Randomized trial on the use of rhEPO in neonates with Rhesus alloimmunization.

No registrations found.

Ethical review	Positive opinion
Status	Suspended
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26568

Source
NTR

Brief title
EPO-4-Rhesus study

Health condition

Recombinant Human Erythropoietin (rhEPO)
Hemolytic Disease of the Newborn
Red blood cell alloimmunization
Intrauterine red cell transfusion

Sponsors and support

Primary sponsor: Leiden University Medical Center (LUMC)
Source(s) of monetary or material Support: LUMC

Intervention

Outcome measures

Primary outcome

1. Number of top-up transfusions required per infant;

2. The percentage of infants requiring a top-up transfusion up to 3 months of life.

Secondary outcome

1. Number of days of admission for top-up transfusions;

2. Reduction in ferritin levels;

3. Long term neurodevelopmental outcome at 2 years of age using the BSID-III test.

Study description

Background summary

Neonates with hemolytic disease of the newborn (HDN) due to red cell alloimmunization often require top-up (red blood cell) transfusions to treat late anemia during the first 3 months of life. Late anemia in neonates with HDN may be due to depressed erythropoiesis (hyporegenerative anemia) and/or persisting (intra-marrow) destruction of erythrocytes by remaining antibodies, which is not necessarily associated with parameters of hemolysis. Hyporegenerative anemia occurs in particular in neonates treated with intrauterine red cell transfusions (IUT) due to bone marrow suppression. Up to 80% of infants with rhesus hemolytic disease (RHD) treated with IUT require at least one top-up transfusion. In infants with HDN treated without IUT up to 65% require at least one top-up transfusion (personal data).

Since more than a decade recombinant Human Erythropoietin (rhEPO) has been applied in small studies and casuistic reports, although it is controversial whether neonates with HDN treated with or without IUT may benefit from this treatment to reduce the risk of delayed anemia and subsequent the need for top-up transfusions. Due to the lack of evidence, routine use of rhEPO is currently not recommended.1 To determine whether rhEPO has a role in treatment of this group of patients, a well-designed randomized controlled clinical trial of sufficient sample size is required.

The aim of this study is to determine if treatment with rhEPO reduces the need for top-up transfusions in neonates with HDN due to red cell alloimmunization treated with or without IUT.

Study objective

To determine if treatment with rhEPO reduces the need for top-up transfusions in neonates with red cell alloimmunization treated (with or without intrauterine transfusions).

Study design

Complete blood counts including hemoglobin level and reticulocyte count are determined weekly in both groups (standard practice). The number of top-up transfusions received during the first 3 months of life and hemoglobin levels prior to the top-up transfusion are recorded. In addition, EPO-levels and iron tests (serum iron, ferritin, transferrin and total iron binding capacity) will be determined weekly (therefore 0.6 ml extra blood is taken) and liver enzymes (ASAT, ALAT, gammaGT and LDH) will be determined monthly.

Intervention

After informed consent, stratification into two groups (with and without intrauterine blood transfusion) will be accomplished. After stratification, included neonates will be randomized at birth to treatment with rhEPO (intervention group) or 'standard of care' (no EPO). In the treatment group, RhEPO is administered subcutaneously at a dosage of 250 U/kg three times a week (Mondays, Wednesdays, and Fridays), starting at the end of the first week, for a period of 8 weeks. Treatment is administered during out-patient visits (once a week) and at home through domiciliary care services (twice a week). Concomitant therapy with folate (0.5 mg/day) is given in all groups (standard practice). Concomitant iron therapy is given if ferritin level drops below 75 microg/l. Weekly measurements of complete blood counts (including hemoglobin level and reticulocyte count) will be performed in all groups (standard practice). RhEPO is discontinued if hemoglobin level is ≥ 13 g/dL after at least 4 weeks of treatment with rhEPO. Monthly measurements of liver enzymes (aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT), gamma-glutamyl transferase (gammaGT) and lactate dehydrogenase (LDH)) will also be performed in all groups (standard practice). In addition, EPO-levels and iron tests will be determined weekly. The number of top-up transfusions received during the first 3 months of life and hemoglobin levels prior to the top-up transfusion are recorded. A uniform transfusion trigger according to our transfusion guidelines will be followed. After initial discharge from the LUMC, top-up transfusions are performed when hemoglobin levels fall below 8.0 g/dL or when hemoglobin is between 8.0 and 9.8 g/dL if clinical symptoms of anemia (lethargy, feeding difficulties or failure to thrive) are present. At two years of age a physical and neurological examination and an assessment of cognitive and neurological development using the Dutch version of the Bayley Scales of Infant Development, 3d edition (BSID-III) will be performed (standard practice). BSID-III scores provide mental developmental indexes (MDI) and psychomotor development.

Contacts

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Eligibility criteria

Inclusion criteria

All (near)-term neonates (gestational age ≥ 35 weeks) with HDN (due to Rhesus-D, -C, -c, -E, Kell or other red blood cell alloimmunization) treated with or without IUT and admitted to the Leiden University Medical Center (LUMC) are eligible for the study. The LUMC is the single national referral center in the Netherlands for pregnancies complicated by maternal red blood cell alloimmunization.

Exclusion criteria

Preterm neonates (gestational age < 35 weeks).

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Control:	Active

Recruitment

NL

Recruitment status:	Suspended
Start date (anticipated):	21-01-2013
Enrollment:	132
Type:	Anticipated

Ethics review

Positive opinion

Date:	22-01-2013
Application type:	First submission

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
NTR-new	NL3661
NTR-old	NTR3807
Other	METC LUMC : P10.227
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results

1. Smits-Wintjens VE, Walther FJ, Lopriore E. Rhesus haemolytic disease of the newborn: Postnatal management, associated morbidity and long-term outcome. Semin Fetal Neonatal Med. 2008;13:265-271.
2. De Boer IP, Zeestraten EC, Lopriore E, van Kamp IL, Kanhai HH, Walther FJ. Pediatric outcome in Rhesus hemolytic disease treated with and without intrauterine transfusion. Am J Obstet Gynecol. 2008;198:54.
3. Rath ME, Smits-Wintjens VE, Lindenburg I, Brand A, Oepkes D, Walther FJ, et al. Top-up transfusions in neonates with Rh hemolytic disease in relation to exchange transfusions. Vox Sang. 2010;99:65-70.