Blood Transfusion Strategies in Patients Supported by Extracorporeal Membrane Oxygenation

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Since red blood cell (RBC) transfusion was first performed by English obstetrician James Blundell 200 years ago,[1] it has become one of the most commonly used life-saving therapies. Historically, RBC transfusion have been viewed as a safe and effective means of treating anemia and improving oxygen delivery to tissues. However, in the early 1980s, transfusion practice began to come under systematic scrutiny.[2,3] The early concern about the safety of blood transfusion revolved around transfusion-related infection. However, the concern about risks of blood transfusion have become diverse and complicated over the last three decades, according to research findings.

In the recent literature, blood transfusion has been confirmed as an independent risk factor for mortality, perioperative infection, postinjury multiple organ failure, systemic inflammatory response syndrome, and admission to the intensive care unit(ICU).[4-7] Problems about blood transfusion are particularly important in the critically ill patients.

Many data suggest that critically ill patients can tolerate hemoglobin levels as low as 7 g/dL and that a “liberal” RBC transfusion strategy may in fact lead to worse clinical outcomes.[8] Actually, RBC transfusion impairs physiologic control of regional vascular tone, induces coagulopathy and negatively impacts immune function and antioxidant system.[9]

The 2012 Cochrane analysis reported that restrictive transfusion strategies were more effective than liberal transfusion strategies in reducing hospital mortality significantly among 6,264 patients from 1986 to 2011.[10,11] As such, newer “restrictive” hematocrit threshold for transfusion (e.g., 21%) are now appreciated to be at least noninferior to more “liberal” hematocrit thresholds (e.g., 30%) for broad array of conditions.[9]

The efficacy of transfusion in critically ill pediatric patients has been also questioned as is still uncertain for adult critically ill patients. Lacroix et al. suggested, based on their TRIPICU study, that there was no difference in outcomes of stable critically ill children between restrictive (hemoglobin threshold of 7 g/dL) and liberal (hemoglobin threshold of 9.5 g/dL) transfusion strategies.[12]

Subgroup analysis of postsurgical and postcardiac surgical patients from the TRIPI-CU study revealed similar findings. Among pediatric cardiac surgical patients, greater RBC transfusion volumes are associated with prolonged duration of mechanical ventilation, an increase in nosocomial infection rates and duration of hospitalization.[13,14]

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The discovered association between RBC transfusion volume and morbidity in critically ill patients has promoted the reevaluation of transfusion strategies used for ECMO patients.

ECMO use has been associated with transfusion of large volumes of RBCs and with exposure to a large number of donor RBC units.[15] Diverse hemostatic strategies are presently used during ECMO such as use of a smaller circuit, antifibrinolytic agents and heparin coated circuits. However numerous RBC transfusion are still requested for circuit priming and due to bleeding, coagulopathy and hemolysis during ECMO course.

Although RBC transfusion are performed by bleeding complications, many RBC transfusions are ordered for the purpose of maintaining an arbitrary hemoglobin threshold in these patients. There is no accepted RBC transfusion threshold for patients supported with ECMO. Guidelines published by the Extracorporeal Life Support Organization call for maintenance of a normal hematocrit and define anemia as a hematocrit less than 45%.[16] Others have used hematocrit threshold between 35% and 45%.[17,18] There are no published prospective data describing the utility and safety of restrictive transfusion strategy among patients receiving ECMO. However, several observational trials in patients with ECMO have suggested that more RBC transfusions related to worse outcomes in some patients. Smith et al. [17] reported that greater RBC transfusion volumes among pediatric patients supported with ECMO for non-cardiac indications are independently associated with an increase in odds of mortality. Kumar et al.[18] concluded that exposure to high amounts of blood transfusion while on ECMO increase the risk of death in patients even after successful decannulation. At present, there are no evidence suggesting that a higher hemoglobin is beneficial to patients supported with ECMO. Fisher et al.[19] retrospectively evaluated the efficacy of RBC transfusion on tissue oxygenation in 45 children with ECMO. They reported that RBC transfusion did not significantly improve global tissue oxygenation, as assessed by changes in mixed venous oxygen saturation and cerebral near infrared spectroscopy. RBC transfusion is indicated to improve oxygen delivery to tissue and for no other purpose. The trial reported by Fisher et al. states that increased blood oxygen content as a result of RBC transfusion does not always guarantee the increase in oxygen delivery

to the tissues. It is true that some researchers are also skeptical about the impacts of transfusion on oxygen delivery. The stored blood is depleted of 2,3-diphosphoglycerate (2, 3-DPG), and adenosine triphosphate. Depletion of 2, 3-DPG results in an increased affinity of hemoglobin for oxygen and impairs the release of oxygen to the tissue. Depletion of adenosine triphosphate results in both altered deformability and loss of integrity of the RBC membrane, which in turn can negatively impact microvascular flow and lead to early destruction of transfused RBCs. Also small quantities of free hemoglobin of transfused blood act as scavengers of nitric oxide, perhaps resulting in microvessel vasoconstriction and thus reducing local tissue oxygen delivery.[20-25] In both critically ill adults and pediatric patients, age of stored RBCs are associated with worse tissue oxygenation and organ dysfunction.[26-28] As far as storage lesion is concerned, the rapid massive leakage of potassium from weak RBC membrane into the extracellular space can cause sudden cardiac arrest.[29] Such an adverse effect of stored RBC transfusion on oxygen delivery and worse outcomes in transfused patients underscore the need for reconsideration or resetting of the traditional transfusion thresholds in ECMO patients. Additional studies are needed to establish the appropriate RBC transfusion threshold for patients supported with ECMO. Ideally, ECMO patients would be better off with transfusion strategies that can improve oxygen delivery by addressing patient variables and stress-specific situations instead of hematocrit trigger strategies.

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