Indian Academy of Pediatrics (IAP)

nRICH

Newer **R**esearch and recommendations **I**n **C**hild **H**ealth

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UNDER THE AUSPICES OF THE IAP ACTION PLAN 2023

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Dear fellow IAPans,

nRICH

Newer **R**esearch and recommendations **I**n **C**hild **H**ealth-aims to bring you the abstracts of some of the breakthrough developments in pediatrics, carefully selected from reputed journals published worldwide.

Expert commentaries will evaluate the importance and relevance of the article and discuss its application in Indian settings. nRICH will cover all the different subspecialities of pediatrics from neonatology, gastroenterology, hematology, adolescent medicine, allergy and immunology, to urology, neurology,vaccinology etc. Each issue will begin with a concise abstract and will represent the main points and ideas found in the originals. It will then be followed by the thoughtful and erudite commentary of Indian experts from various subspecialties who will give an insight on way to read and analyze these articles.

I'm sure students, practitioners and all those interested in knowing about the latest research and recommendations in child health will be immensely benefitted by this endeavor which will be published online on every Monday.

Happy reading!

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Two-year outcomes following a randomised platelet transfusion trial in preterm infants.

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BASED ON ARTICLE

Moore CM, D'Amore A, Fustolo-Gunnink S et al. Arch Dis Child Fetal Neonatal Ed. 2023 Feb 21:fetalneonatal-2022-324915.

ABSTRACT

Objective: Mortality and neurodevelopmental outcomes at 2 years of corrected age in children who participated in the PlaNeT-2/MATISSE (Platelets for Neonatal Transfusion-2/Management of Thrombocytopenia in Special Subgroup) study, which reported that a higher platelet transfusion threshold was associated with significantly increased mortality or major bleeding compared to a lower one.

Design: Randomised clinical trial, enrolled patients from June 2011 to August 2017. Follow-up was complete by January 2020. Caregivers were not blinded; however, outcome assessors were blinded to treatment group.

Setting: 43 level II/III/IV neonatal intensive care units (NICUs) across UK, Netherlands and Ireland.

Patients: 660 infants born at less than 34 weeks' gestation with platelet counts less than 50×10^9/L.

Interventions: Infants were randomised to undergo a platelet transfusion at platelet count thresholds of 50×10^9/L (higher threshold group) or 25×10^9/L (lower threshold group).

Main outcomes measures: Composite of death or neurodevelopmental impairment (developmental delay, cerebral palsy, seizure disorder, profound hearing or vision loss) at 2 years of corrected age.

Results: Follow-up data were available for 601 of 653 (92%) eligible participants. Of the 296 infants assigned to the higher threshold group, 147 (50%) died or survived with neurodevelopmental impairment, as compared with 120 (39%) of 305 infants assigned to the lower threshold group (OR 1.54, 95% CI 1.09 to 2.17, p = 0.017).

Conclusions: Infants randomised to a higher platelet transfusion threshold of 50×10^9/L compared with 25×10^9/L had a higher rate of death or significant neurodevelopmental impairment at a corrected age of 2 years. This follow up study further supports the evidence of harm by higher platelet transfusion thresholds in preterm infants.

COMMENTARY

Neonatal thrombocytopenia is common amongst sick newborns and preterm and poses diagnostic and therapeutic challenge in NICU. The low platelet count often creates panic and triggers a transfusion request. The threshold for transfusion remains variable amongst and within neonatal units based on clinician's discretion.

This study is post-hoc analysis of PlaNeT-2/MATISSE infants. Both the studies found a higher incidence of death or major bleeding within 28 days of randomization and a higher incidence of bronchopulmonary dysplasia (BPD) among neonates randomized to a higher platelet transfusion threshold (<50,000), compared to those randomized to a lower threshold (<25,000). Thus they clearly showed harm than benefit for higher platelet threshold (1,2). When these infants were followed up till 2 years of corrected age the long term outcomes (survival or neurodevelopmental impairment) in the high platelet threshold (> 50,000/mm3) group too were poor compared to low platelet threshold (<25,000/mm3).

The strengths of the study include robust methodology, high follow up rate (92%) and practical approach in assessing the neurodevelopment and neurosensory outcomes. Use of formal development assessment in only 40% of the infants and lack of study power to assess the long term outcomes are the major limitations.

Why should platelet transfusion cause increased adverse short term and long term outcome is still not known. It is well known that infants with thrombocytopenia are likely to be more sick and it is difficult to dissociate sickness from thrombocytopenia severity. Studies show there is poor correlation between platelet count and risk of bleeding. This suggests risk of bleeding is not dependent of platelet count alone but also influence by local and systemic hemodynamic factors and vascular integrity. The role of platelets may not be restricted to haemostasis alone but also in immune regulation. Additional studies are required to understand the mechanism of platelet and organ damage.

Our urge to transfuse based on sickness and a platelet threshold of > 50,000/mm3 does not seem to offer short-term or long-term benefit. Our fear of 'bleeding triggering transfusion' should be curbed. When it comes to platelet transfusion, lower threshold is better than higher.

Implications for practice.

1. Platelet transfusions at a higher threshold platelet count of > 50,000/mm3 is associated with adverse short term (death, BPD) and long term outcomes (seizures, cognitive-motor-visual-hearing deficit and or death) compared to low platelet count threshold of < 25,000/mm3
2. The 'restrictive' platelet transfusion policy compared to 'liberal' transfusion policy seems to do more good, both short term and long term.

REFERENCES

1. Curley A, Stanworth SJ, Willoughby K, Fustolo-Gunnink SF, Venkatesh V, Hudson C, et al. Randomized Trial of Platelet-Transfusion Thresholds in Neonates. N Engl J Med 2019; 380 3:242-51.
2. Fustolo-Gunnink SF, Fijnvandraat K, van Klaveren D, Stanworth SJ, Curley A, Onland W, et al. Preterm neonates benefit from low prophylactic platelet transfusion threshold despite varying risk of bleeding or death. Blood 2019; 134 26:2354-60.