Older blood as good as new: no harmful effects of storage time before transfusion

What is this research about?

After blood is collected from donors, red blood cells are isolated from the blood and stored at 4°C in a solution containing anti-clotting agents and nutrients. This allows the cells to survive for several weeks (up to 42 days) before transfusion. Red blood cell transfusions help save lives at risk due to severe blood loss, low red blood cell levels as a result of chemotherapy, or diseases related to dysfunctional red blood cells.

During storage, red blood cells remain biologically active and gradually use up their energy stores. The red blood cell membranes become more fragile, and some cells burst, releasing their contents into the storage bag. These accumulated changes are referred to as the “storage lesion”. However, it is unclear whether these cellular changes have any effect on transfusion outcome.

Since the 1970s, red blood cells have been stored in Canadian blood banks for up to 42 days. In the late 2000s, several studies raised concerns that blood stored longer than 14 days could be associated with a worse patient outcome (increased morbidity and/or mortality) than fresher blood. This elicited several large randomized trials to evaluate the accuracy of these findings and determine whether the 42-day storage limit should be revised. One of those studies was the Informing Fresh versus Old Red Cell Management (INFORM) trial, a large multinational randomized trial.

What did the researchers do?

Prof. Heddle and her collaborators at six hospitals in four countries (Canada, the United States, Australia and Israel) randomly assigned hospital patients who required transfusions to receive blood that had been stored for different lengths of time. The average storage time was 13 days for the fresher blood and 24 days for the older blood. The main analysis was done with 20,858 patients of the two most common blood types (A and O) to have the maximum possible difference in blood storage time. A secondary analysis was also done including patients of all blood types (24,736 total).

What did the researchers find?

Red blood cell storage time did not affect mortality; 9.1% of type A and O patients transfused with fresher blood died in-hospital versus 8.7% of patients transfused with older blood. Similar results were found when patients of all blood types were included. Within higher risk subgroups (cancer, cardiovascular surgery or intensive care unit patients), red blood cell storage time again did not affect mortality. No significant interactions were found for diagnosis, blood type or hospital location. Hospitalization duration was not altered by blood cell storage time (median of 10 days for both groups).

How can you use this research?

The INFORM study is the largest of several recent randomized trials to confirm that older blood is just as effective as newer blood. Randomized trials are usually considered the “gold standard” for a clinical trial because they are less likely to be biased by confounding factors that affect group selection and outcome. In contrast, observational trials (such as the studies initially suggesting a link between blood storage time and mortality) are useful for discovering patterns and generating hypotheses. These hypotheses must then be tested in more rigorous randomized trials to determine whether the observed pattern is caused by a real effect. In this case, the INFORM study and similar randomized trials have determined that the observed pattern was not real; storage time of red blood cell units does not increase mortality after transfusion.
This is good news for blood operators, blood banks, clinicians and patients. Red blood cell units are often used within a few weeks, but variability in the blood supply sometimes requires the use of older blood. In these cases, it is reassuring to know that patients will do just as well as those given fresher blood.

Despite its high-quality study design, the INFORM trial had several limitations. Because the study was based on electronic database reports from each hospital, detailed information about illness progression was not available. This study design reduced costs, making it possible to examine mortality data for a large number of patients, but prevented more detailed analysis of patient health (morbidity).

Furthermore, these results could only be confirmed for patients with blood types A or O. However, there is no reason to think that the other blood types would show any differences in sensitivity to blood storage time.

Based on the findings of INFORM and several other recent studies, clinicians should not hesitate to use older red blood cell units as long as they are kept in appropriate storage conditions for less than the current 42-day limit.

About the research team: The lead author, Prof. Nancy Heddle, is a professor in the department of medicine at McMaster University, Hamilton, ON, and an adjunct scientist at Canadian Blood Services. Dr. Kathryn Webert is the medical director of utilization for Canadian Blood Services and an associate professor in the department of pathology and molecular medicine at McMaster University. Dr. Donald Arnold is a medical officer for Canadian Blood Services and an assistant professor in the department of medicine at McMaster University. This research was conducted with many collaborators, including Richard J. Cook, Yang Liu, Rebecca Barty, Mark A. Crowther, P.J. Devereaux, Jack Hirsh, Theodore E. Warkentin, David Roxby, Magdalena Sobieraj-Teague, Andrea Kurz, Daniel I. Sessler, Priscilla Figueroa, Martin Ellis, and John W. Eikelboom.

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Want to know more? Contact Prof. Nancy Heddle at heddlen@mcmaster.ca.