

“Efficacy and Safety of Epoetin Alfa in Critically Ill Patients.”
NEJM, 2007; 357: 965-976

Background

- Anemia often occurs in critically ill patients with mechanism thought to be similar to anemia of chronic disease with decreased circulating levels of erythropoietin.
- Previous studies have shown that limiting red blood cell transfusions to patients with hemoglobin less than 7 causes a decrease in mortality as published in the TRICC trial.
- It can be speculated that administration of recombinant human erythropoietin (epoetin alfa) would raise hemoglobin concentrations in these patients, therefore preventing the need for blood transfusions.

Hypothesis

- Treatment with epoetin alfa might decrease the need for red blood cell transfusion.

Study Design

Study type: Prospective, randomized, double-blind, placebo-controlled trial

Setting: 115 medical centers

Time period: Patients recruited from 12/03 to 6/06

Inclusion Criteria:

- Admitted to medical, surgical or medical-surgical ICUs and remained in that ICU for 2 days
- Age 18 years or older
- Hemoglobin concentration of less than 12 g per deciliter
- Written informed consent

Exclusion Criteria: Discharge from ICU within 48 hours after the second day of admission, acute ischemic heart disease, a stay for more than 48 hours in the transferring hospital, left ventricular assist device, history of pulmonary embolism, deep venous thrombosis, ischemic stroke, other arterial or venous thrombotic event, hypercoagulable disorder, dialysis, uncontrolled hypertension (SBP>200mmHg or DBP>110mmHg), , new onset or uncontrolled seizures, third-degree burns on >20% total body surface area, pregnancy, significant GI bleed, transfusion at time of enrollment, treatment with epoetin alfa within past 30 days, inability or unwillingness to receive blood products, participation in another study, hypersensitivity to epoetin alfa or its components

Randomization: N = 1460, were randomized into two groups

- Epoetin alfa (N = 733): Only 618 patients completed the study as others were lost to follow-up, discontinued drug, withdrew or other reasons not specified.
- Placebo (N = 727): 593 completed the study.

Patient characteristics: See Table 1, which were strangely very similar between the 2 groups.

Outcomes:

- The primary endpoint was the percentage of patients who received a red-cell transfusion.
- Secondary endpoints were the number of red-cell units transfused, mortality and change in hemoglobin concentration from baseline.

The Evidence

Variable	Epoetin alfa (N = 733)	Placebo (N = 727)	Relative Risk (95% CI)	P value
Received Transfusion no. (%)	337 (46.0)	351 (48.3)	0.95 (0.85-1.06)	0.34
Admission Group				
Trauma	215/402 (53.5)	216/391 (55.2)	0.97 (0.85-1.10)	
Surgical, nontrauma	59/162 (36.4)	74/168 (44.0)	0.83 (0.63-1.08)	
Medical, nontrauma	63/169 (37.3)	61/168 (36.3)	1.03 (0.78-1.36)	
Units transfused per patient				
Mean	4.5±4.6	4.3±4.8		0.42
Median	3.0	3.0		0.69
Total number of days alive	10,073	10,879		

Comments

- The administration of epoetin alfa does not reduce the incidence of red blood cell transfusion among critically ill patients; however in the small subset of trauma patients it showed a reduction in mortality.
- Given that this study failed to prove its primary outcome, any results drawn from the secondary endpoints cannot be considered valid until more studies are done.
- This study incidentally showed an increase in incidence of thrombotic events with the use of epoetin alfa.