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RED BLOOD CELL TRANSFUSION IN THE EMERGENCY DEPARTMENT

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☐ **Abstract—Background: Transfusion of red blood cells (RBCs) is the primary management of anemia, which affects 90% of critically ill patients. Anemia has been associated with a poor prognosis in various settings, including critical illness. Recent literature has shown a hemoglobin transfusion threshold of 7 g/dL to be safe. This review examines several aspects of transfusion. Objective: We sought to provide emergency physicians with an updated review of indications for RBC transfusion in the emergency department. Discussion: The standard hemoglobin transfusion threshold was 10 g/dL. However, the body shows physiologic compensatory adaptations to chronic anemia. Transfusion reactions and infections are rare but can have significant morbidity and mortality. Products stored for <21 days have the lowest risk of reaction and infection. A restrictive threshold of 7 g/dL is recommended in the new American Association of Blood Banks guidelines and multiple meta-analyses and supported in gastrointestinal bleeding, sepsis, critical illness, and trauma. Patients with active ischemia in acute coronary syndrome and neurologic injury require additional study. The physician must consider the patient's hemodynamic status, comorbidities, risks and benefits of transfusion, and clinical setting in determining the need for transfusion. Conclusions: RBC transfusion is not without risks, including transfusion reaction, infection, and potentially increased mortality. The age of transfusion products likely has no effect on products before 21 days of storage. A hemoglobin level of 7 g/dL is safe in the setting of critical illness, sepsis, gastrointestinal bleeding, and trauma. The clinician must evaluate and transfuse based on the clinical setting and patient hemodynamic status rather than using a specific threshold.** © **2016 Elsevier Inc. All rights reserved.**

☐ **Keywords—blood product; indications; product age; RBC; transfusion; transfusion reaction**

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INTRODUCTION

Transfusion of red blood cells (RBCs) has been a standard of care for the management of anemia for >100 years. RBC transfusion is common, with approximately 15 million units transfused annually in the United States (US), with 85 million units transfused worldwide (1,2). It was thought that patients would not tolerate anemia and regular transfusion would improve outcomes with little risk. The definition of anemia includes hemoglobin (Hgb) <12 g/dL in females and 13 g/dL in males (3). In fact, anemia affects almost 90% of patients in the intensive care unit during their admission, with 30% of intensive care unit (ICU) admissions possessing a Hgb <9 g/dL and 70% <12 g/dL at the time of admission (4–6). Approximately 40% of critical patients will receive a transfusion during hospitali-zation, receiving on average 2 to 5 units of RBCs (7,8). Anemia in the setting of older age, critical illness, trauma, and surgery has been associated with poor prognosis, as indicated in several studies (9–16).

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Patients in the setting of critical illness have multiple causes of anemia, including active hemorrhage, blunted erythropoietin production, inflammatory cytokine production, increased hepcidin, iron deficiency, and underlying disease (e.g., renal failure). RBC transfusion in anemia can increase oxygen delivery, increase cell mass, and potentially resolve anemic symptoms; however, transfusion can contribute to fluid overload, fever, reaction, immunomodulation, multiple organ dysfunction, hypothermia, and coagulopathy (17).

The standard level for transfusion was considered to be Hgb of 10 g/dL or hematocrit (Hct) <30% (15,18–20). Therefore, many transfusions occurred in patients with little to no symptoms in an effort to maintain Hgb levels above this number, considered a liberal strategy for transfusion. Several recent studies have questioned the liberal transfusion threshold in patients with sepsis, gastrointestinal (GI) bleeding, acute coronary syndrome (ACS), and trauma, as well as other components of product transfusion, including the physiologic effects of transfusion, product reactions, and effect of RBC product age.

The question for providers caring for patients ultimately revolves around the threshold for transfusion. Within emergency medicine, critical care, and in-hospital settings, little debate currently exists on restrictive strategy for hemodynamically stable admitted patients. Most would also agree that transfusion can be life-saving in patients with hypoperfusion and severe bleeding. This review will discuss the recent literature on these points and provide emergency physicians with an evidence-based review on the indications for RBC transfusion.

DISCUSSION

Physiologic Effects of RBC Transfusion

Oxygenation is dependent on Hgb concentration, Hgb saturation, oxygen supply, cardiac output, and pulmonary extraction and perfusion. Oxygen delivery to tissues occurs predominantly through attachment to Hgb. A large reservoir of oxygen delivery exists, as the rate of delivery in the normal individual exceeds the consumption of oxygen by a factor of 4; however, if Hgb decreases, oxygen delivery may be affected (21,22).

In a healthy adult, the normal daily production of RBCs is 0.25/kg, with an average RBC lifespan of 120 days—transfused blood cells have a lifespan of 60 days (23). One unit of RBCs increases Hgb by 1 g/dL and Hct by 3%, but these levels may not be reached in the setting of occult bleeding, repeated laboratory draws, fever, hypersplenism, immunologic disease, or hemolysis (23–26). RBCs can be stored to a maximum of 42 days. The process of storing RBCs changes cell wall deformability, increases proinflammatory cytokines, and decreases 2,3-diphosphoglycerate (2,3-DPG), which shifts the oxyhemoglobin dissociation curve to the left. In fact, levels of 2,3-DPG are depleted within 2 weeks of storage, decreasing the ability of RBCs to release oxygen to peripheral tissues. Product transfusion can increase intrinsic blood viscosity and decrease cardiac output, and these effects actually diminish the ability of RBCs to improve oxygenation in critically ill patients (4,15–17,22,24,25). Whether product storage age affects patient morbidity and mortality is controversial, which will be discussed later.

Exogenous RBC ability to increase oxygenation of tissues is not well established in the literature. In the setting of anemia, the body shows a number of physiologic compensatory methods by increasing cardiac output and oxygen extraction in the tissues, as well as an increased ability to offload oxygen in the peripheral tissues through increased 2,3-DPG levels in RBCs. Coronary artery blood blow increases, and blood flow can redistribute through intravascular vasodilators to where it is most needed. With these measures, the body can adapt to chronic anemia (21,22,27).

Types of Products

There are several types of RBCs, each with specific indications to reduce the risk of transfusion reaction. The majority of these situations involve patients with comorbidities, usually immunosuppression, or patients who have received multiple transfusions.

Leukoreduced. The indications for leukoreduced or leukodepleted RBCs include prevention of febrile nonhemolytic reaction, caused by the presence of antibodies to white blood cells (WBCs). Other indications include reduction in the risk of cytomegalovirus (CMV) infection (e.g., bone marrow transplant patients, pregnant women, and patients with HIV/AIDS), reduction in the risk of transplant rejection, and intrauterine transfusions. Leukocyte-reduced products contain fewer WBCs ($<5 \times 10^6$ WBCs) through leukocyte reduction filters (28,29).

Washed. Washed RBCs are used to prevent allergic reactions, specifically in patients with immunoglobulin A deficiency, and in patients with recurrent severe transfusion reactions not prevented by pretreatment with antihistamines and corticosteroids. Centrifugation separation removes close to 98% to 99% of the plasma constituents, decreasing antigens in the plasma and RBC membrane. Washed units often do not provide the full 1-g/dL increase in Hgb, because 10% to 20% of the cells are lost (28,29).