Pathogen inactivation for safer blood transfusion: What are the limitations?

What is this research about?

Despite many safety improvements, blood transfusion still has some risks. These include the risk of illness if blood is contaminated with microorganisms called ‘pathogens’ such as viruses and bacteria that cause disease. Many approaches are used to reduce or prevent pathogen contamination in the blood supply. For example, donors are screened and blood donations are tested. However, testing only works for known pathogens. Unknown pathogens that cannot be tested for, called ‘emerging’ pathogens, are a risk to the blood system. This and other issues including the sensitivity limits of pathogen testing means there is a need for alternative ways to improve blood safety.

Several new technologies to reduce pathogen contamination, called pathogen inactivation (PI), have recently been developed and shown to improve transfusion safety. Generally, whole blood donations are separated into components after collection. One of the separation processes used at Canadian Blood Services, called the buffy coat method, results in three components: platelets, red blood cells (RBCs), and plasma. These components can be transfused separately to patients as they are needed. Before transfusion into patients, PI would treat these blood components with ultraviolet (UV) light with or without a chemical called a photosensitizer. UV light damages nucleic acids (DNA and RNA) which contain the cells’ genetic information. When a pathogen’s nucleic acids are damaged they can no longer reproduce and cause illness. PI offers protection against known and ‘emerging’ pathogens and also destroys residual white blood cells which can cause transfusion-related complications. However, blood components contain nucleic acids, and previous studies have shown that PI can damage plasma and platelet components. Very little is known about the effect of PI on RBCs. The researchers examined the UV light/riboflavin PI method. Rather than treating individual blood components with PI, they treated whole blood with PI, separated the blood and investigated the quality of all three components.

What did the researchers do?

In total, 48 whole blood units were collected from blood donors. Half of the whole blood units were treated with PI, and the other half were left untreated. RBC, plasma and platelet components were produced from both the treated and untreated whole blood. The platelet components that were produced from the untreated whole blood were then treated with PI. The quality of all the components was monitored during their storage using standard laboratory-based tests.

- For RBC and plasma, components produced from PI-treated whole blood were compared to components produced from untreated whole blood.
- For platelets, the researchers also wanted to understand the impact of treating platelet components with PI. Therefore, platelets produced from PI-treated whole blood were compared to platelet components produced from untreated whole blood and then treated with PI.

What did the researchers find?

The quality of RBC components produced from PI-treated whole blood decreased more quickly than components produced from untreated blood. At the end of RBC storage (day 42), the average number of burst RBCs (called

In brief...

Pathogen inactivation is known to improve blood transfusion safety, but also impact quality. More research is needed to determine the best approach to ensure safety and optimize blood component quality.
Plasma components produced from whole blood treated with PI showed a three to 44% decrease in activity for several clotting factors.

Platelet components from PI-treated whole blood were of significantly better quality than platelet components treated directly with PI. However, compared to untreated platelet concentrates, the quality of PI-treated platelets was reduced regardless of whether whole blood or the component was treated. Overall, components produced from PI-treated whole blood did not meet all Canadian Standards Association criteria for quality. However, these standards are based on untreated components, so whether they can be applied to PI-treated products is unclear. PI treatment of platelet concentrates and plasma is known to affect quality parameters, but treatment of these products does not appear to change patient outcomes. Whether the lower quality seen impacts the clinical effectiveness of the RBCs is unknown.

How can you use this research?

This important study is the first to provide a glimpse into the quality of all components produced by the buffy coat processing method following PI treatment of whole blood using the UV/riboflavin approach. The results show that PI treatment damages blood components even when treatment is performed on whole blood before component separation. For platelets, the damage is less when whole blood is treated with PI than when platelets are treated directly. This difference is likely related to hemoglobin, an iron-containing protein in RBCs. Hemoglobin can absorb some of the UV light and, when whole blood is treated, it may lessen the dose of PI received by platelets. Despite this, treatment of whole blood is known to be as effective against pathogens as direct treatment of platelet components. Clinical trials are underway in the USA, Europe and Africa to investigate the impact of whole blood PI treatment on the clinical effectiveness of blood/components. The laboratory-based findings in this study should help researchers interpreting the clinical trial results. Studies such as this one inform decisions by Canadian Blood Services about how PI technologies might be used to provide safe and effective blood components to patients in need. More research on this and other PI methods is needed before a decision can be made on which approach is best to ensure maximum safety and optimum product quality.

About the research team: Dr. Dana V. Devine is the Canadian Blood Services chief medical and scientific officer, a Canadian Blood Services’ centre for innovation scientist and a professor at the department of pathology and laboratory medicine at the University of British Columbia. This study was conducted in Dr. Devine’s laboratory, led by Dr. Peter Schubert, a Canadian Blood Services’ centre for innovation research associate and clinical associate professor in the department of pathology and laboratory medicine at the University of British Columbia. Dr. Katherine Serrano and Dr. Elena Levin are a Canadian Blood Services’ centre for innovation research associate and research assistant, respectively, and are affiliated with the department of pathology and laboratory medicine at the University of British Columbia. Brankica Culibrk, Simrath Karwal and Daniel Bu are members of Dr. Devine’s laboratory. Dr. William P. Sheffield is the associate director of research and a scientist at Canadian Blood Services’ centre for innovation, and a professor of pathology and molecular medicine at McMaster University, Hamilton ON. Varsha Bhakta is a research assistant in Dr. Sheffield’s laboratory at McMaster University. The work was conducted in collaboration with Dr. Raymond P. Goodrich, vice president scientific and clinical affairs, TerumoBCT, Lakewood, CO.

This ResearchUnit is derived from the following publication:

Acknowledgements: Canadian Blood Services is grateful to blood donors for making this research possible. This research received financial support from TerumoBCT and Canadian Blood Services’ centre for innovation funded by the federal government (Health Canada) and the provincial and territorial Ministries of Health. The views expressed herein do not necessarily reflect the views of the federal government.

Keywords: Blood components, pathogen inactivation, quality, platelets, red blood cells, plasma.

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