HPA-1a antigen tolerance induction by maternal-fetal antigen exposure

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Aim of the study is to evaluate wether exposure of HPA-1a negative fetuses to the maternal HPA-1a antigens during fetal life induces tolerance which may reduce the risk that HPA-1a antibodies are developed later in life.We postulate that 1) women...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON30661

Source
ToetsingOnline

Brief title
tolerance induction by maternal-fetal antigen exposure

Condition

- Other condition
- Immune disorders NEC

Synonym
Neonatal AlloImmune thrombocytopenia AND platelet antagonism AND shortage of platelets in newborns

Health condition

Allo immunisatie tegen een trombocyten antigeen

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Grandmother, HPA-1a, NAIT, tolerance

Outcome measures

Primary outcome

Primary study parameter is HPA-1a type of the "grandmothers".

2% of the Caucasian population is HPA-1a negative (HPA-1b1b). If HPA-1a antibodies are only produced by HPA-1a negative women with HPA-1a negative mothers (grandmothers) 20 cases will be enough to show statistical significance.

Calculation:

In the Caucasian population the HPA-1 fenotyping is distributed as follows:

HPA-1a1a 72%

HPA-1a1b 26%

HPA-1b1b 2%

HPA-1b1b mothers will have a HPA-1a1b or HPA-1b1b mother (grandmother). The ratio HPA-1a1b:HPA-1b1b for these grandmothers is 93:7. If there is a 100% tolerance induction all grandmothers must be HPA-1b1b and the statistical significance (Chi Square $p<0.001$) will be shown with only a few grandmothers.

Possible tolerance induction will be depending on the amount of HPA-1a exposure of the fetus. It is likely the amount of exposure varies. Possibly a certain

amount of HPA-1a exposure is necessary for tolerance induction. To show skewing (more HPA-1b1b grandmothers than expected) we will include as many cases as possible (goal is between 40 and 60 cases), retrospective and prospective.
To show a significant skewing at least 20% of 40 and 18% of 60 grandmothers need to be HPA-1b1b.

Maybe there will be a partial suppression of the HPA-1a antibody production because of fetal exposure to HPA-1a. To see if there is a correlation between the antibody titer and the HPA-1 fenotype of the grandmother, we will include 20 women with a high HPA-1a antibody titer (>1:64) and 20 women with a low antibody titer (<1:16).
A significant higher number HPA-1b1b grandmothers (>4 of 20) is expected in the high antibody titer group but not in the low antibody titer group.

Secondary outcome

no secundary study parameters

Study description

Background summary

Neonatal AlloImmune Thrombocytopenia (NAIT) is caused by a platelet bloodgroup antagonism that occurs in about 1 in 1300 random births and results from maternal alloimmunization against platelet antigens present on fetal platelets but absent on maternal platelets. Although 98% of the Caucasian population is positive for the Human Platelet Antigen 1a (HPA-1a), it is the most frequently offending antigen (75%). Approximately 10% of HPA-1a negative women produce HPA-1a alloantibodies
Because of severe thrombocytopenia in utero, in up to 5 percent of cases

intracerebral haemorrhage occurs, often leading to severe neurological sequelae or death.

Study objective

Aim of the study is to evaluate wether exposure of HPA-1a negative fetuses to the maternal HPA-1a antigens during fetal life induces tolerance which may reduce the risk that HPA-1a antibodies are developed later in life.

We postulate that 1) women who were exposed to maternal HPA-1a antigens in the fetal period will not produce HPA-1a antibodies or 2) will have a weaker immune response and therefore a lower HPA-1a antibody titer.
To investigate 1) we will type a cohort of 40-60 grandmothers to observe a skewing of the HPA-1bb typing. To investigate 2) we will include 20 women with a high HPA-1a antibody titer (>1:64) and 20 women with a low antibody titer (<1:16).

Study design

Retrospective and prospective cases that are refered to the platelet/leukocyte serology department for suspected NAIT and for whom maternal HPA-1a antibodies are detected do serve as basis for this study.
Grandmothers of NAIT patients will be asked by the treating physician to give 8 ml of EDTA unclothed blood for HPA-1 genotyping.
For this treating physicians who send material for NAIT investigation to our laboratory will be asked, if mother shows to have HPA-1a antibodies, to ask grandmother to participate. Information and an informed consent form will be provided by our laboratory. In case of participation, only once 8 ml of EDTA unclothed blood will be drawn and send, by a Sanquin Courier, to our laboratory. In this way we hope to include 40-60 cases in 2 years time.
Grandmothers will be genotyped for the HPA-1 system.
maternal HPA-1a antibody titer/quantification will be performed in the Monoclonal Antibody Immobilization of Platelet Antigens Assay and a Logit quantification Program

Study burden and risks

8 ml of EDTA anticoagulated blood will be drawn once by venapunction.
This study will provide knowledge concerning the risk for HPA-1a immunisation of HPA-1a negative women and can be used in the future for the estimation of risk of immunisation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Mothers of women with HPA-1a antibodies

Exclusion criteria

no specific exclusioncriteria

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2007
Enrollment:	60
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
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
CCMO	NL11748.018.06