Treating bleeding during cardiac surgery: Is prothrombin complex concentrate a substitute for plasma?

What is this research about?

During cardiac surgery patients may experience a disruption in their coagulation system (ability to form blood clots). This causes excessive bleeding. Managing bleeding and improving clotting in these patients requires that insufficient levels of an enzyme called thrombin, which helps form blood clots, be replenished.

A number of clotting factors need to be present in blood to improve thrombin generation. Frozen plasma (FP), which contains clotting factors, is used in Canada to manage clot formation in cardiac patients despite the lack of data supporting its effectiveness and risk of causing adverse transfusion reactions, particularly heart failure. Prothrombin complex concentrates (PCCs), which contain selected clotting factors, may be a potential alternative to FP in the management of bleeding. PCCs have multiple advantages since they do not require ABO blood type matching, are provided in lower volumes (lower risk of adverse transfusion reactions) and are pathogen-reduced (lower risk of transfusion-transmitted infections). However, PCCs do not contain the full complement of procoagulants and anticoagulants that are present in FP and may carry a higher thrombotic risk.

A pilot study in bleeding patients undergoing cardiac surgery was conducted to compare PCC and FP in terms of safety and bleeding management effects and to assess the feasibility of a larger trial.

IN BRIEF: During cardiac surgery, bleeding outcomes were similar (and possibly better) when using prothrombin complex concentrate compared to frozen plasma. Large multi-centre trials are warranted to determine the benefits and risks of the intervention.

What did the researchers do?

A pilot trial was implemented in two Canadian hospitals. 101 adult patients undergoing cardiac surgery and requiring clotting factor replacement for bleeding were randomized to one of two treatment groups: the **PCC group** received 1500 IU for patients weighing ≤60 kg and 2000 IU for patients weighing >60 kg; and the **FP group** received 3 U for patients weighing ≤60 kg and 4 U for patients weighing >60 kg. For each group, treatment was repeated once as needed within 24 hours and FP was used for any additional doses.

The effectiveness of the treatments in stopping bleeding (hemostasis) were primarily measured by assessing if patients received hemostatic therapies after initiation of the treatment; number of blood component units (red blood cells, platelets and FP) administered within 24 hours after surgery, and avoidance of RBC transfusion 24 h after start of surgery. Other measures of hemostatic effects and study feasibility were also assessed.

What did the researchers find?

PCC was found to have similar (and possibly better) bleeding control compared to FP in adult cardiac surgery patients experiencing excessive bleeding. Patients in the PCC group had lower requirements for transfusion and hemostatic agents, and significantly lower chest tube blood loss compared to the FP group. Excluding the FP administered as part of treatment assignment, the median number of blood component units was 8.6 and 10.8 in the PCC group and the FP group, respectively. Patients treated with PCC needed fewer RBCs. Duration of mechanical ventilation, ICU and hospital stay, thromboembolic and adverse events, were similar.

How can you use this research?

Because this was a pilot study, the findings should be considered exploratory. However, the findings show that a multi-centre randomized controlled trial comparing PCC with FP is feasible and warranted to see if PCCs are in fact superior as a treatment to FP for cardiac surgery patients with impaired clotting.

This Research Unit is derived from the following publication(s):
Karkouti K, Bartoszko J, Grewal D, Bingley C, Armali C, Carrol J, Hucke H, et al. Comparison of 4-factor prothrombin complex concentrate with frozen plasma for management of hemorrhage during and after cardiac surgery: A randomized pilot trial. *JAMA Netw Open.* 2021 Apr 1; ;4(4):e213936. doi: 10.1001/jamanetworkopen.2021.3936.

Author: This Research Unit was written by Amie Kron, Clinical Research Coordinator, Quality, Utilization, Education, and Safety in Transfusion (QUEST) research program.

About the research team: This research was led by **Dr. Jeannie Callum** and **Dr. Keyvan Karkouti**. Dr. Callum is a transfusion medicine specialist and hematologist at Kingston Health Sciences Centre, professor in pathology and molecular medicine at Queen's University, and lead for the QUEST transfusion research program at the University of Toronto. Dr. Karkouti is professor of anesthesiology at the University of Toronto and chief of anesthesiology and pain management at University Health Network, Sinai Health System, and Women's College Hospital.

Acknowledgements: The University of Toronto QUEST research program receives funding support from Canadian Blood Services (Transfusion Medicine 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. The trial was supported by the Heart and Stroke Foundation of Canada and by an unrestricted grant from Octapharma AG (Lachen, Switzerland). Frozen plasma and 4-factor prothrombin complex concentrate were provided by Canadian Blood Services.

Keywords: Bleeding disorder, coagulopathy, cardiac surgery, clinical trials, blood bank, transfusion medicine, hematology

Want to know more? Contact Dr. Jeannie Callum at jeannie.callum@kingstonhsc.ca