Endothelial dysfunction and pregnancy complications in women with congenital heart disease: an addendum to the ZAHARA-II study (ZAHARED study)

Published: 11-10-2007
Last updated: 10-05-2024

Primary Objectives: To prospectively investigate the changes in cardiac parameters (echocardiography, NT-pro-BNP) and uteroplacental flow (pulsatility index, diastolic notching) during/after pregnancy in women with CHD and compare these changes with…

Ethical review	Approved WMO
Status	Pending
Health condition type	Congenital cardiac disorders
Study type	Observational non invasive

Summary

ID

NL-OMON31812

Source
ToetsingOnline

Brief title
ZAHARED

Condition

- Congenital cardiac disorders
- Cardiac and vascular disorders congenital
- Pregnancy, labour, delivery and postpartum conditions

Synonym
congenital heart disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Nederlandse Hartstichting

Intervention

Keyword: congenitalheartdisease, endothelial dysfunction, pregnancy

Outcome measures

Primary outcome

- Change in cardiac parameters: Significant deterioration in size/function of subpulmonary or systemic ventricle; aggravation of valve regurgitation >= 1 grade; persistent (1 year) significant aggravation of valve stenosis; significant elevation of NT-pro-BNP, compared to healthy controls

- Difference of uteroplacental flow parameters between healthy controls and CHD patients: pulsatility index, % persistent diastolic notching

- Composite endpoint of cardiac complications

- Composite endpoint of obstetric complications

- Composite endpoint of neonatal complications

- Composite endpoint of uteroplacental flow related complications (PIH, pre-eclampsia, eclampsia, intrauterine growth retardation, small for gestational age birth weigt, premature delivery, neonatal mortality).

endpoints for the substudy:

-Change in endothelial function parameters in women with CHD with the same parameters in healthy pregnant women during and after pregnancy.

-Change in endothelial function parameters in these women in relation to uteroplacental flow parameters and to pregnancy outcome (cardiac, obetetric and neonatal complications).

-Change in endothelial function parameters in these women to underlying disease, genetic profile and cardiac function (nT-pro-BNP, echocardiography, pre-pregnancy and post-pregnancy exercise capacity).

Secondary outcome

Change in exercise capacity (exercise test) 1 year post pregnancy compared to pre-pregnancy.

Deterioration of NYHA class during / after pregnancy in CHD patients, compared to healthy women.

For the substudy:

To find genes that cause ED and pregnancy complications in women with CHD.

Study description

Background summary

In the Netherlands, the population of at least 25.000 adult CHD patients is rapidly increasing due to the surgical progress made in the last decades, which has improved long-term outcome. Pregnancy and fertility are important issues in everyday practice of the grown-up congenital heart disease cardiologists. The retrospective ZAHARA I study (Zwangerschap bij Aangeboren HARtAfwijkingen = Pregnancy in Congenital Heart Disease Study, showed an increased incidence of cardiac, obstetric and fetal/neonatal complications in pregnant women with CHD. However, this retrospective study provided no detailed (such as echocardiographic,

neurohumoral) data concerning the impact of the hemodynamic burden of pregnancy on the diseased maternal heart. Therefore identification of high risk pregnancies is up till now insufficient. In the proposed study we have the unique opportunity to prospectively investigate the underlying mechanisms that determine the occurrence of cardiac, obstetric and fetal/neonatal pregnancy complications.
in addition to the abovementiond, Endothelial dysfunction (ED) plays an important role in the pathophysiology of Pre-eclampsia and other pregnancy complications. In the ZAHARA II study, a prospective multicentre ICIN study supported by the Netherlands Heart Foundation (NHS2007B75), we will study the changes in cardiac parameters (i.e. Nt-pro-BNP, echocardiography) as well as the changes in uteroplacental flow parameters in 160 pregnant women with CHD and in 60 healthy controls, and relate these to the occurrence of cardiac, obstetric and neonatal complications. This will give insight in the underlying mechanisms that determine the occurrence of pregnancy complications, thus improving risk stratification and counselling of CHD women. We hypothesize that ED occurs more frequently in pregnant women with CHD than in healthy pregnant women and is associated with the increased occurrence of obstetric and neonatal complications that is found in CHD women. ED may be related to underlying CHD and to cardiac function.

