Long term follow-up after intrauterine transfusion

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Identify, in the heavily RBC alloimmunized population of females after HDN treatment whether particular MHC class II alleles are associated with presence or absence of particular RBC immunization. The second aim of this study is to determine the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Foetal complications
Study type	Observational invasive

Summary

ID

NL-OMON31534

Source
ToetsingOnline

Brief title
LOTUS study

Condition

- Foetal complications
- Developmental disorders NEC

Synonym
Rhesus-baby, Severe anemia with intrauterine transfusion of the fetus

Research involving
Human

Sponsors and support

Primary sponsor: Sanquin Bloedbank
Source(s) of monetary or material Support: Sanquin

Intervention

Keyword: Erythrocyte antibodies, Intrauterine transfusion, Long term follow-up, Neuromotor development

Outcome measures

Primary outcome

1. Identify, in the heavily RBC alloimmunized population of females after HDN treatment whether particular MHC class II alleles are associated with presence or absence of particular RBC immunization.

2. Determine the long-term neuromotor development, cognitive development and psychosocial well-being in a large group of children treated with IUT for fetal anemia.

Secondary outcome

1. Role of chimerism: investigate whether antibodies that had been identified after delivery still persist and whether the fetus or the IUT donor (or both) had provided the offending antigen. Evaluate whether fetal and/or donor chimerism is associated with persistence of RBC antibodies.

2. High and low respondership: investigate whether females, who produced multiple additional red cell antibodies, are high responders against HLA and HPA antigens as well.

3. Other genetic factors: investigate whether polymorphic genes relevant for co-stimulatory APC-T cell activation and T-B cell interactions determine occurrence of RBC allo-immunization. This subquestion is joined together with a wider investigation in other cohorts of immunized patients (Match-study) and carried out in collaboration with Prof. vd Schoot.

4. Long-tern outcome: explore the association of adverse long-term outcome with risk factors, including: gestational age at birth, cause and severity of fetal anemia, presence and severity of hydrops fetalis, and number of IUT procedures.

5. Long-term health effects: a protocolled questionnaire aiming to identify possible immune deviations as a result from the treatment (autoimmune diseases)

Study description

Background summary

Intrauterine transfusions (IUT) are nowadays the mainstay for severe fetal anemia. The main cause of fetal anemia is maternal red blood cell (RBC) alloimmunization. Other frequent causes include Parvo B19 infection and feto-maternal hemorrhage (FMH).
Pregnant women with Rh-D hemolytic disease of the fetus, receive a median of 3 (range 1-8) intrauterine transfusions. We found that 25% of these women develop additional erythrocyte antibodies after IUT and that >70% of these females possess multiple antibodies at delivery, which complicate transfusion treatment and future pregnancies. Such high incidence of red cell immunization exceeds the immunization rate of any poly-transfused patient group. The mechanism of this high immunization rate is unknown. Several factors may contribute, such as an altered immune state of pregnancy, the way and small volume of the transfusion, the dual exposure to MHC-haplotype-shared fetal cells in combination with random donors, prolonged donor cell survival and genetic factors of recipient, child and donors. In particular, MHC-restriction more or less efficiently presentation of RBC antigens may play a role. This study will address several of the putative mechanisms associated with RBC (and HLA/HPA) antibody formation with the aim to identify factors to predict the risk for alloimmunization against particular RBC antigens. This can lead to a change in transfusion policy, in particular future avoidance of certain mismatches for transfusion thereby increasing transfusion safety. Moreover the study creates the opportunity to determine factors leading to the persistence of antibodies against fetal or transfusion antigens.
Although several studies have reported on the much improved short-term outcome after IUTs, only few studies have focused on the long-term neurodevelopmental outcome. Most follow-up studies show that despite the severity of fetal hemolytic disease, developmental outcome for children treated with intrauterine transfusions can be expected to be normal. The main limitation of these studies is the small number of patients included. Moreover cognitive development and quality of life assessment was not always included in the follow-up studies.

The second aim of this study is to determine the long-term neuromotor development, cognitive development and psychosocial well-being in a large group of children treated with IUT for fetal anemia.
In addition, the contact after 20 or more years offer the opportunity to evaluate long-term health sequelae as chimeras has been associated with autoimmune diseases in females.

Study objective

Identify, in the heavily RBC alloimmunized population of females after HDN treatment whether particular MHC class II alleles are associated with presence or absence of particular RBC immunization.
The second aim of this study is to determine the long-term neuromotor development, cognitive development and psychosocial well-being in a large group of children treated with IUT for fetal anemia.

Study design

Observational cohort study
All women and their live-borne children, who have been treated with intra-uterine transfusions for severe fetal anemia in the past 20 years will be asked to participate in the study. After informed consent, a blood sample is withdrawn. From young children, in-stead of a blood sample, a mouth-swap or a saliva sample will be taken.
The follow-up visit includes a physical and standardized neurological examination in children.
The mothers will be asked to fill in a protocolled questionnaire.

Study burden and risks

Study persons will be invited to come to the LUMC, where blood or saliva sampling or mouth swab and filling in questionnaires will take place. The follow-up visit also includes a physical and standardized neurological examination.
The risks are those associated with routine venepuncture. Participation does not result in any direct benefit.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Mothers and their live offspring who were treated with intrauterine transfusion.

Exclusion criteria

None

Study design

Design

Study type: Observational invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-07-2008
Enrollment:	800
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL21240.058.08