

Reducing bleeding after cardiac surgery: fibrinogen concentrate vs cryoprecipitate

After cardiac surgery, it's common for patients to lose so much blood that they need to replace some blood components (red blood cells, platelets, plasma) through transfusion. Excessive bleeding can happen when fibrinogen, a protein essential to the blood clotting process, is in short supply in a patient's blood. Having abnormally low levels of fibrinogen for reasons that are not hereditary is a condition called acquired hypofibrinogenemia.

Hypofibrinogenemia is treated by replacing the patient's fibrinogen with either cryoprecipitate or fibrinogen concentrate. Although both products come from blood plasma, they differ in purity, fibrinogen content and shelf life. They also have different storage and shipping requirements. In North America, cryoprecipitate is the most common product used, while in most European countries, fibrinogen concentrate is the preferred product.

This study examined whether fibrinogen concentrate performs as well as cryoprecipitate in patients who have cardiac surgery and require fibrinogen replacement.

IN BRIEF: Fibrinogen concentrate may be considered for fibrinogen replacement in cardiac surgery patients who experience bleeding related to acquired hypofibrinogenemia.

What did the researchers do?

The researchers conducted a randomized controlled trial, considered the gold standard in evidence-based medicine for the rigorous way it evaluates the effectiveness of a treatment. The trial was conducted at 11 hospitals in Canada.

- The study involved 735 adult patients who had cardiac surgery and needed fibrinogen replacement because of excessive bleeding due to acquired hypofibrinogenemia.
- Patients were randomly assigned to one of two treatment groups:
 1. **The fibrinogen concentrate group** received 4 g of fibrinogen concentrate, given over roughly 10 minutes (and repeated as needed during the first 24 hours after surgery).
 2. **The cryoprecipitate group** received one dose (10 units) of cryoprecipitate (estimated to contain approximately 4 g of fibrinogen), given according to local practice (and repeated as needed during the first 24 hours after surgery).

- To see how effective the fibrinogen or cryoprecipitate treatments were in limiting bleeding, researchers compared the number of blood component units (red blood cells, platelets, plasma) given within 24 hours of the cardiac surgery. They also looked at other measures of bleeding severity, such as the number of transfusions needed from the start of surgery to seven days after surgery.

What did the researchers find?

The primary finding was that fibrinogen concentrate was noninferior to cryoprecipitate, as measured by the number of blood components transfused 24 hours after cardiac surgery. The mean number of blood component transfusions was 16.3 units in the fibrinogen concentrate group and 17.0 units in the cryoprecipitate group. Both treatment groups were similar in other measures of health too, such as the number of adverse events they experienced after treatment and the duration of their hospital stay. Patients in the fibrinogen concentrate group undergoing elective surgery received less allogenic blood components compared to the cryoprecipitate group.

How can you use this research?

Very few studies have directly compared the use of cryoprecipitate and fibrinogen concentrate for fibrinogen replacement after cardiac surgery. By showing that fibrinogen concentrate is as effective as cryoprecipitate—the most common treatment currently used in Canadian hospitals—this study suggests that fibrinogen concentrate may be considered for fibrinogen replacement.

Although both products were shown to be equally effective, product preference may be influenced by other considerations. Unlike cryoprecipitate, fibrinogen is pathogen-reduced and consequently carries a lower risk of transmitting disease-causing microorganisms to a patient. Another advantage of fibrinogen concentrate is that it is logistically simpler to deliver to a patient's bedside: its freeze-dried, powdered form makes it easier to transport, store, reconstitute and administer than cryoprecipitate, which must remain frozen until use. Although fibrinogen concentrate is slightly more expensive than cryoprecipitate, the full costs associated with using these products, including potential costs of managing disease transmission, have not been evaluated.

About the research team: This research was led by **Dr. Jeannie Callum** and **Dr. Keyvan Karkouti**. Dr. Callum is director of utilization, department of laboratory medicine and molecular diagnostics at Sunnybrook Health Sciences Centre, and professor, department of laboratory medicine and pathobiology at the University of Toronto. Dr. Karkouti is professor of anesthesiology at the University of Toronto, chief of anesthesiology and pain management at University Health Network, Sinai Health System, and Women's College Hospital, and senior scientist at the Toronto General Research Institute and the Peter Munk Cardiac Centre.

This **Research Unit** is derived from the following publication:

[1] Callum J, Farkouh ME, Scales DC, Heddle NM, Crowther M, Rao V, et al. Effect of fibrinogen concentrate vs cryoprecipitate on blood component transfusion after cardiac surgery: The FIBRES randomized clinical trial. *JAMA*. 2019 Oct 21:1-11.

Acknowledgements: This research received funding support from Canadian Blood Services (Transfusion Medicine Research Program Support Award), funded by the federal government (Health Canada) and the provincial and territorial ministries of health. The views herein do not necessarily reflect the views of Canadian Blood Services or the federal, provincial or territorial governments of Canada.

Keywords: massive blood loss, fibrinogen concentrate, cryoprecipitate, fibrinogen, cardiac surgery

Want to know more? Contact Dr. Keyvan Karkouti at keyvan.karkouti@uhn.ca