Study objective

Primary Objectives: To prospectively investigate the changes in cardiac parameters (echocardiography, NT-pro-BNP) and uteroplacental flow (pulsatility index, diastolic notching) during/after pregnancy in women with CHD and compare these changes with with age/parity-matched healthy controls.
To relate the cardiac parameters (prepregnancy and during pregnancy) with the occurrence of cardiovascular, obstetric and neonatal complications.
To relate the cardiac parameters (prepregnancy and during pregnancy) and uteroplacental flow measurements with the occurrence of obstetric complications and neonatal complications.
Secondary Objective(s):
To elucidate the mechanisms behind the increased incidence of obstetric and neonatal complications in CHD patients by focusing on changes in utero-placental perfusion.
To evaluate the incidence of permanent (1 year) decline of exercise tolerance in women with CHD and compare this with healthy women.
To evaluate the risks scores for cardiac and neonatal complications in pregnant women developed by Siu et al and by the ZAHARA1 investigators prospectively in women with CHD.
To continue the (worlds largest) registration (ZAHARA registration) of pregnancy outcome in CHD women, primarily to facilitate the future assessment of long-term effects of pregnancy on survival and morbidity in CHD patients.

Study design

Prospective multi-center cohort study. All pregnant patients with a congenital heart anomaly presenting before 20 weeks of gestation in the participating medical centres will be asked to participate by their cardiologist. Data concerning underlying heart disease/obstetric medical history will be retrieved from medical records. In the participating centers it is common practice to perform echocardiograms in CHD patients yearly/2-yearly, therefore prior echocardiograms will be
available in most patients. Currently standardised outpatient follow-up (including standardised echocardiograms)
are being developed by the Dutch 'Werkgroep Congenitale Cardiologie bij Volwassenen' to improve uniformity.
Serial (20, 32 weeks of pregnancy, 1-year postpartum) standardised echocardiograms will be performed. Foetal
growth and utero-placental perfusion (e.g. flow velocity measurements of uterine and umbilical artery) will be
studied by Doppler ultrasound evaluations (20, 32 weeks; for healthy control women only at 20 weeks). Neurohumoral parameters (Nt-pro-BNP) will be assessed during/after pregnancy. Data concerning pregnancy complications will be collected. Exercise testing will be performed 1-year postpartum in patients who had undergone this test less than 1 year before pregnancy. It is estimated based on the ZAHARA I study that 160 women with CHD and 60 healthy pregnant controls will be enrolled during a 3-year period.

Study burden and risks

In this selected patientgroup of pregnant women with a congenital heart anomaly, the number of study assessments are kept down to a minimum:
20 weeks, 32 weeks, 1 year post partum: Standardised echocardiography; NTpro-BNP
20 weeks, 32 weeks: foetal ultrasound evaluation of intra-uterine growth and amniotic fluid volume, obstetric
clinical evaluation. Uteroplacental Doppler flow registration
20 weeks, 32 weeks:totaal eiwit in 24uurs urine
20 weeks, 32 weeks: biomarkers for endothelila function
32 weeks: IMT measurement
1 year post partum: In the subgroup of patients who had pre-pregnancy exercise testing, an exercise test will
be performed (preferably VO2max).
The proposed study assessments are risk-free.

For control women:
20 weeks, 32 weeks, 1 year post partum: Standardised echocardiography; NTpro-BNP
20 weeks, 32 weeks: biomarkers for endothelila function
32 weeks: IMT measurement
20 weeks, 32 weeks:total protein in 24h urine
20 weeks: foetal ultrasound evaluation of intra-uterine growth and amniotic

fluid volume, obstetric
clinical evaluation.
20 weeks, 32 weeks: Uteroplacental Doppler flow registration

In zwangerschap op 20 + 32 weken: 24-uurs urine voor de bepaling van totaal eiwit

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
9700 RB Groningen
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
9700 RB Groningen
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

All pregnant patients with a congenital heart anomaly presenting before 20 weeks of gestation in one of the participating medical centres; 60 healthy controls

Exclusion criteria

Congenital heart disease: no exclusion criteria. Healthy women: Women who are on chronic medication; women who are under specialist control for chronic disease; drug addicts and smokers

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:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2007
Enrollment:	195
Type:	Anticipated

Ethics review

Approved WMO

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

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	NL19125.042.07