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Risks and Indications of Blood Transfusions/Pros and Cons in the International Context

Abstract

Seit Anfang des 20. Jahrhunderts, als Bluttransfusionen erstmals in die Medizin Einzug hielten, haben sich die Indikationen für Bluttransfusionen vervielfacht, während die Risiken von Transfusionen stetig abnahmen. Dank der eingehenden Untersuchung von Blutspendern und von Bluttests konnte die Übertragung von Infektionskrankheiten durch Transfusionen deutlich reduziert werden, sodass heute die größten verbleibenden (wenn auch sehr unwahrscheinlichen) Risiken auf menschliche Fehler oder auf nach der Blutspende verdorbene oder infizierte Blutkonserven zurückzuführen sind. Reaktionen auf allogene Bluttransfusionen sind immer noch relativ häufig und führen bei etwa 20 % der Patienten zu Fieber, Schüttelfrost, Ausschlag oder Juckreiz. Nichtsdestotrotz besteht die größte Sorge von Ärzten und Patienten nach wie vor in der Übertragung von Infektionskrankheiten wie HIV oder Hepatitis. In beiden Fällen ist das Risiko sehr gering. Vor allem durch die aktuellen Bestrebungen, die Indikation zur Verabreichung von Bluttransfusionen einzuengen, kann das Risiko noch weiter verringert werden.

Dieser kurze Artikel beleuchtet die aktuelle Indikationsstellung für Bluttransfusionen sowie die damit verbundenen Risiken im internationalen Kontext. Ferner wird über die Anwendung von Erythropoetin als weitere Möglichkeit zur Verringerung von Erythrozyten-Transfusionen berichtet.

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Red blood cell (RBC) transfusions are frequently used to treat anemia that is symptomatic or severe (as evidenced by the patient's hemoglobin [Hb] level) but are associated with well-known risks and shortcomings, prompting the search for safer and more effective alternatives.

Anemia, albeit defined as any Hb level below normal, can be more precisely categorised by various grading systems such as those developed by the World Health Organization (WHO).[1] WHO measures Grade 1 anemia as a Hb level of 9.5 to 10.9 g per dL. For the more severe grades of anemia, it uses a Hb level of 8.0 to 6.5 g per dL as the lower limit of Grade 3 (serious) anemia, with a Hb level of less than 6.5 g per dL considered Grade 4 or life-threatening anemia.

The decision to transfuse an anemic patient is often based solely on the haemoglobin value. Patients are frequently transfused when haemoglobin values fall below 8.0 g/dL (grade 3). While this is a reasonable "transfusion trigger," studies in patients requesting bloodless or conservative care have demonstrated that lower transfusion triggers in otherwise stable patients are reasonable.[2-4] Of course, the decision to transfuse should also be based on clinical symptoms related to any degree of anemia, such as dyspnea unrelieved by oxygen, lightheadedness, syncope, chest pain, palpitations, decreased urinary output, and change in cognitive function. Multiple factors other than the Hb value can be used to determine the need for intervention, and individual hospital or clinic guidelines are encouraged for a given region to conserve, yet appropriately use blood transfusion as much as possible. For example, one could attempt to identify the expected blood loss associated with a specific type of surgical procedure, allowing a target Hb to be identified and guiding transfusion practice.

Although transfusions of red blood cells (RBCs) ameliorate anemia, transfusions are associated with well-known risks, primarily related to the risk of transmission of infectious disease. Improved screening of the blood supply has substantially reduced the risk of transmitting HIV and hepatitis C.[5] However, the potential for transmitting other infectious organisms remains. At the time of writing, nucleic acid technology screening is not available for viral entities such as hepatitis A and B, Parvovirus B19, and West Nile virus. Transmitting parasitic contaminants, including malaria and *Trypanosoma cruzi* (the organism responsible for Chagas disease), is also a concern that cannot be alleviated via contemporary routine blood screening. Evidence also exists that a new variant form of Creutzfeldt-Jakob disease (CJD), a rare and fatal neurodegenerative condition, may be transmitted through blood transfusions, albeit rarely.[6,7]

