Autoantibodies in cord blood of offspring from women with rheumatoid arthritis? A pilot study to investigate placental transfer of autoantibodies in women with RA

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To answer the following questionsDo RA-specific autoantibodies cross the placenta, and can they be found in fetal cord blood in the offspring of mothers suffering from RA?Do RA-specific autoantibodies in fetal cord blood display different...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON38801

Source
ToetsingOnline

Brief title
RA autoantibodies in cord blood

Condition

- Autoimmune disorders
- Neonatal and perinatal conditions

Synonym
rheumatism, rheumatoid arthritis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: autoantibodies, cord blood, placental transfer, rheumatoid arthritis

Outcome measures

Primary outcome

The study design is observational with the primary endpoint: presence/absence

and characteristics of autoantibodies in maternal blood and cord blood.

Autoantibody-negative women will serve as a negative control.

Secondary outcome

Characteristics of autoantibodies in RA

Study description

Background summary

Rheumatoid arthritis (RA) is a common autoimmune disease characterized by persistent synovitis, systemic inflammation and the expression of autoantibodies. Although RA affects 0.5-1% of the population, knowledge concerning disease pathogenesis remains relatively limited. (1)
The *oldest* autoantibody in RA is rheumatoid factor (RF). RF targets the Fc-part of human IgG and is mostly present as IgM-RF although IgG-RF and IgA-RF have also been described in subgroups of patients.
In the past decade, anti-citrullinated protein antibodies (ACPA) have been identified as a new class of autoantibodies in RA and are now important diagnostic and prognostic biomarkers. Patients with ACPA positive RA are prone to suffer from a severe course of the disease with more joint destruction than ACPA-negative patients. (2) Intriguingly, ACPA can be detected in serum many years before disease onset.(3)
In 2011, autoantibodies recognizing carbamylated (homocitrulline-containing) antigens (anti-CarP antibodies) have first been described as a new serological marker for patients with ACPA negative RA. In this group of patients, anti-CarP antibodies associate with more severe joint destruction compared to joint

destruction in anti-CarP negative patients.

In most female patients, symptoms of RA ameliorate during pregnancy. Postpartum, the disease frequently flares. In contrast, other autoimmune disorders such as systemic lupus erythematodes and pemphigus vulgaris often worsen during pregnancy, but can also cause placental insufficiency, growth retardation and premature birth. In addition, these disorders pose an increased risk for the child because of placental transfer of autoantibodies, which can lead to neonatal lupus or pemphigus, respectively.
Interestingly, no cases of neonatal RA have so far been described, and no detailed analysis has been performed to investigate whether and to what extent autoantibodies from RA patients cross the placenta and can be found in fetal cord blood.
In principal, placental transfer of antibodies in the human is mediated by the neonatal Fc receptor that specifically recognizes IgG. The majority of ACPA and anti-CarP antibodies are of the IgG isotype and, therefore, should be able to cross the placenta. Consequently, these antibodies can be expected in neonatal cord blood. Recent evidence indicates, however, that at least ACPA are different from *conventional* IgG molecules. For example, the vast majority of ACPA carries highly sialylated N-glycans in the variable region. In contrast, such glycans are found in only a minority of non-citrulline specific IgG and have so far not been detected on other autoantibodies. Also, analysis of glycans in the Fc region revealed important differences between ACPA and the rest of circulating serum IgG. These observations are relevant, as glycans are known to modulate the structure of antibodies and the extent to which a molecule can interact with its receptor.
Given that offspring of mothers with autoantibody positive RA do not show signs and symptoms of disease, the question arises whether ACPA and other disease specific autoantibodies do indeed cross the placenta in the same way as has been described for non-self reactive IgG and other autoantibodies.

Study objective

To answer the following questions
Do RA-specific autoantibodies cross the placenta, and can they be found in fetal cord blood in the offspring of mothers suffering from RA?
Do RA-specific autoantibodies in fetal cord blood display different characteristics (such as fine-specificity, avidity, glycosylation) than their maternal counterparts?

Study design

pilot study

Study burden and risks

Minimal risk for patient because of venous puncture

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

pregnant women with RA diagnosed according to the revised EULAR/ACR 2010 criteria or the 1987 ACR criteria

Exclusion criteria

women under 18 years of age are not eligible to participate for ethical reasons

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-02-2014
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	11-12-2013
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	NL45676.058.13

Study results

Date completed:	14-06-2017
Actual enrolment:	12