

Whole blood: longer holding times before leukoreduction may be a safe to explore option

What is this research about?

Whole blood transfusion is receiving renewed interest as a lifesaving alternative to component therapy for actively bleeding patients. In Canada, all blood products for transfusion must be leukoreduced. Leukoreduction removes white blood cells that could potentially cause infectious disease transmission or unwanted immune responses. Canadian Blood Services is evaluating a platelet-sparing filter to prepare leukoreduced whole blood for transfusion. The manufacturers of the platelet-sparing filter licensed for use in Canada recommend that whole blood be filtered within eight hours of collection. This is not always operationally feasible, especially in Canada where distances between collection and processing sites can be large. This research examined whether the whole blood collection bag, leukoreduction filtration, and the timing of filtration significantly affects whole blood quality during 21 days of cold storage. Exploring and validating alternative processing parameters, such as longer hold times before leukoreduction, could offer greater operational flexibility for blood operators.

IN BRIEF: A longer hold time before leukoreduction of whole blood for transfusion did not significantly impact quality and could allow for greater operational flexibility for blood operators.

What did the researchers do?

This was an eight-arm, non-pool and split study using whole blood collected from healthy type O blood donors. The researchers assessed the impact of the collection bag used, whether the unit was leukoreduced or not, and the time from donation to leukoreduction and refrigeration (cold storage) on in vitro properties of whole blood during 21 days of cold storage. The study compared "early" leukoreduction filtration and refrigeration (3-8 hours after collection) and "late" leukoreduction filtration and refrigeration (18-24 hours after collection). For the unfiltered arm of the study, "early" and "late" referred to when the units were placed in the refrigerator. The in vitro qualities of unfiltered or filtered whole blood, at early or late timepoints, were assessed at day 0/1, 7, 14, and 21 days of cold storage. Measurements included assessments of whole blood supernatant and hemostatic profile (using a machine called a ROTEM), and red blood cell, platelet, and plasma in vitro quality assays.

What did the researchers find?

Leukoreduction of whole blood resulted in some loss of platelets but this loss was not enough to significantly impact the ability of the blood to clot, as seen by ROTEM hemostatic profiles. There

was also no major loss in hemoglobin and hematocrit levels, consistent with previously published data. Comparing early versus late leukoreduction, longer whole blood holding times resulted in increased metabolic activity, shown as higher rate of glucose consumption and lactate generation, and lower pH. However, these initial differences diminished throughout the 21-day cold storage period. Clotting time was slightly longer in the late filtered whole blood units, but the level did not change throughout storage. Prothrombin, factor V and factor VIII activity, fibrinogen levels and prothrombin time were not significantly different after leukoreduction or impacted by filtration timing. Leukoreduction did not result in contact activation (i.e. clotting due to the interaction of factors with a surface such as the filter). Overall, there were some small statistical differences in quality parameters between early and late leukoreduction, but none were considered biologically relevant. There were also no consistent, significant differences in whole blood in vitro quality between the two blood collection bags used.

How can you use this research?

A refined understanding of the production processes and the parameters which impact final product quality is critical to safely and reliably introducing leukoreduced, cold-stored whole blood. By exploring several processing parameters in depth, including the hold time before leukoreduction, this study showed that hold times of up to 24 hours before leukoreduction are possible, which extends the parameters put forward by the filter's manufacturer (up to 8 hours). This study provides important evidence that will be submitted to the regulator as part of Canadian Blood Services' planned license amendment to obtain approval to add whole blood to its product formulary. A complementary study recently published has shown that extended time prior to filtration of whole blood may not pose a significant bacterial contamination safety risk to transfusion patients. Together, these findings will support Canadian Blood Services and other blood operators to tailor their whole blood production process to fit within their operational paradigms.

About the research team: This research was led by **Dr. Peter Schubert**, Canadian Blood Services senior scientist, with **Dr. William Sheffield**, Canadian Blood Services associate director, research; **Dr. Dana Devine**, Canadian Blood Services chief scientist, and **Ken McTaggart**, Canadian Blood Services associate director, product and process development. The study involved members of their laboratories and the Blood4Research facility.

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