Research Unit

Plasma: what's in the bag?

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What is this research about?

Plasma is the protein-rich, fluid portion of blood. It contains proteins important for blood clotting and fighting infections. Biological drugs derived from plasma are essential, life-saving treatments for a variety of diseases. They include coagulation factors used to treat bleeding disorders and immunoglobulins, including intravenous immunoglobulin (IVIg), which are used to treat immune disorders. To manufacture these drugs, blood plasma from thousands of donations is pooled together, treated to reduce the risk of transfusion-transmitted infections, and fractionated into components that are used to manufacture biological drugs.

In brief…

Processing time impacts the quality of recovered plasma. Yields of immunoglobulin could be improved if the maximum time between blood donation and processing into plasma is reduced.

Most plasma that is sent for fractionation into biological drugs comes from apheresis donations (called "source plasma"). Plasma that is made from whole blood donations can also be sent for fractionation (called "recovered plasma"), although the majority is used directly for transfusion to patients. Plasma for transfusion must be manufactured and frozen within 24 hours of donation, whereas recovered plasma must be processed within 72 hours of donation. Unlike plasma for transfusion, which is well-studied and regulated, there are no standards that address the biological quality and protein composition of recovered plasma for fractionation.

In this study, the researchers characterized recovered plasma manufactured from whole blood by the two manufacturing methods which are used by Canadian Blood Services: the buffy-coat method or the whole blood filtration method. They also tested whether waiting longer to process plasma from a whole blood donation impacts the quality of the plasma product.

What did the researchers do?

This study was designed to assess and compare three kinds of recovered plasma:

- Recovered plasma produced by the buffy coat method and processed within 24 hours of collection;
- Recovered plasma produced by the whole blood filtration method and processed within 48 hours of collection;
- Recovered plasma produced by the whole blood filtration method and processed between 48 and 72 hours after collection.

Recovered plasma was produced at four production sites across Canada and sent to a central laboratory where the activities of important plasma factors for coagulation and blood clotting were tested. The prothrombin time (PT), which tests how effectively blood clots, was also measured. Total amounts of protein and the concentration of immunoglobulins, from which the plasma-derived drug IVIg is made, were also tested.

What did the researchers find?

All recovered plasma tested met the quality thresholds for frozen plasma set by regulators in Canada. The researchers saw no differences in activity of coagulation factors (F)VII, fibrinogen, prothrombin or von Willebrand Factor between recovered plasma produced by the buffy coat method or the whole blood filtration

method. However, the length of time between the blood donation and processing into plasma impacted the quality of recovered plasma manufactured using the whole blood filtration method. The researchers found that:

- Unexpectedly, immunoglobulin levels – and therefore predicted yields of the important plasma-derived drug, IVIg – were about 15 per cent lower in blood donations held for longer (72 hours). Processing the blood into recovered plasma less than 48 hours after donation was associated with higher IVIg levels.
- FVIII activity was also found to be lower in blood donations held for longer before processing into plasma (72 hours).

How can you use this research?

Historically, the plasma fractionation process was driven by the need to maximize the yield of FVIII, to provide concentrates to treat patients with hemophilia. However, these days many patients with hemophilia are treated with recombinant (engineered) FVIII, so this is no longer the most pressing need. In contrast, the need for IVIg has been growing steadily in recent years, and this trend is likely to continue. This means immunoglobulin yield has become the most important concern for plasma fractionation. The results of this study suggest that on average about 15 per cent more immunoglobulin could be available for fractionation if the maximum allowed time, between donation of blood and processing into recovered plasma, is reduced to 48 hours. The high cost and low rates of national immunoglobulin product self-sufficiency would justify such a change in practice.

There has been a steady increase in the use and demand for plasma-derived drugs in Canada and around the globe. In response to the growing demand, Canadian Blood Services is increasing the amount of source plasma we collect from donors so we can continue to ensure security of supply of plasma-derived drugs for Canadian patients. While source plasma remains the major source of plasma for fractionation, this study provides valuable information on the quality and characteristics of recovered plasma produced by Canadian Blood Services. Understanding and optimizing “what’s in the bag” provides valuable baseline data as we continue to improve our products, and to maximize to value of the blood donations we gratefully receive.

About the research team: This work was conducted by **William Sheffield**, associate director of research at the Centre for Innovation, Canadian Blood Services scientist, and professor in the department of pathology and molecular medicine at McMaster University, Hamilton, ON, **Varsha Bhakta**, a senior research assistance in Dr. Sheffield’s laboratory, and **Craig Jenkins**, senior manager, product and process development at the Centre for Innovation.

This ResearchUnit is derived from the following publication(s):

[1] Sheffield WP, Bhakta V, & Jenkins C: Extending the pre-processing holding time of whole blood beyond 48 h reduces coagulation FVIII activity and immunoglobulin G content of recovered plasma. Transf Apher Sci 2018; https://doi.org/10.1016/j.transci.2018.09.016.

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Want to know more? Contact Dr. Sheffield at william.sheffield@blood.ca