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만성 신부전 환자에서 혈중 Klotho 수치와 신사구체 여과율과의 관련

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Circulating Klotho Level is Decreased in Patients with Chronic Kidney Disease and Its Deficiency is Associated with Low eGFR

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Background: Klotho is mainly expressed in the renal distal tubules and exerts coreceptor function for FGF23. It can also be released into the circulation by proteinase-induced cleavage or alternative splicing and acts like a hormone that can have anti-oxidative stress and anti-senescence effect. However, it is unknown whether circulating klotho levels are altered and associated with estimated glomerular filtration rate (eGFR) in patients with chronic kidney disease (CKD).

Methods: We conducted a cross-sectional study in 215 subjects who were diagnosed as CKD between January 2006 and December 2011 at our institute. 30 subjects who had only microhematuria and no evidence of other kidney diseases were considered a control group. Demographic and clinical data were reviewed based on medical records. We measured serum concentrations of klotho, FGF23, high-sensitivity C-reactive protein (hsCRP), and parathyroid hormone (PTH).

Results: The mean age of the subjects was 45.9 years and 54.4% were male. The median klotho and FGF 23 level was 565.0 (107.4 to 5142.0) and 101.2 (34.2 to 472.1) pg/ml, respectively. The mean eGFR and random unrine protein-to-creatinine ratio (UPCR) was 47.9 (4.08 to 165.26) ml/min/1.73m^2 and 3.41 (0.02 to 34.03). Compared with control group, patients with CKD had lower circulating klotho levels (1090.3±1068.2 vs. 433.5±370.7 pg/ml, p=0.003). When subjects were categorized into 5 groups according to eGFR (CKD 1, GFR >90; CKD 2, 60<eGFR<89; CKD 3, 30-59; CKD 4, 15-29; CKD 5, <15 ml/min/1.73m^2), circulating klotho level gradually decreased as CKD stage increased (P for trend <0.01). In addition, log-transformed klotho was negatively correlated with age (γ=-0.404, p<0.001), log-transformed UPCR (γ=-0.373, p<0.001), log-transformed FGF23 (γ=-0.278, p<0.001), log-transformed hsCRP (γ=-0.302, p<0.001), phosphorus (γ=-0.174, p=0.011), and log-transformed PTH (γ=-0.255, p=0.004), whereas it was positively correlated with eGFR (γ=0.553, p<0.001). In a multivariate linear regression adjusted for these factors, log-transformed klotho was independently associated with eGFR (β=0.187, p=0.005).

Conclusion: We demonstrated that circulating klotho level was decreased as kidney function declined and was associated with multiple covariates that are widely altered in CKD patients. Although this study did not aim to clarify mechanism for the effect of klotho on kidney function, our findings suggest that klotho may play a role in attenuation of disease progression.

Key Words: 클로토, 만성신부전, 신사구체여과율
Klotho, CKD, eGFR