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Neonatal Plasma Transfusion: An Evidence-Based Review

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ABSTRACT

Several clinical scenarios for plasma transfusion are repeatedly identified in audits, including treatment of bleeding in association with laboratory evidence of coagulopathy, correction of disseminated intravascular coagulation, prevention of intraventricular hemorrhage, management of critically ill neonates (eg, during sepsis or as a volume expander), or correction of markers of prolonged coagulation in the absence of bleeding. The findings of at least one national audit of transfusion practice indicated that almost half of plasma transfusions are given to neonates with abnormal coagulation values with no evidence of active bleeding, despite the limited evidence base to support the effectiveness of this practice. Plasma transfusions to neonates should be considered in the clinical context of bleeding (eg, vitamin K dependent), disseminated intravascular coagulation, and very rare inherited deficiencies of coagulation factors. There seems to be no role for prophylactic plasma to prevent intraventricular hemorrhage or for use as a volume expander.

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Box 1. Why is plasma commonly transfused in neonatal intensive care units to prevent intraventricular hemorrhages when there is no evidence to support this?

For those practicing on the "front line" of neonatal care, when looking after another family's baby, you want to do your absolute best to give that family the best possible outcome for their child. What do you do when caring for an infant at a high risk of bleeding, for example, a baby born at 24 weeks' gestation who has coagulation tests well out of your local reference range? You are aware that the reference ranges are not validated for such a small infant but the results do seem quite abnormal. It is also at the back of your mind that the child could be septic but is it only just becoming clinically apparent? After all, the mother's membranes were ruptured for some time before delivery. Should you wait or should you "do something" about those coagulation test results? After all, your colleagues would "do something."

Reasons previously described to explain why health care professionals continue to use treatments that do not work include the following:

- Clinical experience
- Overreliance on a surrogate outcome
- A need to do something
- No one asks the question [1]
- Local practice/unit culture
- Parental expectations/assumptions

The pressure to "do something" is great and what we need is better evidence to base our critical clinical decisions upon. There are significant gaps in neonatal transfusion medicine research, and as a highly transfused patient group, they deserve better. To base clinical decisions today on research performed more than 20 years ago does not seem ideal.

Conflict of interest: The authors have no conflicts of interests to declare.

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Clinical Scenario

An extremely premature growth–restricted infant at 27 weeks' gestation weighing 500 g was delivered after a planned cesarean birth for suspected fetal compromise. She is admitted to the neonatal intensive care unit (NICU) and routine admission blood tests reveal that the prothrombin time (PT) and the activated partial thromboplastin time (aPTT) are elevated outside the reference ranges provided by the laboratory. The attending neonatologist requests plasma from the Blood Blank to prevent an intraventricular hemorrhage (IVH). There are no signs of active bleeding, and the infant is not displaying any signs of sepsis.

Background

Up to 15% of neonates admitted to the NICU are transfused with plasma when all birth weights and gestational ages are included [2-4]. Several clinical scenarios for plasma transfusion exist and are repeatedly identified in audits. Reasons given by health care professionals to support administration of neonatal plasma transfusion commonly include hypovolemia, bleeding with abnormal coagulation test results, abnormal coagulation test results without bleeding, intraoperative bleeding, sepsis, and partial exchange for polycythemia [5-7]. The findings of a national comparative audit of transfusion practice have indicated that almost half of plasma transfusions are given to neonates with abnormal coagulation values with no evidence of active bleeding [8]. There remains, however, marked variation in plasma transfusion practices in NICUs around the world [7]. Moreover, a recent study found that up to 60% of neonatal plasma transfusions were not consistent with guideline recommendations [2]. Additional uncertainty around transfusion of plasma stems from the unique development of the neonatal coagulation system and a lack of appreciation of reference ranges to define neonatal coagulopathy; of note, the most widely quoted reference range in preterm neonates did not evaluate the coagulation profile of neonates born at less than 30 weeks' gestation [9-11].

In most cases, use of plasma is linked in the minds of health care professionals with increased risk of bleeding. Bleeding, at varying degrees of severity, is common in neonates admitted to the NICU [12]; however, clinically significant bleeding is relatively uncommon. Types of major bleeding include rectal or pulmonary, but intracranial bleeding carries the greatest risk for adverse neurodevelopmental outcome. However, the etiology of IVH is most often attributed to the fragility of the germinal matrix vasculature and disturbances in the cerebral blood flow [13], rather than a primary abnormality in coagulation.

This review will consider the background and indications, and summarize the evidence and highlight where research is needed in neonatal plasma transfusion. Inevitably, we recognize the challenges of randomized studies being undertaken to address these diverse clinical settings, and the need to consider how best to approach these scenarios and provide sensible advice to health care professionals on the front line of neonatal clinical care.

Plasma for Neonatal Transfusion

Fresh-frozen plasma is human donor plasma frozen within a short specified period after collection (often 8 hours) and then stored at a defined temperature, typically at −30°C. Plasma frozen at slightly later intervals (typically up to 24 hours) after collection is referred to as FP24. After thawing, although diluted with citrate anticoagulant, plasma contains near normal levels of many plasma proteins, including procoagulant and inhibitory components of the coagulation cascades, acute-phase proteins, immunoglobulins, and albumin. Levels of the labile coagulation factors V and VIII are slightly lower in FP24 by comparison to fresh-frozen plasma, but both components are usually considered clinically equivalent. However, the marginally lower levels for some coagulation factors in FP24 may be clinically important, for example, in the context of low-volume transfusions to neonates, although there are no relevant data to inform this issue. Similarly, there is evidence that pathogen reduction technologies may impact on coagulant content [14,15], but the clinical implications of this in the context of neonatal transfusions have not been evaluated.

Reported Indications for Use of Plasma in Neonates

In neonatal practice, plasma is predominantly given to reduce perceived bleeding risk (prophylaxis) in nonbleeding patients. However, it should be accepted that all critically ill neonates might display some features of bleeding risk, for example, oozing at sites of venepuncture. Other usages include as a volume expander, bleeding with abnormal coagulation test results, intraoperative bleeding, sepsis, partial exchange for polycythemia, and exchange transfusions.

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