Managing Thrombocyte transfusions in a Special Subgroup: NEonates

Published: 20-01-2014
Last updated: 24-04-2024

To assess whether a higher prophylactic platelet transfusion threshold is superior to the lower thresholds in reducing the proportion of patients who experience a major bleed or death up to study day 28.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Platelet disorders
Study type	Interventional

Summary

ID

NL-OMON45117

Source
ToetsingOnline

Brief title
MATISSE

Condition

- Platelet disorders
- Congenital and peripartum neurological conditions
- Neonatal and perinatal conditions

Synonym
bleeding, Hemorrhage

Research involving
Human

Sponsors and support

Primary sponsor: National Health Services Blood and Transplant (NHSBT), UK
Source(s) of monetary or material Support: Sanquin Research

Intervention

Keyword: Hemorrhage, Premature neonate, Thrombocyte transfusion, Thrombocytopenia

Outcome measures

Primary outcome

The proportion of patients who either die or experience a major bleed up to and including study day 28.

Secondary outcome

• Proportion of patients surviving to go home following a major bleed

• Proportion of patients surviving to go home without having had a major bleed

• Proportion of patients who have died up to study day 28

• Proportion of patients who sustain a major bleed up to study day 28

• The rate and time from randomization of minor, moderate and major bleeding derived from the bleeding assessment tool up to study day 14, and for major bleeds up to study day 28.

• Number of platelet units transfused up to study day 28

• Time to discharge home

• Neuro-developmental outcome as assessed by the Bayley III scale of infant development or a Dutch self-completion questionnaire (PARCA-R: Parent Report of Children*s Abilities for very Premature Infants) and a supplementary questionnaire designed specifically for MATISSE. This assessment will take place at 2 year corrected postnatal age.

• Platelet transfusion-related adverse events up to discharge

Study description

Background summary

Preterm neonates with thrombocytopenia are often treated with prophylactic thrombocyte transfusions, with the aim of preventing major bleeding. Practice in many Dutch neonatal units has seen the adoption of thresholds for prophylactic platelet transfusions at around 25-50 x10^9/L. However, the effectiveness and safety of any thresholds in preterm neonates has not been established in randomised controlled trials. Several observational trials show that more restrictive guidelines do not cause increased bleeding risk.

Study objective

To assess whether a higher prophylactic platelet transfusion threshold is superior to the lower thresholds in reducing the proportion of patients who experience a major bleed or death up to study day 28.

Study design

MATISSE is a randomized, parallel group, superiority trial. Preterm neonates with severe thrombocytopenia are randomized between a high transfusion threshold (50x10^9/L) and a low transfusion threshold arm (25x10^9/L). Regular observational bleeding scores and cranial ultrasounds will be performed to assess the presence of bleeding. Follow up continues until a gestational age of 38 weeks or discharge. A follow-up visit to assess neurologic development at 2 years corrected age will also be performed.

Intervention

Randomization between a thrombocyte transfusion threshold of 50x10^9/L and a thrombocyte transfusion threshold of 25x10^9/L.

Study burden and risks

Daily bleeding scores are based on standard observations and do not require extra manipulation of the neonates. Cranial ultrasounds are known to be safe and will be combined with standard ultrasound regimes where possible. No extra blood draws will be performed for this study. The two year neurodevelopmental follow up visit is standard care for the majority of preterm neonates, but will be scheduled on top of standard care for a small subset. Risk of an excess of severe bleeding events in either arm of the trial will be addressed by close monitoring of all neonates using the pre-piloted bleeding assessment tool by trained clinical staff, education to highlight bleeding events and severity, and immediate reporting of all major bleeding events. In addition, the PlaNet-2

trial has already performed an interim analysis and the Independent Data Monitoring Committee (IDMC) is closely monitoring the primary outcome (mortality and major bleeds) as well as safety data for any imbalance between the two arms. It is possible that neonates will benefit from receiving either more of fewer transfusions. Because of the current lack of evidence, it is impossible to predict whether this will be the case. We do not expect neonates to be harmed by this study, based on observational studies suggesting that lowering the transfusion threshold does not increase the number of major bleeds. This study has to be conducted in this study population because preterm neonates are a very distinct population with organ systems (including the hemostatic system) that are still immature and high risk of specific age-related diseases such as necrotizing enterocolitis (NEC) and other diseases. Results from adult or pediatric studies can therefore not be extrapolated to this population.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1. Written informed consent obtained
2. Admission to a participating NICU (includes postnatal transfer)
3. <34 weeks gestational age at birth
4. A platelet count of <50 x10^9/L
5. Cranial ultrasound scan must have been undertaken less than 6 hours prior to randomisation in order to rule out recent major intraventricular hemorrhage

Exclusion criteria

1. Major/life-threatening congenital malformations (e.g. chromosomal anomalies, Fanconi*s anaemia, Thrombocytopenia Absent Radius syndrome (TAR));
2. The occurrence of a major/ severe bleed within the previous 72 hours. However, the neonate may be eligible for randomisation later, once 72 hours has elapsed, provided there are no further major bleeds and the baby meets all the inclusion criteria;
3. All foetal intracranial haemorrhages excluding subependymal haemorrhage from any antenatal ultrasound scan;
4. Known immune thrombocytopenia or family history of alloimmune thrombocytopenia or maternal antiplatelet antibodies or maternal idiopathic thrombocytopenic purpura;
5. Neonates judged by the attending neonatologist to be unlikely to survive more than a few hours at the time of proposed randomisation;
6. Neonates who were not given parenteral Vitamin K after birth.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-02-2014

Enrollment:	315
Type:	Actual

Ethics review

Approved WMO Date:	20-01-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-09-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	De MATISSE centra staan als Nederlandse includerende centra genoemd bij de registratie van de Engelse Planet-2 studie.
CCMO	NL45931.018.13