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Safety of erythropoietin administration among End-Stage Renal Disease patients

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Objectives : Anemia is an important risk factor for cardiovascular disease (CVD) and mortality in patients with chronic kidney disease (CKD). Erythropoietin (EPO) has been used to care for anemia in both CKD patients and those with cancer. Concerns of EPO were included an increased risk CVD and tumor progression, but definite association was not fully confirmed. We performed the study to validate safety of EPO among End-Stage Renal Disease (ESRD) patients.

Methods : A total of 3432 ESRD patients were included to a prospective observational study in Clinical Research Center for ESRD (CRC-ESRD) registry. The patients were divided into hemodialysis (HD) group and peritoneal dialysis (PD) group by dialysis methods. A dose of EPO use, IV iron use and serum hemoglobin (Hb) levels, CVD and cancer mortality were collected in the registry. Cox proportional hazard analysis was conducted to estimate hazard ratio (HR) for the EPO use, doses and Hb levels with mortality of CVD and cancer after adjusting for risk factors including age, sex, comorbidities including diabetes, hypertension.

Results : The mean hemoglobin (Hb) levels of all the patients were 10.5±1.33 g/dL, and EPO doses were 148.52± 101.7 U/kg/week. IV iron was administered to 139 patients. Mean Hb levels, EPO doses and number of patients received IV iron were higher in HD group than PD group (p=0.001 for both). The mortality rate of CVD was 1.71% in HD and 1.94% in PD. CVD mortality was increased by EPO use in PD group (HR 1.72, 95% CI, 1.05-2.88, p=0.04). But the mortality has no correlation with EPO doses (95% CI, 0.99-1.02, p=0.62) and Hb level (95% CI, 0.69-1.17, p =0.44). On the other hand, any factor did not relate to CVD mortality in HD group. The mortality rate of cancer in ESRD patients was 0.94% in HD group and 0.78% in PD group. Most frequently observed cancer related to mortality was colon cancer in PD group and lung cancer in HD group. Hb levels, EPO use and doses were not associated with cancer mortality in both groups. In risk factor analysis by multivariate Cox-regression analysis, the mortality of CVD was associated to diabetes (p<0.01) and age (p<0.001) in

both groups. However, the mortality of cancer was not related with any factor.

Conclusions : EPO use was associated with an increase of CVD mortality in PD patients. Diabetes and age were independent risk factors of CVD mortality in ESRD patients treated with EPO. On the other hand, the mortality of cancer in ESRD patients was not affected to EPO use.

Keywords : erythropoietin, dialysis, complication, cardiovascular disease, cancer,