Anemia and Red Blood Cell Transfusion

Advances in Critical Care

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KEYWORDS

• Anemia • Red blood cell transfusion • Transfusion • Blood transfusion • Hemoglobin • Critical care • Critically ill

KEY POINTS

- Anemia is common in all critically ill patients and is due to anemia of inflammation (high hepcidin levels resulting in iron-restricted erythropoiesis) and low erythropoietin (EPO) levels.
- A new hormone (erythroferrone) has been identified, which mediates hepcidin suppression to allow increased iron absorption and mobilization from iron stores.
- In general, in critically ill patients and those with severe sepsis and septic shock, a restrictive strategy (consider red blood cell [RBC] transfusion when hemoglobin [Hb] $\leq$7 g/dL) is recommended; in patients with acute coronary syndrome, consider RBC transfusion when Hb $\leq$8 g/dL.
- The decision to transfuse RBCs should not be solely based on the hemoglobin level and should include clinical factors and patient preferences with use of a Patient Blood Management approach.
- All strategies to prevent anemia in the intensive care unit (decreased phlebotomy, low volume sampling tubes, medical treatment of anemia) should be implemented.

INTRODUCTION

Anemia is common in the intensive care unit (ICU), resulting in frequent administration of red blood cell (RBC) transfusions. Significant advances have been made in understanding the pathophysiology of anemia in the ICU that will be reviewed. Most studies document that approximately 30% to 50% of patients receive RBC transfusions while in the ICU with an average of 5 units transfused during their ICU stay.[1–9] Higher RBC transfusion rates are reported in burn patients.[10] RBC transfusions are most commonly administered to ICU patients with anemia, and not bleeding. Several recent

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randomized controlled trials (RCTs) have providing increased evidence regarding the safety of restrictive RBC transfusion strategies in ICU patients, and this review summarizes the findings of these important studies. ICUs with evidence-based restrictive transfusion protocols significantly reduced the risk of transfusion in ICU patients controlling for patient and ICU factors, confirming the effectiveness of restrictive transfusion protocols.[11]

Anemia in the Intensive Care Unit: Pathophysiology

The pathophysiology of anemia in critical illness is consistent with an "anemia of chronic disease" and "anemia of inflammation."[12] Anemia in ICU patients is the result of 3 main abnormalities related to the host inflammatory response: (1) dysregulation of iron homeostasis due to increased hepcidin concentrations; (2) impaired proliferation of erythroid progenitor cells; and (3) blunted erythropoietin response. Hepcidin is the master regulator of iron homeostasis. Increased hepcidin concentrations reduce iron availability via 2 mechanisms: (1) internalization and destruction of the iron-exporting protein ferroportin, which in turn leads to an inability to export iron out cells, locking iron primarily in macrophages of the reticuloendothelial system (RES); and (2) decreased absorption of iron through the gastrointestinal tract (**Fig. 1**).[13] High hepcidin concentrations result in a state of functional iron deficiency.[14]

Reduced production of erythropoietin and a blunted response of the bone marrow to erythropoietin further contribute to anemia in critically ill patients (**Fig. 2**). A new hormone (erythroferrone, ERFE) has been identified, which mediates hepcidin suppression to allow increased iron absorption and mobilization from iron stores.

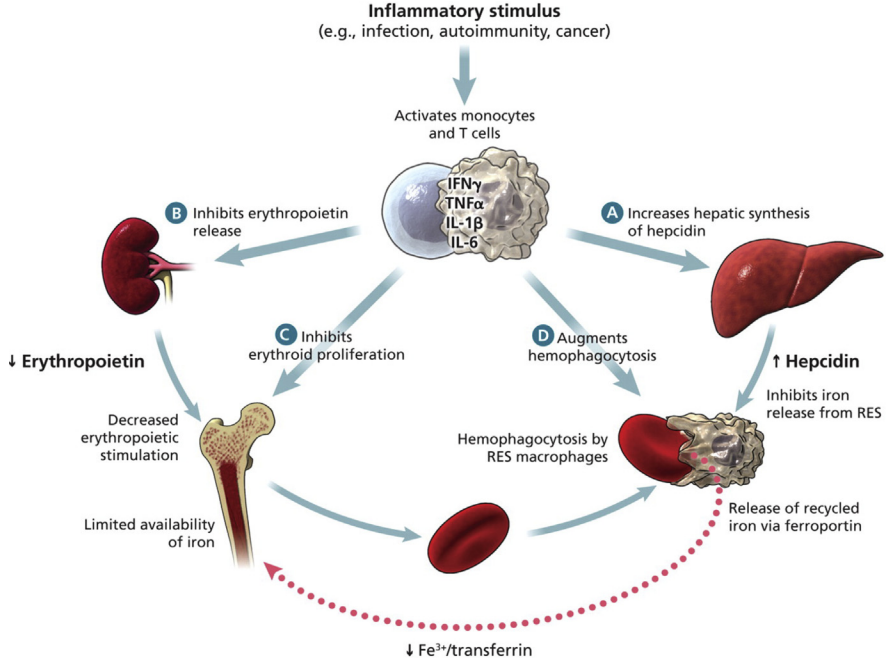

Fig. 1. Anemia in critically ill patients is related to high hepcidin and low erythropoietin levels. IFNγ, interferon γ; IL-1β, interleukin-1β; IL-6, interleukin-6; TNFα, tumor necrosis factor α. (*From* Zarychanski R, Houston DS. Anemia of chronic disease: a harmful disorder or an adaptive, beneficial response? CMAJ 2008:179;333–7.)