Since blood transfusions are used quite often in the intra-operative setting, it is important to examine any additional risks that they may pose. Data from over 30 observational studies suggests that blood transfusions are associated with up to a 10-fold increased risk of developing postoperative infections.[8] For example, data from the Project IMPACT

database that included 1717 patients admitted to a medical-surgical-trauma intensive care unit found that the nosocomial infection rate for those receiving a transfusion was 15.4% compared with 2.9% for those who did not receive a transfusion ($P < 0.005$).[9] The risk of nosocomial infection was dose dependent. For each unit of packed RBCs infused, the risk of developing a nosocomial infection increased by a factor of 1.5. A subgroup analysis found that there was an increase in the risk of nosocomial infection regardless of age. Of course, while this may be a consequence of blood transfusion, it may also simply indicate that patients receiving transfusions are sicker to begin with.

A meta-analysis was recently conducted to assess whether leukoreduction is effective in reducing the risk of postoperative infections.[10] This analysis pooled data from randomised trials involving patients undergoing a wide variety of types of surgery. The overall risk of postoperative infection was reduced by 40% among transfused patients who received leukoreduced blood compared with those who received non-leukoreduced blood. There was also a 39% reduction in mortality for those receiving leukoreduced versus non-leukoreduced blood.

A UK haemovigilance study, SHOT (Serious Hazards Of Transfusion) examined the incidence of adverse reactions to blood transfusions experienced in patients between 1996-2003. During this time period, of the 23 million units of blood transfused, the adverse reaction rate was 0.2 per 100,000 units transfused with a morbidity rate of 1.1 per 100,000 units (0.6 due to transfusion related acute lung injury (TRALI) and 0.2 due to infection).[11]

The mechanism by which transfusions may adversely affect survival has not been definitively established; however, it is speculated that it may be related to transfusion-related immunosuppression.[12] The antigens infused during allogeneic transplantation produce a wide variety of adverse reactions that likely stem from the production of antibodies and specific cytotoxic T-cells, as well as the suppression of immune responses.[8] Leukocytes are a known contaminant of RBC and platelet transfusions. Some data has suggested that the immunomodulatory effects associated with allogeneic leukocyte transfusion are associated with worse clinical outcome and that leukoreduction techniques can help avoid this effect. For example, in a randomised, controlled trial among patients undergoing cardiac surgery, leukocyte-depleted blood was associated with a postoperative mortality rate that was more than 50% lower than that of non-depleted transfusions[13]. However, in a more recent study at this same institution, there was no significant benefit on cancer recurrence or overall 5-year survival in colorectal cancer patients receiving perioperative leukocyte-depleted transfusions.[14]

Recombinant human erythropoietin (EPO) has been used to treat the anemia associated with HIV, renal disease, cancer, and anemia of chronic disease in the US for over 10 years. Despite its FDA approval in 1996 for use in the presurgical setting, clinicians often

do not think of optimising a patient's Hb level preoperatively via erythropoietin. Given a normal hemoglobin lower limit of 12 g/dL, EPO could reasonably be considered for patients without other reversible causes of anemia as their hemoglobins fall below this level. However, EPO is not without expense and cost benefit issues must be taken into account. In the HIV and oncology settings, consideration of EPO is recommended after Hb levels fall below 11 g/dL and definitely after a Hb decline below 10 g/dL.[15,16] Similar guidelines exist in nephrology for dialysis and predialysis anemic patients.[17] EPO is effective for driving RBC production and iron supplementation is an equally important component of anemia management to ensure the production of RBCs with adequate Hb content.

In summary, anemia is a global problem. Identification of anemia in a patient should always require a brief evaluation of the cause of the anemia before treatment. If Hb related symptoms or values are severe enough, transfusion should be considered. While transfusion is increasingly safe, it will never be totally without infectious, adverse reactions, or clerical error related risk. EPO therapy provides an acceptable alternative treatment strategy for those patients who do not require immediate correction of the anemia.

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