Female blood donors linked to better outcomes for transfused preterm infants

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Premature or very low birth weight infants often need transfusions of red blood cells (RBCs) while in the neonatal intensive care unit. New research from Emory and Children's Healthcare of Atlanta suggests that
the sex of adult blood donors may affect the risk of common complications.

A typical very-low-birth-weight infant who received red blood cell \textit{transfusion} from only female donors had a risk of negative outcomes that was more than three times less than one who received red blood cells from only male donors.

The results are published on September 3 in \textit{JAMA Network Open}.

Common negative outcomes that can occur with very low birth weight infants include necrotizing enterocolitis, meaning intestinal damage caused by infection and inflammation, lung damage or retinopathy of prematurity. Some prior studies indicate that transfusions might be connected to these risks, although other studies show no relationship.

The protective effect of female donors also increased with older \textit{donor} age. Although not examined in this study, some potential explanations for the protective effect could be reduced breakdown during storage of RBCs from female donors, along with less inflammation and more antioxidant capacity, the authors write.

Ravi Patel and colleagues followed 181 very-low-birth-weight infants born at 3 Atlanta hospitals (Grady, Emory Midtown and Northside) from 2010 to 2014. Dr. Patel is director of neonatal research in the Department of Pediatrics at Emory University School of Medicine and Children's Healthcare of Atlanta.

Q&A with Ravi Patel

\textbf{How common is it for preterm infants to receive RBC transfusions while in the NICU?}
RBC transfusion is common, with about half of very low birth infants receiving at least one RBC transfusion while in the NICU.

**Why are RBC transfusions necessary in this situation?**

RBC transfusion is necessary to treat anemia related to prematurity.

**Could you discuss the benefits and risks of RBC transfusion in preterm infants?**

RBC transfusion can benefit preterm infants by improving the amount of oxygen than can be carried and delivered to tissues, but may, in rare circumstances, lead to an infection or transfusion reaction. There is uncertainty about whether RBC transfusion increases the risks of some adverse clinical outcomes.

**Explain the study design—in particular, the decision to compare only those infants with female donors vs male donors, while excluding those who received RBCs from both male and female donors?**

We included those infants receiving transfusions from only male donors or only female donors to allow for a consistent assessment of the type of blood donor sex an infant was exposed to. This was the closest approximation to a trial design in which infants would be transfused red blood cells from only female or only male blood donors.

**Is it correct to say that the suspected mechanism for the difference in risk has to do with the characteristics of the RBCs, rather than immune**
differences, the suspected reason for the reverse effect in adults?

We don't know what the potential mechanisms are that could explain our epidemiologic findings. However, we believe evaluating the potential role of inflammation or antioxidant capacity of red blood cells would be important areas of inquiry. Importantly, these mechanisms may differ from those that are postulated to affect adults.

**What should we conclude from your findings? What type of additional investigation or policy change is necessary?**

Our findings suggest that the characteristics of blood donors, such as their sex and age, may be important in the effects of red blood cell transfusion. If these findings are confirmed, we believe randomized trials transfusing blood from only males or only females would be justified, which could inform changes in practice.

The analysis took advantage of data from a previous study on transfusions and cytomegalovirus (CMV), which included very-low-birth-weight infants born at three Atlanta hospitals: Grady Memorial Hospital, Emory University Hospital Midtown, and Northside Hospital.
