High disease activity and prednisone use during pregnancy; lifelong consequences for children of mothers with rheumatoid arthritis?

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The aim of the current study is to get insight into the in potential lifelong consequences of active disease and or prednisone use during pregnancy on the children of women with rheumatoid arthritis. As readout it uses indicators (risk factors) for…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON40087

Source
ToetsingOnline

Brief title
FEtal Programming by Rheumatoid Arthritis (FEPRA)

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Neonatal and perinatal conditions

Synonym
chronic, systemic inflammatory disorder

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,Reumafonds;Nederland

Intervention

Keyword: 1) rheumatoid arthritis, 2) prednisone, 3) pregnancy, 4) fetal programming

Outcome measures

Primary outcome

Anthropometric data of the child

- Height

- Weight

- Sitting height

- Head circumference

- Arm/waist/hip circumference

Blood pressure of the child

- 3 times measurement on one day

Parents:

- weight

- height

- head circumference

- blood pressure

Information on:

- Familiy medical hisory

- Medication use of mother

- Growth chart from birth onwards

Secondary outcome

Data on body composition & fat percentage

- Lean body mass

- Holtain skin fold caliper

- Abdominal ultrasound

- Dual Energy X-ray Absorptiometry (DXA)

Venapuncture

- glucose

- glucose fasting levels

- C-peptide

- Insulin

- Cortisol

- Total cholesterol

- HDL

- LDL

- Triglycerides

- Free fatty acid

- Adiponectin

- DNA analysis (genetic variation and epigenetic changes)

24 h cortisol levels in saliva

- 4 measurements on one day

Buccal epithelial cells obtained by mouth swab

- DNA analysis, 1 measurement

Study description

Background summary

To prospectively study the mutual influence of rheumatoid arthritis pregnancy and pregnancy outcome the PARA-study (Pregnancy induced Amelioration of Rheumatoid Arthritis) was started in 2002. A main finding of the study is that both high disease activity (above median) during pregnancy as well as prednisone use were associated with lower birth weight.
Babies born to women with active disease and prednisone use weighted on average 460 gram less. This is more pronounced then other known factors that influence the birth weight like that of smoking (100-200gram less) or of the World War II Dutch famine (100-250 gram less).
Low birth weight has been associated with cardiovascular disease, hypertension, noninsulin dependent diabetes mellitus (DM) and neuropsychiatric disorders in adulthood. This association is already present for a lower birth weight within the normal range. Risk factors for the above mentioned disease associations can already be demonstrated at a very young age and can be tracked from young age into adulthood. Whether the lower birth weight of children born to women with rheumatoid arthritis has similar consequences is not known.
The influence of medication (like prednisone) could depend on the genetic variation of an individual person (e.g. single nucleotide polymorphisms, SNP's). The phenomenon that events during early life (pregnancy) may have lifelong consequences is referred to as the developmental origin of disease. Epigenetic processes are thought to be one of the mechanisms underlying the developmental origin of disease. Of these, DNA-methylation has been most extensively studied. Most pronounced changes occur in early pregnancy. Factors that have been shown to influence DNA-methylation include maternal disease and malnutritions, smoking, placental insufficiency, corticosteroids, folate depletion and cytokines. It is plausible that inflammatory disorders, like acitve RA may also influence the methylation.

Study objective

The aim of the current study is to get insight into the in potential lifelong consequences of active disease and or prednisone use during pregnancy on the children of women with rheumatoid arthritis. As readout it uses indicators (risk factors) for future development of cardiovascular disease and non-insulin dependent diabetes mellitus that are suitable at very young age. Moreover, it attempts to elucidate potential pathogenic mechanism.

If there are consequences found in the study on the children, another RA treatment strategy durring the pregnancy can be considered to minimize the potential lifelong risk factors for the newborn.

Study design

Translational epidemiological research study

Study burden and risks

a) minimal radiation durring the dual-energy X-ray absorptiometry
b) potential hematoma after venepunction
c) there aren't any expected complications of the mouth swabs

Contacts

Public
Reumafonds

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

mother has participated in the PARA study (MEC 214.320/2002/117)

Exclusion criteria

a) twins
b) non-Caucasian children
c) children with congenital abnormalities

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-10-2010
Enrollment:	378
Type:	Actual

Ethics review

Approved WMO Date:	21-12-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-07-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL28432.078.09