

## Association between High-Dose Erythropoiesis-Stimulating Agents, Inflammatory Biomarkers, and Soluble Erythropoietin Receptors

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### Abstract

#### Background

High-dose erythropoiesis-stimulating agents (ESA) for anemia of chronic kidney disease (CKD) have been associated with adverse clinical outcomes and do not always improve erythropoiesis. We hypothesized that high-dose ESA requirement would be associated with elevated inflammatory biomarkers, decreased adipokines, and increased circulating, endogenous soluble erythropoietin receptors (sEpoR).

#### Methods

A cross-sectional cohort of anemic 32 CKD participants receiving ESA were enrolled at a single center and cytokine profiles, adipokines, and sEpoR were compared between participants stratified by ESA dose requirement (usual-dose darbepoetin- $\alpha$  ( $< 1 \mu\text{g}/\text{kg}/\text{week}$ ) and high-dose ( $\geq 1 \mu\text{g}/\text{kg}/\text{week}$ )).

#### Results

Baseline characteristics were similar between groups; however, hemoglobin was lower among participants on high-dose ( $1.4 \mu\text{g}/\text{kg}/\text{week}$ ) vs usual-dose ( $0.5 \mu\text{g}/\text{kg}/\text{week}$ ) ESA. In adjusted analyses, high-dose ESA was associated with an increased odds for elevations in c-reactive protein and interleukin-6 ( $p < 0.05$  for both). There was no correlation between high-dose ESA and adipokines. Higher ESA dose correlated with higher levels of sEpoR ( $r_s = 0.39$ ,  $p = 0.03$ ). In adjusted analyses, higher ESA dose (per  $\mu\text{g}/\text{kg}/\text{week}$ ) was associated with a 53% greater odds of sEpoR being above the median ( $p < 0.05$ ).

#### Conclusion

High-dose ESA requirement among anemic CKD participants was associated with elevated inflammatory biomarkers and higher levels of circulating sEpoR, an inhibitor of erythropoiesis. Further research confirming these findings is warranted.