HBV isolates, 4 were of nonUS origin (B, C, D, F; all from VBI donors) and 3 were of US origin (A2; 2/3 from VBI donors); A2 is the vaccine genotype. 6/7 were wild type in the pre-S/S region. **Conclusions:** HBV MP NAT yield rates exceed those projected by models and likely reflect the absence of VBI in the models. The high yield suggests the efficacy of HBV MP NAT for donor screening even in the absence of known transmissibility of VBI. The public health aspects of HBV infection in VBI donors require further study.

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P4-020A

Harmful Effects of Red Blood Cell Transfusions: Iron and Inflammation

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Background: Clinical studies suggest that transfusion of packed red blood cells (RBCs) after prolonged storage is associated with increased mortality, infection, and multi-organ failure in hospitalized patients. We hypothesized that iron delivered to the monocyte-macrophage system by rapid clearance of a damaged subpopulation of stored RBCs causes adverse effects and we developed a mouse model to study the mechanism(s) responsible. **Methods:** RBCs from FVB/NJ mice were filter leukoreduced and stored in CPDA-1 for <2 weeks at a hemoglobin of 17.0 g/dL at 4°C, under conditions previously reported to meet FDA 24-hr post-transfusion survival guidelines. Male C57BL/6 mice were transfused with 200 or 400 μL of fresh or stored RBC and sacrificed 2 hr post-transfusion. Plasma cytokine levels were quantified by a multiplex flow cytometric assay, organ iron levels were measured by a wet ashing method, and serum non-transferrin bound iron (NTBI) was determined by a nitrilotriacetic acid-ultrafiltration assay. Acute-phase protein serum amyloid A1 (SAA1)-luciferase transgenic mice were also transfused and bioluminescence was measured for up to 24 hr using the In Vivo Imaging System (Caliper Life Sciences). **Results:** In contrast to fresh RBC transfusions, transfusions with RBCs stored for 2 weeks (i) induced dose-dependent increases in circulating pro-inflammatory cytokines (monocyte chemoattractant protein-1, interleukin (IL)-6, CXCL1, and tumor necrosis factor-α; all $p < 0.05$), (ii) increased serum NTBI levels (undetectable vs. 2.4 ± 0.3 μM; $p < 0.05$), and (iii) led to substantial iron deposition in liver and spleen ($p < 0.05$). Stored RBC transfusions also increased luciferase activity (320-fold) in the hepatic region of SAA1-luciferase reporter mice at 4 hr post-transfusion ($p < 0.05$). To determine if this inflammatory state was caused by the RBCs themselves or by a substance accumulating in the supernatant during storage, normalized doses of washed RBCs, supernatant, or RBC ghosts were transfused; only washed RBC transfusions significantly increased circulating cytokine and NTBI levels ($p < 0.05$). Finally, to examine the role of iron in the inflammatory response, mice were injected with 3 mg of deferoxamine, an iron chelator, just prior to transfusion; this significantly blocked the cytokine response (e.g. reducing IL-6 from 212.8 ± 30.8 pg/mL to 98.4 ± 10.1 pg/mL; $p < 0.05$). In addition, iron chelation inhibited hepatic SAA1 induction by 54% at 4-hr post-transfusion. **Conclusions:** Transfusing mice with older stored RBCs acutely produces serum NTBI and induces a pro-inflammatory response. Iron chelation can decrease the pro-oxidant effects of the iron released following rapid clearance of a damaged subpopulation of stored RBCs, which is responsible, at least in part, for the observed "cytokine storm."

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P5-020A

Clinical Effectiveness and Safety of Pooled, Random Donor Platelet Concentrates, Leucoreduced and Stored up to Seven Days in Either Plasma or Additive Solution with and Without Pathogen Reduction in Hemato-oncological Patients

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Introduction: Extending storage time combined with maintaining or improving the safety of platelet products are the main features in the development of new platelet products. In a multicenter randomised controlled trial we have investigated the transfusion efficacy in hemato-oncological patients of three different buffy-coat derived platelet products: Platelets stored in plasma (plasma-PC), platelets stored in PAS III (Intersol, PAS III-PC) and platelets stored in PAS III treated with psoralen pathogen reduction (Intercept, PR-PAS III-PC). Platelets were stored up to seven days. Here we report on the data of the interim analysis of this study, comparing plasma PC with PR-PAS III-PC. **Methods:** Patients were randomised to receive up to a maximum of five platelet transfusions with either plasma-PC, PAS III-PC or PR-PAS III-PC. Inclusion criteria were: age ≥ 18 years, hemato-oncological disease, expected number of PC transfusions >2 and informed consent. Exclusion criteria were: known or suspected HLA/HPA-immunisation, pregnancy or clinically relevant auto-immune thrombocytopenia. Primary endpoint of the study was 1-hour corrected count increment (CCI). Secondary endpoints were 24-hour CCI, bleeding CTC grade ≥2, transfusion requirement of red blood cell concentrates and PC, PC transfusion interval and adverse transfusion reactions. The study was designed as a non-inferiority study, in which inferiority is defined as a >20% decrease of mean 1-hour CCI. **Results:** The study started March 2007 and at the time of interim analysis, December 2008, there were 199 evaluable patients (plasma-PC n = 68, PAS III-PC n = 64, PR-PAS III-PC n = 67). Based on data from the interim analysis, we report on the PC transfusion data and bleeding complications from the first 135 patients included in the plasma PC arm and the PR-PAS III-PC arm. Transfusions with PR PAS-III PCs (n = 252) resulted in a mean 1-hour CCI of 11.4 ± 5.4 as compared to 17.5 ± 7.1 with plasma PCs (n = 212), resulting in a mean difference of 34.2% ($P < 0.0001$). The 24-hour CCI was 8.0 ± 5.6 and 13.0 ± 7.9, respectively, resulting in a mean difference of 33.5% ($P < 0.0001$). 24 patients in the PR PAS-III arm experienced bleeding episodes as compared to 14 in the plasma PC arm ($P = 0.045$). After reviewing these data, the independent Data Safety Monitoring Board advised us to halt inclusion in the PR-PAS III-PC. **Conclusion:** Although the final analysis of the study still has to be completed, data of the second interim analysis strongly suggest inferiority of platelets stored in PAS III treated with pathogen reduction. As the study has just finished enrolling patients we expect to complete the analysis of all included patients in September 2009.

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