII) has been shown to play an important role in several renal diseases including IgA nephropathy (IgAN). Although it is well recognized that angiotensin-converting enzyme (ACE)-dependent AngII-generating system is a major source of intrarenal AngII production, chymase (CMA)-dependent pathway is also reported to be upregulated in intrarenal cells in diabetic nephropathy (DN) and other glomerulonephritides. The polymorphisms of genes involved in the synthesis of AngII have been reported to be related to the clinical outcomes in DN and IgAN. We investigated the association of ACE and CMA gene polymorphisms with the development and progression of IgAN among Korean patients.

Methods : Korean patients with biopsy-proven IgAN (N=261) with a minimal follow-up of 4 years (mean±SD: 103.4±52.6 months) were recruited. Three hundred healthy subjects with normal renal function, normal urinalysis and normotension were included as controls. The polymorphisms of ACE gene (I/D, A2350G) and CMA gene (G-1896A, C-1794T) were determined by the dynamic allele specific hybridization or 5' nuclease allelic discrimination assay.

Results : The genotype and allele frequencies of ACE and CMA were not different significantly between IgAN patients and controls. There was no significant association between genotypes of ACE and CMA and initial renal function, amount of daily proteinuria, and frequency of hypertension. The frequency GG genotype in CMA G-1896A polymorphism was significantly higher in patients with stable disease course than in those with progressive course (61.4% vs. 46.8%, p=.041). In Kaplan-Meier analyses, the renal survival rate was good in patients carrying GG homozygote at CMA G-1896A (p=.045). Moreover, G-1896A polymorphism remained an independent risk factor for the progression after multivariate analysis (Cox regression model, HR for AA genotype: 6.086, 95% CI 2.057-18.005, p=.001; HR for GA genotype: 1.986, 95% CI 1.226-3.219, p=.005).

Conclusions : Our results suggest that CMA G-1896A polymorphism affect the progression rate of IgAN in Korean patients.

Key Words : 안지오텐신 II, IgA 신장병, 카이메이즈
Angiotensin II, IgA Nephropathy, Chymase