Commentary

Blood management in intensive care medicine: CRIT and ABC – what can we learn?

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Abstract

In 284 US intensive care units the CRIT study (Anemia and blood transfusion in the critically ill – Current clinical practice in the United States) assessed allogeneic red blood cell (RBC) transfusion and outcome in 4892 patients. As in the former European ABC study (Anemia and blood transfusion in the critically ill), the mean pretransfusion hemoglobin was approximately 8.5 g/dl and RBC transfusions were independently associated with an increased mortality. These studies were purely observational and, therefore, despite the finest statistical models indicating that RBC transfusions were independently associated with a higher mortality, it remains possible that this adverse outcome is not due to a harmful effect of RBC transfusion in itself, but merely reflects the fact that transfused patients were sicker to start with. The definitive call is still out, but one mechanism by which RBC transfusion might be harmful now appears less likely; namely, storage lesion. In the CRIT study, mortality was not increased in patients receiving 'old' RBCs (>14 days stored) versus 'fresh' RBCs. The effect of leukoreduction could not be assessed since mainly nonleukoreduced RBCs were transfused. The evidence is mounting, however, that RBC transfusions are efficacious only when oxygen delivery is compromised. What can be done to diminish the use of RBC transfusions, its costs and side effects in intensive care medicine? There are two important options available today: decreasing blood loss for diagnostic purposes using pediatric sampling tubes, and establishing restrictive multidisciplinary transfusion guidelines and implementing them in daily clinical practice.

Keywords: blood transfusion, morbidity, mortality

Between August 2000 and April 2001, data on red blood cell (RBC) transfusion and outcome were prospectively collected in the CRIT study (Anemia and blood transfusion in the critically ill – Current clinical practice in the United States) in 284 intensive care units (ICUs) in 213 US hospitals. Data on 4892 patients were analyzed [1]. The mean pretransfusion hemoglobin was 8.6 ± 1.7 g/dl and did not differ much between surgical ICUs, medical ICUs and combined ICUs nor between community ICUs and academic ICUs. Allogeneic RBC transfusions were independently associated with a longer ICU stay, with a longer hospital length of stay and with higher mortality. The association between RBC transfusion and mortality was particularly pronounced with more than 2 RBC units transfused.

A similar study (the ABC study; Anemia and blood transfusion in the critically ill) was performed in Europe in November 1999, which yielded very similar results. The mean pretransfusion hemoglobin was 8.4 ± 1.3 g/dl, and the mortality and morbidity were also increased in transfused patients versus nontransfused patients. This effect again was clear with more than 2 RBC units transfused [2].

Both these studies ask two questions: Are allogeneic blood transfusions beneficial or harmful in intensive care medicine? How can blood management be improved in intensive care medicine?

ABC = Anemia and blood transfusion in the critically ill; CRIT = Anemia and blood transfusion in the critically ill – Current clinical practice in the United States; ICU = intensive care unit; RBC = red blood cell.

Benefit or harm from allogeneic RBC transfusion

Both studies are large and data acquisition was prospective, but the studies are purely observational. Therefore, despite the finest statistical models used showing that allogeneic blood transfusions were independently associated with a higher mortality [1,2], it remains possible that this adverse outcome is not due to a harmful effect of allogeneic RBC transfusion in itself, but merely reflects the fact that transfused patients were sicker to start with. Indeed, there is some evidence that this was the case.

In the ABC study transfused patients were older, had a lower baseline hemoglobin, had higher Sepsis-related and Organ Failure Assessment scores and Acute Physiological and Chronic Health Evaluation II scores, and were more frequently in shock at hospital admission [2]. This potential confounding can only be avoided in prospective, randomized trials [3,4]. The largest is the study by Hébert and colleagues comparing a restrictive transfusion regimen (hemoglobin $<$7.0 g/dl) with a liberal transfusion regimen (hemoglobin $<$9.0 g/dl), finding a lower 30-day mortality in the restrictive transfusion regimen in patients younger than 55 years of age and in patients with an Acute Physiological and Chronic Health Evaluation II score $<$20 [3]. But also, when combining all available prospective randomized trials comparing restrictive and liberal transfusion regimens with mortality data ($n = 1568$, referenced in Carson and colleagues [4]), a higher mortality was found in the liberal transfusion group (15.2% versus 12.0%, chi-square $P < 0.06$). The potential is therefore real that RBC transfusions are efficacious only in very specific situations in intensive care medicine, such as when pretransfusion oxygen delivery is low [5], or that RBC transfusions are associated with significant side effects so that the overall balance is negative.

Immunosuppressive effects and storage lesions have been considered potential explanations for the relative ineffectiveness or even harmfulness of allogeneic blood transfusions [6,7]. Since the immunosuppressive effect may be mediated via leukocytes, universal leukoreduction has been introduced in many countries. Its effect on transfusion-related side effects, however, was only very modest: post-transfusion fever decreased but serious nosocomial infections remained unchanged and the effect on mortality was borderline [8]. No in-depth information regarding the type of RBCs transfused and the effect of transfusion on outcome are available in the CRIT and ABC studies, so this remains an open question.

In contrast, the age of the transfused RBCs was recorded in both studies: 16.2 ± 6.7 days in the ABC study [2] and 21.2 ± 11.4 days in the CRIT study [1]. Interestingly, older blood was not associated with a higher mortality or a higher morbidity [1,2]. This is in keeping with a recent observational study in 897 cardiac surgery patients, in which no association between the age of transfused RBCs and outcome was observed other than the risk of pneumonia increases with RBCs older than 28 days [9]. The mechanism(s) by which potentially harmful effects of allogeneic blood transfusions are mediated therefore remains largely unknown.

Improvement of blood management in intensive care medicine

Given the high costs of allogeneic blood transfusions [10], their very selective efficacy [5] and their side effects [7], an improved blood management in intensive care medicine is mandatory. Such options include decreasing blood loss for diagnostic purposes using pediatric sampling tubes [2], establishing restrictive multidisciplinary transfusion guidelines and implementing them in daily clinical practice [11], using recombinant human erythropoietin [12] and developing artificial oxygen carriers [13].

On average, 41 ml blood is drawn each day from a typical ICU patient. This becomes a main source of blood loss during the ICU stay [2]. By simply using pediatric sampling tubes this diagnostic blood loss could easily be cut in half. This measure is probably too simple to be taken seriously! Have you introduced it in your ICU?

Establishing restrictive multidisciplinary transfusion guidelines may also appear trivial. In the real world, however, it is not – and strictly implementing them in daily clinical practice is even less so [11]. Interestingly, in the CRIT study the presence or absence of a transfusion protocol did not influence the pretransfusion hemoglobin [1]. What does this mean? Did the transfusion protocols ask for the same traditional (high) hemoglobin transfusion triggers as used by the physicians anyway? Or were existing (restrictive) transfusion guidelines simply neglected? Have you introduced restrictive transfusion guidelines in your ICU and meticulously followed physicians' adherence?

Using recombinant human erythropoietin in intensive medicine resulted in clear reductions of allogeneic blood transfusion needs [12]. Its use in daily clinical practice may be limited by its relatively high price but, sooner or later, recombinant human erythropoietin will find its place in intensive care medicine.

Artificial oxygen carriers are fascinating new drugs in clinical development. Although perioperative transfusion requirements were reduced in several phase III studies [13–15], none of these substances is yet licensed in the Western world for human use and their use in intensive care medicine is very limited.

So, let us continue to work on future options but let us simultaneously implement the practical changes that can already make a difference today.

Competing interests

None declared.

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