Review

Transfusion trigger: when to transfuse?

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Abstract

The decision to transfuse a hospitalized patient must balance the known risks of transfusion with the need to provide adequate tissue oxygenation and the appropriate utilization of blood as a scarce resource. The minimum tolerated hemoglobin level is not well established, and considerable variation exists in intensivists' transfusion practices. Conventional transfusion triggers of 100 g/l have been challenged by reports indicating that aerobic metabolism is supported by hemoglobin levels of 50 g/l or less. Evidence from randomized trials also indicates that withholding transfusions may result in improved outcomes. Arbitrary numeric hemoglobin triggers, however, cannot supercede intervention based on individual physiologic need and clinical circumstances.

Keywords blood transfusion, hemoglobin level, tissue oxygenation

The normal hemoglobin level in the healthy individual is greater than 130 g/l. In the ambulatory patient levels below this are considered to represent anemia and trigger a search for potentially correctable causes, including sources of occult blood loss. However, the hemoglobin level of most hospitalized patients and, in particular, patients in an intensive care unit (ICU) falls substantially below this normal range. Multiple factors are responsible, including acute blood loss, dilution secondary to fluid retention and depressed hematopoiesis. At a certain level of anemia, the surgeon becomes concerned that reduced oxygen-carrying capacity may be detrimental to the patient's welfare and considers transfusion. The level that should trigger this decision has until recently been largely unknown.

The rationale for blood transfusion is rooted in the physiology of oxygen delivery. Oxygen delivery to the tissues (Do_2) depends upon the concentration of hemoglobin (Hb), the percent saturation of that hemoglobin (Sao_2), and the cardiac output (CO):

$$Do_2 = Hb \times \%Sao_2 \times CO$$

A reduction in oxygen delivery below a critical level deprives tissues of the oxygen necessary for oxidative metabolism and results in a shift to anaerobic metabolism. Because oxygen requirement by tissues may be increased during acute stresses, it is intuitive that maintaining adequate oxygen delivery will result in improved clinical outcome. Indeed, the concept that supranormal oxygen delivery was desirable led intensivists to devise strategies to increase oxygen delivery in critical illness to supraphysiologic levels [1]. The benefits of such an approach, however, have not been borne out by randomized controlled trials [2].

In theory, manipulation of hemoglobin, oxygen saturation, and/or cardiac output should increase oxygen delivery. However, hemoglobin is normally almost fully saturated with oxygen, and increasing cardiac output in the face of adequate filling pressures requires the use of inotropic agents. Thus, augmenting hemoglobin level is a potentially attractive strategy to increase oxygen delivery. Clinical studies, however, demonstrate the fallacy in such an approach; isovolemic hemodilution evokes reflex increases in cardiac output, with the result that oxygen uptake at the tissue level remains constant [3].

The benefits of transfusion must be weighed against the risks [4]. Transfusion is in essence a transplant of allogeneic cells, and its risks, although modest, are not negligible. Transfusion carries a small risk for transmission of viruses such as HIV

ICU = intensive care unit.

Table 1

Outcomes following transfusion: the TRICC trial

	Strategy		
Parameter/outcome	Restrictive ($n = 418$)	Liberal ($n = 420$)	*P*
Average hemoglobin (g/l)	85 ± 7	107 ± 7	<0.01
Units transfused	2.6 ± 4.1	5.6 ± 5.3	<0.01
MOD score	10.7 ± 7.5	11.8 ± 7.7	0.03
Hospital mortality (%)	22.2	28.1	0.05

MOD, multiple organ dysfunction. Data from the Transfusion Requirements in Critical Care (TRICC) trial [8].

and hepatitis, although with application of adequate screening methods this risk is low. The potential for transmission of unidentified viruses is unknown. Transfusion is also known to be immunosuppressive, and transfusion is an independent risk factor for nosocomial infection or for recurrence of malignancy [5]. Perhaps most importantly, blood is an increasingly scarce resource that must be used responsibly.

If transfusion to supranormal levels is not intrinsically helpful, then what is the minimum level of hemoglobin that can be tolerated by a healthy individual? The answer is unknown, but studies in human volunteers have demonstrated that isovolemic hemodilution to a hemoglobin of 50 g/l or less does not result in biochemical evidence of anaerobic metabolism [3]. Anecdotal reports documenting the course of Jehovah's Witness patients who have experienced major bleeding episodes confirm the ability to tolerate hemoglobin levels well below those conventionally accepted by physicians. Until quite recently, physicians accepted the maxim that patients should be transfused so that the hemoglobin was greater than 100 g/l, and that transfusion should be given 2 units at a time. The basis for this recommendation lies more in tradition than in science.

A recent Canadian initiative was undertaken to define patterns of blood transfusion in critical illness and to determine optimal transfusion strategies in critically ill patients [6]. Using a scenario-based questionnaire, it was determined that transfusion triggers vary widely and are strongly influenced by the geographic locale of the individual clinician's practice. In general, clinicians selected a higher transfusion trigger for patients with underlying cardiac disease or for patients with sepsis in whom supply dependency might be present. Substantial variability was documented in a retrospective survey of transfusion practices in four Canadian ICUs [7]. Again, physician factors accounted for a significant proportion of the variability in practice.

The Transfusion Requirements in Critical Care (TRICC) Trial [8], a multicenter, randomized, controlled trial, was conducted between 1994 and 1997. A total of 838 patients from 25 centers were randomly assigned to a liberal transfusion strategy (maintenance of the hemoglobin >100 g/l) or a restrictive transfusion strategy (maintenance of hemoglobin >70 g/l). Eligible patients were those who had a hemoglobin of 90 g/l or less within 72 hours of ICU admission. Patients enrolled in the two study groups had comparable baseline demographic features, and compliance to the protocol was excellent. Patients in the restrictive arm received half the volume of transfused blood that patients in the liberal arm did. Surprisingly, when outcome data were analyzed, patients in the restrictive arm exhibited a strong trend toward improved 30-day survival and a significant improvement in hospital survival. The development of new organ dysfunction in the ICU was significantly less in patients randomly assigned to the restrictive arm (Table 1). There was a trend toward decreased 30-day mortality among patients who were treated according to the restrictive transfusion strategy. The significant differences in mortality rates during hospitalization, rates of cardiac complications, and rates of organ dysfunction all favored the restrictive strategy. A review of the adverse events in both groups revealed that the major morbidity in the liberal group was the sequelae of transfusion – acute respiratory distress syndrome, congestive heart failure, and volume overload. Subsequent review of patients with a cardiac diagnosis showed that, even in this high-risk population, a restrictive transfusion policy resulted in improved clinical outcomes, although the differences were not statistically significant [9].

The deleterious consequences of blood transfusion arise from many sources. Improved techniques of screening the donor pool for infecting organisms have reduced rates of infection. Although hard data are not available, it is likely that leukodepletion has reduced the frequency of symptomatic adverse events associated with transfusion [10]. Marik and Sibbald [11] showed that transfusion of old blood (>12 days) was associated with worsening oxygen delivery because stored red blood cells lose their deformability and hence their ability to pass through the microvasculature and unload oxygen.

The best evidence currently available suggests that transfusion can safely be withheld as long as the hemoglobin remains above 70 g/l and the patient is not actively bleeding.

Such a policy appears not only to be safe but also perhaps even preferable to a more liberal strategy, even in patients with underlying cardiac disease. Whether a lower transfusion trigger is superior is unknown. Ultimately, however, the decision to transfuse should be based on expectation of individual physiologic benefit rather than on adherence to an arbitrary numeric transfusion trigger.

Competing interests

None declared.

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