Red blood cell transfusion: Does it matter how old it is?

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None related to this topic.

Approximately 13.8 million units of allogeneic RBCs are administered in the U.S. annually, with over 2 million units alone going to patients undergoing cardiovascular surgery. Allogeneic RBCs that are stored in modern preservative solutions are approved for use within 42 days after collection. This 42 day shelf life is based largely on the ability of these cells to persist in the circulation for > 24 hours. As previously summarized[1], it is well known that RBCs undergo significant biochemical and structural changes during the 42 day period of storage (e.g. decreased RBC deformability, decreased ATP and 2,3-DPG, and a significant increase in abnormally shaped RBCs).

For example we have recently published the most comprhensize assessment of stored red blood cells[2]. We analyzed changes occurring during RBC storage focusing on RBC deformability, RBC-dependent vasoregulatory function, and S-nitrosohemoglobin (SNO-Hb). Five hundred ml of blood from each of 15 healthy volunteers was processed into leukofiltered, additive solution 3-exposed RBCs and stored at 1-6 °C according to AABB standards. Blood was subjected to 26 assays at 0, 3, 8, 24 and 96 h, and at 1, 2, 3, 4, and 6 weeks. Numerous changes occurred including previously described deterioration in levels of 2,3-DPG and potassium. RBC deformability assayed at a physiological shear stress decreased gradually over the 42-day period. In addition, SNO levels, and their physiological correlate, RBC-dependent vasodilation, become depressed soon after collection, suggesting that even "fresh" blood may have developed adverse biological characteristics. Time courses vary for several storage-induced defects that might account for recent observations linking blood transfusion with adverse outcomes.

There is growing evidence from "association studies" that the administration of allogeneic RBCs of longer storage duration is an independent predictor of mortality in surgical, trauma, and other critically ill patients. For example, Zallen et al[3] and Purdy et al[4] demonstrated an association between the administration of "older blood" and mortality in trauma and septic ICU patients, respectively.

Studies in cardiac surgery have yielded inconsistent results[5-9]. For example, Vamvakas et al. studied a cohort of 416 consecutive patients undergoing low risk CABG surgery[7]. From their data they concluded that "After adjustment for the effects of the risk factors for pneumonia and the number of transfused RBCs, an association was observed between the length of storage of transfused RBCs and the development of postoperative pneumonia. This association should be investigated further in future studies of the outcomes of blood transfusion". However, the same investigators subsequently studied a cohort of 268 patients undergoing CABG surgery at the same institution[8]. In their most recent publication they reported that "This study did not corroborate the previously reported association between transfusion of old RBCs and increased morbidity. However, there is surprisingly little research on the clinical outcomes of the transfusions of old RBCs, and this hypothesis should be investigated further"[8]. Leal-Noval et al. studied a cohort of 897 low risk patients undergoing cardiac surgery in Spain[6]. From their data they concluded that "Prolonged storage of erythrocytes does not increase morbidity in cardiac surgery. However, storage for longer than 28 days could be a risk factor for the acquisition of nosocomial pneumonia". Van de Watering et al. observed no independent association of storage duration and adverse outcome[9], although the lack of complete leuokodepletion in these patients makes it unclear how generalizable these results are to a setting with universal prestorage leukodepletion. However, in a large dataset (n > 4,000), DeSimone et al. (Duke University) observed an independent association between increased duration of storage of allogeneic RBCs and mortality after cardiac surgery[5]. More recently an observational study of

6,002 cardiac surgical patients by Koch et al. published in the *New England Journal of Medicine* showed that increased storage duration was an independent predictor of mortality and other adverse outcomes[10].

No large randomized trial has examined the impact of duration of stored RBCs on organ dysfunction and mortality in high risk patients. In humans there is no Level I evidence to guide clinicians, and most of the existing data come from non-randomized cohort studies (Level 3) described above. Therefore, high risk hospitalized patients routinely receive allogeneic RBCs that have been stored for a prolonged period of time, largely because there is no definitive proof that the duration of storage of RBCs is of clinical relevance.

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