American Red Cross

Pathogen Reduced Cold-Stored Platelets (CSP)

The American Red Cross Now Offers PR PAS-Stored CSP

Cold-stored platelets (CSP) are a recent hot topic. Prior to the 1960s, refrigerated whole blood contained red cells, plasma, white cells and (cold-stored) platelets transfused as one product to bleeding patients. With broad advancement in medical treatments and manufacturing technology, transfusion therapy became component-based whereby a single donation could yield specific blood products for multiple patients. Researchers sought to find the optimal storage conditions for each blood component. In 1969, Murphy and Gardner showed that CSP did not survive as long as room temperature (RT)-stored platelets after transfusion in healthy research donors.[1] That led to the change to RT storage of platelet concentrates, which has since remained the standard.

For an oncology or stem cell transplant patient, platelets are transfused to maintain a platelet count high enough to prevent bleeding until the patient's recovery. In actively bleeding patients, transfused platelets are immediately needed to form clots at sites of injury, and the shorter circulation time of CSP is less of a consideration. In-vitro testing suggests CSP create stronger clots that are more resistant to fibrinolysis (clot breakdown),[2] while an in-vivo study showed faster reversal of bleeding with transfusion of CSP vs. RT-stored platelets.[3] While the U.S. military and several centers described positive experiences in using CSP under previous FDA variances, little peer-reviewed data on clinical outcomes is published. A pilot trial randomizing adult cardiac surgery patients to receive either CSP or RT-stored platelets while on cardiopulmonary bypass showed similar bleeding outcomes and transfusion needs in both groups, suggesting non-inferiority of CSP in this setting.[4] The larger ongoing CHIPS (Chilled Platelet Study) trial uses an adaptive study design to compare outcomes in pediatric and adult cardiac surgery patients randomized to receive CSP up to day 21 of storage or standard RT-stored platelets, which expire in 5 days.

RT-stored platelet inventory shortages remain a common challenge due to short product shelf life, fluctuations in donor turnout, and supply chain disruptions. As RT-stored platelets have a higher risk for septic transfusion reactions, the FDA mandates that they undergo bacterial mitigation, typically either pathogen reduction (PR) or large-volume delayed sampling (LVDS) for bacterial culture.[5] These measures delay

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release from suppliers to hospitals and shorten usable shelf life of platelets. With data showing that early platelet transfusion is beneficial in the treatment of coagulopathy seen in trauma and during massive hemorrhage,[6,7] there is a resurgence of interest in CSP given its current shelf life of 14 days compared to 5 days for PR RT-stored platelets.

Following the June 2023 FDA guidance on alternative procedures for CSP manufacturing,[8] the Red Cross began to plan for its production. CSP are stored at 1-6° C which slows metabolic activity and inhibits growth of bacterial pathogens; additionally, they do not require agitation or bacterial mitigation.The Red Cross will offer PR CSP stored in platelet additive solution (PAS). PR removes the need for irradiation and for CMV-seronegative units for vulnerable patient populations. Large platelet aggregates are frequently observed in CSP stored in full plasma,[9] but decreasing the plasma content by cold storage in PAS reduces aggregate formation.[10] Additionally, PAS storage reduces allergic transfusion reactions[11] and should further decrease the already low risk of hemolysis due to ABO isohemagglutinins in non-type-specific platelet transfusion.[12]

Per the aforementioned FDA guidance, CSP use is "intended for the treatment of active bleeding when conventional platelets are not available, or their use is not practical."[8] The FDA has recommended that hospitals create their own standard operating protocols to define their individual institutional plans for CSP use. Additional clinical data on CSP use in bleeding patients will hopefully be published in coming years with recently completed enrollment in the CriSP-HS (The Cold-Stored Platelet Early Intervention in Hemorrhagic Shock) and CriSP-TBI (The Cold-Stored Platelet Early Intervention in Traumatic Brain Injury) studies and ongoing enrollment in CHIPS. CSP use for non-bleeding patients has not yet been studied, and the appropriate use of CSP vs. RT-stored platelets to meet the needs of specific patient populations is likely to remain a popular area of future research and discussion.

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