CRITICAL CARE

COMMENTARY

New versus old blood – the debate continues

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See related research by Ranucci *et al.*, http://ccforum.com/content/13/6/R207

Abstract

Since the inception of blood banking, refinements in laboratory processes have allowed for progressively longer storage times of red blood cells. Whilst advantageous for the logistics of stock management, the clinical impact of the duration of red blood cell storage prior to transfusion remains uncertain, and a topic of growing interest.

The current standard red blood cell (RBC) storage time of up to 42 days is not based upon a demonstrable therapeutic benefit, but instead on the observed return of 70% of the viable transfused RBCs at 24 hours after storage for 42 days or less. The structural, biochemical and immunological changes that RBCs undergo during storage are well described, but what remains controversial is the evidence that this storage lesion translates into adverse clinical outcomes for patients receiving older blood. In a previous issue of *Critical Care*, Ranucci and colleagues report an adverse outcome in infants receiving older blood during cardiopulmonary bypass (CPB) [1].

Effects of blood storage

The effects of storage on RBCs include changes in potassium (increased levels), 2,3-diphosphoglycate (decreased levels), lactate (increased levels), pH (decreased values), glucose (decreased levels), adenosine triphosphate (decreased levels), methaemoglobin (increased levels), red cell structure (from biconcave disc, to echinocytes and then to spherocytes), and therefore red cell deformability. Storage effects also include changes to the microenvironment with reduced levels of *S*-nitrosohaemoglobin and nitric oxide. Prolonged storage prior to transfusion also results in an immunomodulatory effect, first described by Opelz and colleagues who demonstrated reduced transplant rejection after stored red cell administration [2]. This effect theoretically increases infection risk, by accumulation of proinflammatory lipids and neutrophil priming, resulting in severely reduced neutrophil function.

The evidence that prolonged storage of RBCs contributes to demonstrable adverse outcomes remains controversial, however, and is hampered by many small retrospective studies with potential selection bias; most evidence is also confounded by relatively recent changes in practice such as leucodepletion of RBCs. Moreover, there is still no consensus on what constitutes old blood, with studies using variable definitions of 5, 12, 14 or 21 days. None of the prospective studies to date have shown a correlation between the age of RBCs and adverse outcome. Two new studies in progress should provide further data – the Age of Blood Evaluation study (Canadian Clinical Care Trials Group) in trauma/intensive care patients and the Red Cell Storage Age Study (US National Heart, Lung, and Blood Institute's Transfusion Medicine/Hemostasis Clinical Trials Network) in cardiac surgery patients.

Intensive care studies

Marik and Sibbald reported in 1993 that older RBCs were associated with a reduced intragastric pHi value (a surrogate for gut ischaemia) and postulated that impaired deformability of RBCs impeded microvasculature flow [3]. A similar study published in 2004, however, failed to confirm these findings [4]. Offner and colleagues suggested that trauma patients receiving blood stored for >2 weeks had higher rates of infection and multiorgan failure [5]; but these patients also received a greater volume of transfusion, were older and had more severe injuries. More recently, Zallen and colleagues reported in a cohort of 63 trauma patients that those who received older blood had a higher risk of developing multiorgan failure [6]; yet again, however, these patients were older and received marginally more RBCs.

Cardiac surgery studies

The largest studies in this field have been performed in cardiac surgery. Van der Watering and colleagues retrospectively reviewed 2,732 patients undergoing CPB [7];

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univariate analysis, but not multivariate analysis, suggested a correlation between storage time and survival. In 2008 Koch and colleagues evaluated an even larger patient group of cardiac surgical cases who received RBCs either ≤14 days old or >15 days old [8]. Their results indicated excess inhospital mortality associated with older blood, but these patients were also more likely to have received more RBCs.

These retrospective studies are now added to by that of Ranucci and colleagues in a previous issue of *Critical Care*, who evaluated outcome in 239 infants receiving blood as either a CPB pump prime or an intra/post-operative top-up transfusion according to whether this blood was ≤4 days old or older. Of 192 infants receiving CPB prime blood, the authors concluded that older blood recipients were more likely to have pulmonary complications. After adjusting for other possible confounders, the RBC storage time remained an independent predictor of major morbidity, although the same association was not found for patients receiving RBCs after CPB.

Red cell transfusion in the critically ill continues to raise many questions – including whether the storage duration of red cells affects measurable outcomes; whether leucodepletion results in fewer storage associated complications; the effect of red cell irradiation on relevant outcomes; and, finally, the appropriate target haemoglobin level in the preoperative, bleeding and stable critically ill patient.

Clearly, more robust evidence from prospective trials is required to support the therapeutic use of blood transfusion in the critically ill, or uncertainty will remain.

Abbreviations

CPB, cardiopulmonary bypass; RBC, red blood cell.

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Competing interests

DW is a co-investigator in the RELIEVE study; A feasibility randomized trial comparing restrictive and liberal blood transfusion strategies in intensive care patients.

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