Leiden's IVIg trial in Rhesus disease of the Neonate

Published: 01-06-2006
Last updated: 14-05-2024

AimTo determine whether the prophylactic use of IVIg reduces the need for ET in neonates with Rh-D hemolytic disease.

Ethical review	Approved WMO
Status	Pending
Health condition type	Haemolyses and related conditions
Study type	Interventional

Summary

ID

NL-OMON29923

Source
ToetsingOnline

Brief title
LIVIN' study

Condition

- Haemolyses and related conditions
- Blood and lymphatic system disorders congenital
- Neonatal and perinatal conditions

Synonym
Rhesus disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Exchange transfusion, Immunoglobulin, Rhesus disease

Outcome measures

Primary outcome

13.1 Primary outcomes

a. Use of ET (%; proportion of children receiving one or more ET)

b. Number of ET performed per infant

Secondary outcome

13.2 Secondary outcomes

c. Duration of phototherapy (number of days)

d. Maximum serum bilirubin (mmol/l)

e. Change in bilirubin in first 24 hours (%)

f. Change in bilirubin in first 48 hours (%)

g. Use of top-up red cell transfusion in first week of life (%; proportion of children receiving one or more red cell transfusion and number of transfusions per infant)

h. Use of simple red cell transfusion after first week and until 3 months of life (%; proportion of children receiving one or more red cell transfusion and number of transfusions per infant)

i. Duration of hospital stay (number of days)

Study description

Background summary

Background
Rh-D disease of the neonate may lead to excessive hyperbilirubinemia and permanent brain damage (i.e. kernicterus). Traditional neonatal treatment of Rh-D disease consists of intensive phototherapy and ET. Phototherapy lowers bilirubin through photo-oxidation, whereas ET removes bilirubin and hemolytic antibodies, and corrects anemia. ET is a high-risk invasive procedure associated with a significant rate of adverse effects. Although the mortality rate associated with ET is nowadays reported to be less than 0.3% in the term infants, the morbidity rate associated with ET is at least 5%.
Neonatal treatment with IVIg has been suggested as an alternative therapy for ET in hemolytic disease of the neonate (HDN). A few small randomized controlled trials (RCT) have suggested that IVIG combined with phototherapy reduces the serum bilirubin and the need for ET in neonates with HDN compared with phototherapy alone6-9. In these studies, treatment with IVIg also reduced the duration of phototherapy and length of hospitalization, but increased the need for late red cell transfusions7. However, the number of patients included in these RCTs was small and the study- design and inclusion criteria varied considerably. In one study, infants with ABO incompatibility were also included. Moreover, an unexpected and large number of these children with ABO incompatibility and HDN required ET8. Finally, the criteria for exchange transfusion were discordant between the various studies.
Therefore, the evidence thus far is considered insufficient to recommend the routine use of IVIg10. A recent Cochrane review suggested that the results of further trials of higher quality should be awaited10. In contrast, the American Association of Pediatrics (AAP) recommended in 2004 the use of IVIg (0.5 - 1 g/kg) in HDN in case of failure of phototherapy, despite the limited data1. Given the conflicting recommendations, a well-designed randomized controlled trial (RCT) for the use of IVIg in HDN is urgently needed.

Study objective

Aim
To determine whether the prophylactic use of IVIg reduces the need for ET in neonates with Rh-D hemolytic disease.

Study design

Prospective randomized double blind placebo controlled trial

Intervention

Prior to randomization, stratification into two groups (with and without intrauterine blood transfusion) will occur. At birth, patients are then randomized to the IVIg treatment group (group A) or placebo control group (group B) by opening a sealed envelop containing a study number. In group A, patients will receive conventional intensive phototherapy plus prophylactic

IVIg as a single dose of 0.75 g/kg within the first 4 hours after birth. In group B, patients will receive conventional intensive phototherapy plus an equal amount of glucose 5% intravenous infusion (placebo) on day one. For details on the phototherapy protocol, see paragraph 18.

Study burden and risks

Apart from the excellent safety profile for transmission of viral disease, all blood products (incl IVIg) have a theoretical risk for transmission of variant Creutzfeldt-Jakob disease. At present, this risk is considered extremely low.

Contacts

Public
Academisch Medisch Centrum

albinusdreef 2
2300 rc Leiden
Nederland
Scientific
Academisch Medisch Centrum

albinusdreef 2
2300 rc Leiden
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

7.1 Inclusion criteria: Neonates of 35 or more weeks of gestation with Rh-D hemolytic disease admitted to the neonatal nursery of the Leiden University Medical Center (LUMC). Rh-D hemolytic disease was defined as (1) Antibody Dependent Cellular Cytotoxicity-test (ADCC) > 50% and (2) positive direct Coombs test in a Rh-D positive fetus/neonate with a Rh-D negative mother and a Rh-D positive father. Previous intra-uterine transfusions and the presence of additional antibodies besides anti-D are not reasons for exclusion.

Exclusion criteria

7.2 Exclusion criteria: (1) Perinatal asphyxia (defined as an Apgar score at 5 minutes less than 3 and/or umbilical cord arterial pH less than 7.0). (2) Neonates with hemolytic disease other than Rh-D. (3) Neonates with Rh-D hemolytic disease presenting > 24 hours after birth.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2006
Enrollment:	68
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
CCMO	NL11345.058.06