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관상동맥 우회술을 시행한 환자에게서 Erythropoietin 치료가 장기적 임상 결과에 미치는 영향

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Erythropoietin Treatment Improves Long-term Outcome in Patients with Higher Level of Urine Neutrophil Gelatinase-associated Lipocalin (NGAL) Undergoing Coronary Artery Bypass Grafting

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Purpose: Erythropoietin (EPO) has been shown to have protective effects on the development of acute kidney injury (AKI). In addition, urine NGAL is known as an early biomarker for AKI. However, few studies were evaluated on the effect of EPO and NGAL on the progression of end stage renal disease (ESRD) or death. The aim of this study was to evaluate the association between urine NGAL and long term outcome as well as AKI, and to test the hypothesis that prophylactic EPO treatment improves long-term outcome after coronary artery bypass grafting (CABG).

Methods: Seventy one patients scheduled for elective CABG randomly received either 300 U/kg of EPO or saline intravenously before surgery. Serial urine samples were analyzed by ELISA for NGAL expression. The primary outcome was AKI defined as an increase in the serum creatinine concentration of ≥0.3 mg/dL or ≥50 percent from baseline within 48hours, or oliguria of less than 0.5 mL/kg/hour for more than six hours. And the secondary outcome was the composite of death or ESRD.

Results: AKI was developed in 21 patients (29.6%). At baseline, 2, 4, 24, and 72 hours after CABG, urine NGAL was significantly higher in AKI group. For concentration in urine NGAL at 2 hours, the area under the receiver-operating characteristic curve was 0.862, and sensitivity was 1.00 and specificity 0.778 for a cutoff value of 4 μg/L in EPO group. The urine NGAL≥4 μg/L at 2 hours after CABG was the independent predictor of AKI by multivariate analysis (p=0.002).

Eleven patients died or developed ESRD during 38.9±12.1 months of mean follow up period. EPO treatment group showed lower incidence of secondary composite outcome compared to placebo group in patients with urine NGAL≥ 4 μg/L at 2 hours after CABG during follow-up period (Log Rank test, p=0.037). However, there was no beneficial effect of EPO in patients with urine NGAL< 4μg/L at 2 hours after CABG. After adjustment for age, gender and univariate risk factors, and compared to placebo group, EPO treatment group had a 0.056-fold decreased risk for death or ESRD (95% confidence interval, 0.004-0.877, p=0.040).

Conclusion: Prophylactic administration of EPO prevents death or ESRD in patient with urine concentration of NGAL≥ 4 μg/L at 2 hours after CABG.

Key Words: Erythropoietin, 사망, 말기 신부전
Erythropoietin, Mortality, End stage renal disease