EDITORIAL

Using a lower platelet transfusion threshold: translating evidence into practice

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Whether to transfuse platelets in an infant with thrombocytopenia is a common decision faced by neonatologists. While there are numerous examples of uncertainty in neonatal medicine, there has been recent expansion in the evidence guiding platelet transfusions, especially in extremely preterm infants. In this edition of the journal, three manuscripts further advance the evidence behind the practice of lower platelet transfusion thresholds reported by the seminal PlaNeT-2 trial [1].

The PlaNeT-2 trial showed that, in a sample of 660 infants born prior to 34 weeks gestation, lower platelet transfusion thresholds were associated with improved outcomes [1]. In the high threshold group (<50,000/μl) 90% of the infants were transfused compared to 53% in the low threshold group (<25,000/μl). Infants in the high threshold group had increased odds (1.57, 95% CI 1.06–2.32) of major bleeding or death prior to 28 days of age [1]. At two year follow-up, the odds of death or neurodevelopmental impairment were increased in the high threshold group (OR 1.54, 95% CI 1.09–2.07) [2]. Despite the strength of the evidence supporting the use of a lower platelet transfusion threshold, the design of the PlaNeT-2 trial left some clinical questions open. Inclusion in the study required a cranial sonogram without evidence of major bleeding within 6 h of study entry, which may not always be available in routine practice when making transfusion decisions. Prior to study entry, 39% of infants in the sample received open label transfusions which could have affected the generalizability of the trial findings and results. Death and bleeding were tracked only through day of life 28. Thus, the safety and efficacy of transfusing platelets between 25 and 50,000/μl in preterm babies in the first week of life prior to known results of a head ultrasound have not been definitively established.

In this issue of the Journal, two manuscripts from single centers utilize quality improvement methodology to provide further clinical translational evidence that build on prior studies showing that lower platelet transfusion thresholds reduce transfusion without a concordant increase in bleeding. The study of Coletti and colleagues included preterm and term infants in a large level IV Neonatal Intensive Care Unit (NICU) [3]. Employing a trigger platelet transfusion threshold of 25,000/μl, the NICU decreased platelet transfusion per 100 patient days by 50% without any increase in negative balancing measures such as hemorrhage. While the PlaNeT-2 trial transfused 15 ml/kg of platelets, Coletti and colleagues also standardized transfusion at a volume of 10 ml/kg and reduced the monthly volume of platelets transfused, again without an increase in bleeding. A transfusion threshold of 25,000/μl was also used by Lalos and colleagues in a single level IV NICU [4]. The authors used a threshold for transfusion of a platelet count < 25,000/μl in babies <1000 g who were not actively bleeding regardless of stability and were able to show a reduction in non-guideline adherent transfusion without an increase in pulmonary hemorrhage or severe IVH. In this study, 93% of transfused infants had a head ultrasound before platelet transfusion. These results are consistent with the work of Davenport et al., which demonstrated a reduction in non-indicated transfusions without an increase in bleeding after changing the threshold for transfusion to <25,000/μl in term and preterm infants in a single center [5]. A transfusion threshold of <50,000/μl was used in the first week in babies <28 weeks and ≤7 days old in this study, and this study was done in a unit caring for outborn patients.

Also in this issue of the Journal, Tweddell and colleagues present the results from a questionnaire presenting 11 scenarios on platelet transfusion after establishing a new restrictive platelet threshold of 25,000/μl in a four NICU hospital system [6]. It should be noted that the new guidelines in this hospital system allowed for transfusion with a platelet count < 50,000/μl in babies <28 weeks and <7 days or before performing a lumbar puncture. While 94% of neonatologists indicated they would abide by the new guidelines, 83% of advanced practice clinicians, and 77% of nurses indicated agreement. Common reasons for non-compliance included a platelet count close to or approaching the threshold demonstrating that clinicians still have some reluctance to transfuse at a lower threshold. Tweddell's study provides neonatologists with important information regarding the barriers to implementing a change in the threshold for platelet transfusion.

In a review published previously in this Journal, Christensen noted the long lag time from publication to implementation of evidence and suggested that most babies should be transfused platelets at a threshold of less than 25,000/μl rather than 50,000/μl [7]. The results of the studies from Coletti [3] and Lalos [4], along with the previous work of Davenport [5] build on the PlaNeT-2 trial and provide "real world" evidence collectively supporting the safety of guidelines with lower platelet transfusion thresholds. While randomized studies remain the gold standard for establishing evidence, the QI methodology used by these two new studies demonstrate how single NICUs can successfully implement a platelet transfusion practice change, while assessing balancing measures such as bleeding. The studies of Coletti [3], Lalos [4], and Davenport [5] all show that it is feasible to translate the evidence from a large randomized multicenter trial and reduce platelet transfusions in a NICU without adverse bleeding consequences. In contrast to randomized trials, outcomes form QI studies do require cautious interpretation as they may have low power to detect changes in outcomes and be biased by confounding from changes in case mix and co-treatments over time.

While many of our practices in neonatology lean towards intervention, evidence continues to emerge that lowering the threshold to transfuse platelets leads to improved outcomes compared to a more aggressive approach to transfusion. Several nuances of approaches to platelet transfusion still need to be

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established. Should clinicians transfuse or avoid platelet transfusion in infants <28 weeks and <7 days of age with a platelet count between 25,000 and 50,000/μl? What is the appropriate threshold for platelet transfusion in term infants with thrombocytopenia at risk for bleeding, including those receiving therapeutic hypothermia? While the Coletti [3] and Davenport [5] studies included term infants, evidence in this population remains limited and was not addressed in PlaNet-2 [1]. What is the optimal volume of platelet transfusion? The use of a 10 ml/kg transfusion volume in Coletti's study [3] confirms the work of some previous small trials [8] but is different from the 15 ml/kg volume used in the PlaNet-2 trial [1]. How might the use of different platelet products impact outcomes and transfusion efficacy?

The studies in this issue of the journal further translate the evidence from the PlaNet-2 trial and show that a transfusion threshold of <25,000/μl can be safely used for babies < 34 weeks gestation beyond the first week of life while informing neonatologists about the difficulties in changing this approach. While we await further evidence, clinicians must cautiously weigh the certainty and generalizability of the evidence when determining the risks and benefits of platelet transfusion in neonates and other populations.

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AUTHOR CONTRIBUTIONS

DAP contributed to the concept of the manuscript, literature review, writing the manuscript, finalizing the manuscript content. SAP contributed to the concept of the manuscript, finalizing the manuscript content. RMP contributed to the concept of the manuscript, finalizing the manuscript content. All authors approved the final version of the manuscript.

COMPETING INTERESTS

The authors declare no competing interests.