Transfusion Evidence Synopsis

Platelet transfusion thresholds in premature neonates (PLANET-2 trial)

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CLINICAL QUESTION: Does transfusing platelets to preterm infants (< 34 weeks) at a higher platelet count threshold count (< 50 x 10^9/L) reduce the risk of major bleeding or death compared to only transfusing platelet when the platelet count drops below 25 x 10^9/L.

BOTTOM LINE: Preterm infants with a low platelet count who were transfused platelets at the higher platelet count threshold had a higher risk of dying or having a major bleed than those who were not. The reasons why this occurred are currently unclear.

Introduction

Platelet transfusions are commonly given to prevent bleeding in preterm infants with a low platelet count (Curley*, et al* 2018). However, there has been a lack of evidence on the appropriate platelet count threshold from randomised-controlled trials (RCTs) (New*, et al* 2016, Sola-Visner and Bercovitz 2016). There has therefore been a wide variation in practice within and between countries (Cremer*, et al* 2011, Sparger*, et al* 2015, Stanworth*, et al* 2009). This is the first RCT that has assessed different platelet count thresholds in neonates with very low platelet counts (< 50 x 10^9/L).

Evidence Box

Study design: Open-label randomised controlled trial

Study years: June 2011 to August 2017

Countries: United Kingdom, Netherlands, Ireland

Setting: Neonatal intensive care

No. of patients: 660 randomised (653 analysed for primary outcome)

Median gestational age (range): 26.6 weeks (22.7 to 33.9)

Median birth weight (range): 740 g (360 to 2490)

Intrauterine growth retardation: 245/659 (37%)

Female: 263/659 (40%)

Inclusion criteria: gestational age < 34 weeks, platelet count < 50 x 10^9/L, cranial ultrasonography (< 6 hours prior to randomisation) no major intraventricular haemorrhage.

Exclusion criteria: major/life-threatening congenital malformation, major bleeding within 72 hours, intracranial haemorrhage, immune thrombocytopenia, parenteral vitamin K not given, very poor life expectancy.

Comparison: platelet transfusion (15 ml/kg) when platelet count < 50 x 10^9/L (high-threshold group) versus when platelet count < 25 x 10^9/L (low-threshold group).

Primary outcome: Death or major bleeding within 28 days.

Secondary outcomes: death, major bleeding, moderate bleeding, minor bleeding, chronic lung disease, retinopathy of prematurity, discharge from hospital, number of platelet transfusions, proportion receiving platelet transfusions, sepsis, necrotizing enterocolitis, serious adverse events, transfusion-related adverse events, neurodevelopmental outcome at 2 years (not yet reported).

This Transfusion Evidence Synopsis summarizes an RCT in the NEJM (Curley*, et al* 2018).

Summary of Study

Many more babies in the high-threshold group (90%) received a platelet transfusion (Table)

Giving platelet transfusions at the higher threshold to prevent bleeding increased the risk of death or major bleeding (Table). This was an unexpected finding, as the study's hypothesis was that it would decrease the risk of death or major bleeding. The reasons for this difference are unknown.

There was an increase in the number of babies with bronchopulmonary dysplasia in the high-threshold group (Table). There was no evidence of a difference in the numbers who developed retinopathy of prematurity (Table); sepsis; necrotising enterocolitis; or any serious adverse event (Table) during the trial. There was borderline evidence of a decrease in the number of babies discharged from hospital by 38 weeks corrected gestational age in the high-threshold group (Table).

Limitations

3.2% (45 of 1393) of platelet transfusions were given when they were not indicated by the protocol, and more of these were given in the low-threshold group (87%; 39/45). There were also 124 episodes when the indications for giving a transfusion were met but no transfusion was given, and more of these occurred in the high-threshold group (76%; 94/124). However, when per-protocol analyses were performed there was no significant difference in the findings.

Only 37% of infants were recruited within 5 days of birth, therefore these findings are more relevant to infants with late onset thrombocytopenia due to sepsis or necrotising enterocolitis rather than thrombocytopenia that develops within the first 3 days of life.

Evidence in context

This is the first large RCT of prophylactic platelet transfusion in premature neonates with very low platelet counts. Previous observational studies have suggested harms associated with giving platelet transfusions (Curley*, et al* 2018).

Implications for practice

This trial supports the advice given by BSH to use a threshold of 25 x 10^9/L to guide administration of platelet transfusions in premature neonates who are not bleeding and do not require surgery (New*, et al* 2016).

References

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Table

Outcomes	**Platelet Tx (50 x 10^9/L)**	**Platelet Tx (25 x 10^9/L)**	**Relative effect Odds ratio (OR) or Hazards ratio (HR) (95% CI)***
Death or major bleeding within 28 days	26% (85/324)	19% (61/329)	OR 1.57 (1.06 to 2.32)
Death within 28 days	15% (48/326)	10% (33/330)	OR 1.56 (0.95 to 2.55)
Major bleeding within 28 days	14% (45/328)	11% (35/330)	HR 1.32 (1.00 to 1.74)
Survived with bronchopulmonary dysplasia at 36 weeks	63% (169/269)	54% (153/281)	OR 1.54 (1.03 to 2.30)
Survived with retinopathy of prematurity at 38 weeks corrected gestational age	29% (82/279)	24% (71/297)	OR 1.38 (0.91 to 2.08)
Discharged from hospital by 38 weeks corrected gestational age	9% (29/326)	12% (41/328)	HR 0.68 (0.46 to 1.00)
At least one platelet transfusion	90% (296/328)	53% (177/331)	HR 2.75 (2.36 to 3.21)
Serious adverse events	25% (81/328)	22% (74/331)	OR 1.14 (0.78 to 1.67)

* The odds ratios and hazards ratios were adjusted for trial site, intrauterine growth restriction, and gestational age at birth.