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만성신질환 환자에서 1,25 Dihydroxyvitamin D과 내인성 에리트로포이에틴 저항성과의 연관

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Serum 1,25 Dihydroxyvitamin D Level Is Independently associated with Endogenous Erythropoietin Resistance in Patient with Chronic Kidney Disease

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Introduction: Resistance to exogenous erythropoietin (EPO) stimulating agent (ESA) has been known to be associated with mortality in patients with chronic kidney disease (CKD). Recent studies have also demonstrated an association between resistance to endogenous EPO and mortality in CKD patients. We aimed to identify factors associated with endogenous EPO resistance, represented by serum EPO concentration and its ratio to hemoglobin (EPO/Hb ratio), with a focus on serum 1,25 dihydroxyvitamin D [1,25 (OH)2D].

Method: This study included 223 CKD patients [glomerular filtration rate (GFR) <60 ml/min/1.73m^2] who were not on dialysis therapy from Pusan National University Yangsan Hospital between 2008 and 2013. The patients were excluded if they were on ESA therapy or had iron deficiency (Transferrin saturation <20% or ferritin <100 ng/ml) at the time of study enroll. The association of endogenous EPO/Hb ratio with clinical (age, sex, diabetes, hypertension, and smoking) and laboratory variables [GFR, serum albumin, total cholesterol, body mass index, 1,25(OH)2D, transferrin saturation, ferritin, high sensitivity C-reactive protein (hsCRP), intact PTH] was investigated by univariate and multivariate linear regression analysis.

Results: Of the 223 patients, 144 were in CKD stage 3, 49 in CKD stage 4, and 30 in CKD stage 5. Mean GFR (ml/min/1.73m^2) was 42.7±7.6 in CKD stage 3, 22.5±4.2 in CKD stage 4, and 10.4±2.5 in CKD stage 5. Mean endogenous EPO level did not vary significantly across CKD stages, whereas Hb level was lower and endogenous EPO/Hb ratio was higher as CKD stage increased. In univariate analysis, endogenous EPO/Hb ratio was significantly associated with GFR (β=-0.405, p<0.001), serum albumin (β=-0.164, p=0.072), 1,25(OH)2D (β=-0.407, p<0.001), and iPTH (β=0.454, p<0.001). In multivariate analysis, 1,25(OH)2D level had independent inverse association with endogenous EPO/Hb ratio (β=-0.248, p<0.001). In addition, hsCRP (β=0.207, p=0.002) and iPTH (β=0.292, p=0.002) level was independently associated endogenous EPO/Hb ratio. No significant association was seen between GFR and endogenous EPO/Hb ratio in multivariate analysis.

Conclusion: In our cohort of CKD patients, serum 1,25(OH)2D was significantly associated with endogenous EPO resistance. The results of this study suggest the association of 1,25(OH)2D with endogenous erythropoietin resistance might play important role in anemia of CKD patients.

Key Words: 비타민 D, 에리트로포이에틴, 만성신질환
1,25 Dihydroxyvitamin D, Erythropoietin, CKD