Supporting evidence to change regulations regarding the storage of cryosupernatant plasma

What is this research about?

Canadian Blood Services is a not-for-profit organization whose mission is to manage the supply of blood and blood products in Canada, except for the Province of Québec. The majority of Canadian Blood Services activities involve collecting, producing, testing, and distributing transfusable products (red blood cells, plasma, and platelets). One of the products produced is cryosupernatant plasma which is made by removing the cryoprecipitate from slowly thawed frozen plasma. Most patients receiving cryosupernatant plasma suffer from thrombocytopenic thrombotic purpura (TTP), a disease in which ADAMTS13 (a plasma protein) fails to trim von Willebrand Factor (VWF) (another plasma protein) to a size appropriate for healthy function.

Cryosupernatant plasma has reduced levels of Factor VIII (FVIII) and von Willebrand Factor (vWF), but it contains other factors that can benefit patients who don’t need FVIII or vWF replacement. Once prepared, cryosupernatant plasma is refrozen and stored until thawed for transfusion into patients. Prior to transfusion, the cryosupernatant plasma must be refrigerated at 1°C - 6°C. Currently, Canadian regulations limit the refrigerated storage time to 24 hours and require that older units be discarded. Although this regulation has been in place for many years, it is not clear how it came to be. Regulated cryosupernatant shelf life varies internationally. In Europe, for example, it must be transfused as soon as possible after it is thawed, while the AABB standards allow for refrigeration for up to five days before transfusion.

The purpose of this study was to determine if cryosupernatant plasma could be refrigerated for up to five days without compromising the safety and quality of the product. Researchers looked at the plasma proteins contained within thawed cryosupernatant plasma to determine the quality of the product at various stages of storage.

What did the researchers do?

The study involved Cryosupernatant plasma units that could be spared without compromising national inventory levels. These units were removed from the supply chain, as an extension of quality control, and shipped Dr. William Sheffield’s laboratory in Hamilton. Because ABO blood type affects VWF levels in plasma, an equal number of units from type O donors and type A donors were tested.

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Cryosupernatant plasma units were thawed and refrigerated for up to 120 hours. A small sample was taken (without compromising sterility) from each unit at thaw and after 24, 48, and 120 hours of refrigerated storage. Changes to ADAMTS13, VWF, fibrinogen, coagulation factors V, VII, and VIII was monitored in the samples. Samples collected at time of “thaw” were also compared to samples collected during refrigeration.

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At the end of the 120 hour study period, the remaining cryosupernatant units were shipped to Dr. Sandra Ramirez-Arcos’s Laboratory in Ottawa, where samples were tested for sterility using the BacT/ALERT bacterial detection system.
What did the researchers find?

Extending the storage time of thawed and refrigerated cryosupernatant plasma from 24 hours to 120 hours did not result in any meaningful differences in product quality.

After 120 hours of refrigerated storage:

- All units remained free from bacterial contamination.
- There was no significant loss of fibrinogen activity.
- Greater than 97% of the ADAMTS13 activity remained present.
- FV activity declined by 8%, and FVII activity declined by 12%. However, these declines are no greater than those seen in previous stability studies of frozen plasma deemed acceptable by regulators. Most of the decline in activity took place in the first 24 hours after thawing.

How can you use this research?

Patients with TTP require plasma exchange, a high-volume transfusion procedure requiring many units of cryosupernatant plasma. If a scheduled procedure is cancelled or postponed, even for 24-48 hours, many units of cryosupernatant plasma can be wasted. The results of this study have been shared with the Canadian Standards Association in hopes of influencing changes to cryosupernatant plasma regulations and eventually clinical practice. We expect these changes to reduce the waste of cryosupernatant units in Canadian hospitals without compromising the quality of the product transfused into the patients.

About the research team: Dr. William Sheffield is a Senior Scientist with Canadian Blood Services and a Professor of Pathology and Molecular Medicine at McMaster University, Hamilton. Varsha Bhakta is a Senior Research Assistant in the laboratory of Dr. Sheffield. Craig Jenkins is Director of the Quality Monitoring Program with Canadian Blood Services in Ottawa. Dr. Sandra Ramirez-Arcos is a Development Scientist with Canadian Blood Services and Associate Professor in the Department of Biochemistry, Microbiology and Immunology at the University of Ottawa.

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