Early erythroferrone levels can predict the long-term hemoglobin responses to erythropoiesis-stimulating agents

Peng Xu¹, Raymond Wong², and Xiaoyu Yan¹

¹The Chinese University of Hong Kong ²The Chinese University of Hong Kong Faculty of Medicine

September 19, 2023

Abstract

Background and Purpose: Our previous study reported that erythroferrone (ERFE), a newly identified hormone produced by erythroblasts, responded to recombinant human erythropoietin (rHuEPO) sensitively but its dynamics was complicated by double peaks and circadian rhythm. This study intends to elucidate the underlying mechanisms for the double peaks of ERFE dynamics, and further determine whether early ERFE measurements can predict hemoglobin (HGB) responses to rHuEPO. Experimental Approach: By expressing recombinant rat ERFE protein and investigating its deposition in rats, the production of ERFE was deconvoluted. To explore the role of iron in ERFE production, we monitored short-term changes of iron status after injection of rHuEPO or deferiprone (DFP). Pharmacokinetic/pharmacodynamic (PK/PD) modelling was used to confirm the mechanisms and examine the predictive ability of ERFE for long-term HGB responses. Key Results: The rRatERFE protein was successfully expressed and purified. The production of ERFE was deconvoluted and showed two independent peaks (2 h and 8 h). Transient iron decrease was observed at 4h after rHuEPO injection and DFP induced significant increases of ERFE. Based on this mechanism, the PK/PD model could characterize the complex dynamics of ERFE. In addition, the model predictions further revealed a stronger correlation between ERFE and HGB peak values than that for observed values. Conclusions and Implications: The complex dynamics of ERFE. The early peak values of ERFE, which occur within a few hours, can predict HGB responses several weeks after ESA treatment.

Hosted file

Manuscript_XiaoyuYan.docx available at https://authorea.com/users/666066/articles/667068early-erythroferrone-levels-can-predict-the-long-term-hemoglobin-responses-toerythropoiesis-stimulating-agents