Intensive Care Med (2013) 39:1002–1004
DOI 10.1007/s00134-013-2900-5

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What's new in transfusion policies?

Received: 6 March 2013
Accepted: 8 March 2013
Published online: 10 April 2013

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Since 1667, when the first blood transfusion was given in humans, many millions of patients have undergone this intervention. However, despite its widespread use, the decision to transfuse is still driven by simplistic and arbitrary triggers, such as the hemoglobin level rather than integrated clinical variables [1]. For many years, the threshold generally used to guide transfusion practice was a hemoglobin concentration of 10 g/dL and a hematocrit of 30 %, the so-called 10/30 rule, derived from John Lundy's clinical experience in the 1940s [2]. Transfused blood was considered a perfect substitute for blood loss and a powerful treatment for anemia, with all its adverse consequences [3]. Nevertheless, the risks related to blood transfusion were well recognized, including errors in cross-matching, risks of transmission of pathogens, transfusion-associated circulatory overload (TACO), storage-lesion consequences, transfusion-related acute lung injury (TRALI), and transfusion-related immunomodulation (TRIM), which may be associated with an increased incidence of infectious complications.

As a result of increasing concern related to the risks of overtransfusion, in the 1990s our Canadian colleagues conducted a multicenter randomized trial in critically ill patients, and showed that lower hemoglobin thresholds were as safe and effective as higher ones, and may even have been superior in younger patients and those with lower disease severity [4]. These data inspired physicians worldwide to decrease hemoglobin transfusion thresholds. Other randomized and observational studies in different populations confirmed these findings and showed a worrisome association of red blood cell (RBC) transfusion with worse clinical outcomes, arguing against a liberal strategy of transfusion [5–7]. In the Transfusion Requirements After Cardiac Surgery (TRACS) study, a randomized clinical trial in cardiac surgery patients, we confirmed the non-inferiority of a restrictive strategy of blood transfusion, using a hematocrit of 24 % as threshold, compared to a more liberal strategy using a hematocrit of 30 % as threshold; we also identified blood transfusion as an independent risk factor for clinical complications and death in these patients [8]. Two other recent studies also argue against a liberal strategy of transfusion. Carson et al. [9] randomized 2,016 patients with cardiovascular disease to a liberal or a restrictive strategy of RBC transfusion after hip-fracture surgery, and observed no benefit associated with the liberal strategy. And, in a single-center study in patients with acute upper gastrointestinal bleeding, Villanueva et al. [10] showed that a restrictive strategy of transfusion improved outcomes, including survival at 6 weeks; patients in the liberal group had a significant increase in portal pressure, which may have promoted further bleeding. Recently published systematic reviews and guidelines have reinforced the safety and efficacy of a restrictive strategy of RBC transfusion compared to a liberal strategy in medical and surgical critically ill patients [11–13].

On an almost daily basis, we are therefore confronted with the dilemma that although anemia increases risk in critically ill patients, RBC transfusion is also associated with increased morbidity and mortality rates; over the last decade, blood transfusion rather than anemia has become the patient's enemy, and a multidisciplinary approach to reduce transfusion rates has been widely adopted in the critical care setting.

However, although the studies discussed earlier warn against excessive use of transfusions in some institutions and in certain groups of patients, the *benefits* of blood transfusions have recently been outlined in other patient populations. Recently published results from a multicenter randomized trial revealed that in patients with sickle-cell disease, preoperative RBC transfusion was associated with a decreased risk of clinically important and severe complications, particularly acute chest syndrome [14]. In a pilot study in neurosurgical patients, Naidech et al. [15] showed that targeting a higher hemoglobin level in patients with subarachnoid hemorrhage seemed to be safe and feasible and may have reduced the incidence of cortical cerebral infarction. These studies included patients with relatively low mortality rates, but in the last few years, several studies have emerged to indicate that more liberal blood transfusion rates may reduce morbidity and mortality rates in more severely ill critical care patients. The Sepsis Occurrence in Acutely Ill Patients (SOAP) study, an observational multicenter study, showed higher 30-day survival rates in critically ill patients who had received a transfusion than in those who had not [16]. Sakr et al. [17], in critically ill surgical patients, reported that blood transfusions were associated with a lower risk of hospital death, especially in older patients, in patients with severe sepsis, in patients with higher admission severity scores and in patients admitted after non-cardiovascular surgery [17]. Similarly, Park et al. [18], in a recent multicenter study of 1,054 patients with sepsis from community-acquired pneumonia, showed using a Cox proportional hazard model that RBC transfusion was associated with a lower risk of 7-day, 28-day and in-hospital mortality.

These findings raise questions about whether the restrictive policy of transfusion adopted in recent years has perhaps been *too* restrictive. Is current restriction of transfusions really safe and effective or are our transfusion thresholds now so low that the benefit of transfusion exceeds the risk? Moreover, blood is now safer, because of advances in blood bank strategies, including collection, storage, infection screening and leukoreduction, which may reduce some of the known adverse effects of blood transfusion. And, if we look back at the study by Hébert et al. [4], we see that only 13 % of the patients screened were actually enrolled, which considerably limits the generalizability of the results. In addition, a re-analysis of their data by Deans et al. [19] suggested an increased mortality rate in patients with coronary artery disease who were in the restrictive strategy group.

There are now sufficient data available to encourage us to rethink our transfusion practice in sicker patients. But we do not believe this necessitates new multicenter studies, like that of Hébert et al. [4]. The SOAP group of investigators launched such a study but rapidly abandoned it. Indeed, the investigators found it difficult to randomize certain groups of patients, e.g., it was believed inappropriate to enroll a young, recently traumatized individual without cardiac problems to the liberal group or an elderly patient with ischemic cardiomyopathy to the restrictive group. Rather, we believe that a standardized 'trigger' or 'threshold' approach to transfusion is just too simplistic [20]. William Osler wrote a century ago that "Variability is the law of life, and as no two faces are the same, so no two bodies are alike, and no two individuals react alike and behave alike under the abnormal conditions which we know as disease" [21]. In a similar fashion, different patients in specific circumstances may or may not benefit from a red blood cell transfusion. How to measure this benefit and to balance the risks of anemia and the risks of transfusion are still big challenges in critical care medicine. At the bedside, the decision whether to transfuse or not must take into account individual patient characteristics, including age and cardiovascular disease, and physiological data, such as hemodynamic measurements and tissue perfusion markers [1, 20]. The decision-making process must combine all these data to determine the correct transfusion trigger for each individual patient.

Conflicts of interest The authors have no conflict of interest to declare.

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