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IgA 신증환자에서 Klotho 유전자 다형성과 신증의 진행 및 생존율과의 연관성

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The Association of Klotho Polymorphism with Clinical Course of IgA Nephropathy

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Backgrounds: IgA nephropathy is most common in primary glomerulonephritis causing end stage renal disease, and the vasculopathy is known to involve disease progression. Klotho, a gene related to aging process, has been reported to play a role in atherosclerosis. We investigated whether Klotho gene polymorphism affect on clinical course of IgA nephropathy.

Methods: The data registered for PREMIER study which enrolled the patients with biopsy proven IgA nephropathy from 34 hospitals and clinics were analyzed. Two single nucleotide polymorphisms for Klotho gene, G395A of promoter region and C1818T of exon 4, were examined using Taqman PCR assay, and investigated the association of genotypes with the progression of IgA nephropathy and patients' survival.

Results: Among 1078 patients, clinical data of 1029 patients confirmed about survival were analyzed. The allele frequency was 0.174 for A allele of G395A and 0.184 for T allele of C1818T complied with Hardy-Weinberg equilibrium. There were no differences of patients with progressive disease which was defined as 50% elevation of serum creatinine between genotypes with G395A and C1818T polymorphisms. However, when patients were categorized into CKD I to V by estimated GFR with modified MDRD equation, the population who advanced to CKD IV and V at the end of the study from CKD I to III initially was larger in T allele carrier of C1818T polymorphism (p=0.03). Death was 54 (5.25%) and proportion of A allele carrier of G395A was higher in non-survivor (4.2 vs 7.6%, p=0.022). A allele carrier of G395A, creatinine, albumin, and hemoglobin were the factors predicting survival in logistic regression analysis.

Conclusion: Klotho gene polymorphism in G395A of promoter region was associated with survival of patients with IgA nephropathy, and progression to advanced CKD stages was related to T allele carrier of C1818T. The pathogenesis and the effect of therapeutic intervention should be studied further.

Key Words: 면역글로불린 A신증, 유전자 다형성, Klotho유전자
IgA nephropathy, Polymorphism, Klotho gene