Is antenatal prednisone exposure associated with chronically elevated cortisol levels in children?

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The aim of this study is to determine whether children between 5-17 years born to women with an autoimmune disorder and prednisone use during pregnancy have chronically elevated cortisol levels compared to children born to women with an autoimmune...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Adrenal gland disorders
Study type	Observational non invasive

Summary

ID

NL-OMON44675

Source
ToetsingOnline

Brief title
Hair cortisol and intrauterine prednisone exposure (HAIR)

Condition

- Adrenal gland disorders
- Neonatal and perinatal conditions

Synonym
autoimmune disorders

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

Intervention

Keyword: 1) reumatoid arthritis, 2) prednisone, 3) pregnancy, 4) hair cortisol

Outcome measures

Primary outcome

I) hair cortisol measurements

- proximal 3 cm hair (with about 100 hairs) will be cut from the back of the

scalp of the child

II) anthropometric data of the child

- bloodpressure: 3 times measured on one day

- height and weight

- waist and hip circumference

- fat percentage using a skin fold measured by Holtain caliper

III) questionnair:

- information on hair, hair products and medication use of the child

IV) since the child*s body composition is related to that of its parents, data

on height and weight of both parents will be obtained

Secondary outcome

I) DNA analysis in buccal epithelial cells obtained by a mouth swab

Study description

Background summary

In 2002 the PARA-study (Pregnancy induced Amelioration of Rheumatoid Arthritis) was started to prospectively study the influence rheumatoid artritis and medication use on the pregnancy outcome.
Recently we have shown in this study group that the children born to women with RA and prednisone use during pregnancy have higher daytime cortisol levels in saliva at age 7 compared to children born to women without prednisone use. This finding correlates with earlier animal studies. Chronically elevated cortisol levels in childhood have been associated with hypertension, cardiovascular disease, and non-insulin dependent diabetes mellitus (DM) in adulthood. Cortisol in saliva is not suitable for long-term cortisol measurements due to the circadian rhythm, pulsatile secretion, daily variation and reactivity to acute (transient) stress. Hair cortisol seems to more adequately reflect the long-term cortisol levels. The aim of current research proposal is to get more insight into the lifelong consequences of antenatal prednisone exposure on the long-term cortisol levels as reflected in the hair cortisol. Additionally, we want to perform DNA analysis in buccal epithelial cells, obtained by mouth swabs, to determine whether the observed findings are related to DNA-polymorphisms or changes in DNA-methylation.

During pregnancy there are limited options for the treatment of autoimmune disorders. Prednisone is a widespread used drug.
The result of this study will inform us about the safety of prednisone use during pregnancy, especially the long-term effects on the offspring.

Study objective

The aim of this study is to determine whether children between 5-17 years born to women with an autoimmune disorder and prednisone use during pregnancy have chronically elevated cortisol levels compared to children born to women with an autoimmune disorder without prednisone use. And whether this is associated with physical signs of higher cortisol levels (body composition, blood pressure).
We will also determine whether the observed findings are related to DNA-polymorphisms or changes in DNA-methylation.

The result of this study could change current treatment strategies of pregnant women with an autoimmune disease to minimize potential life long risk of the offspring.

Study design

case-control study

Study burden and risks

- the hair collection and mouth swab is non-invasive
- the burden is the time investment of one hour for the hair and buccal epithelial cell collection, physical examination (for anthropometric data) and questionnair

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

To be eligible for this trial, children in the study arm must meet all of the following criteria:
- Children between 5-17 years born to women with an autoimmune disorder, primarily RA, and prednisone use with a dose * 5mg/day during at least two trimesters of their pregnancy

- Parents of the child are able and willing to give written informed consent and comply with the requirements of the study protocol;To be eligible for this trial, children in the control arm must meet all of the following criteria:
- Children between 5-17 years born to women with an autoimmune disorder, primarily RA, without prednisone use during their pregnancy
- Parents of the child are able and willing to give written informed consent and comply with the requirements of the study protocol

Exclusion criteria

1) monozygotic twins
2) non-Caucasian children
3) children with congenital abnormalities
4) parental refusal to participate
5) children with hair shorter than 2cm
6) children with chronic illness

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-05-2015
Enrollment:	360
Type:	Actual

Ethics review

Approved WMO Date:	08-10-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-03-2017
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	NL49156.078.14

Study results

Date completed:	05-10-2018
Actual enrolment:	360