Urinary markers for fetal growth restriction: the role of gaseous vasoactive molecules.

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Hypothesis: gaseous signaling molecules influence placental vasomotor activity to compensate for hypoxemia. Metabolites of these vasoactive molecules can be found in the blood and urine and can indicate whether this (compensatory) mechanism is used...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Foetal complications
Study type	Observational invasive

Summary

ID

NL-OMON43012

Source
ToetsingOnline

Brief title
Urinary markers and fetal growth restricton

Condition

- Foetal complications

Synonym
Fetal growth restriction, fetal growth retardation

Research involving
Human

Sponsors and support

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

Intervention

Keyword: fetal growth restriction, gaseous, marker, urine

Outcome measures

Primary outcome

Urinary metabolites and metabolites in blood related to composite neonatal consisting of fetal weight, length, matched for gestational age.

Secondary outcome

Placental histology, Doppler abnormalities, mode of delivery, APGAR scores and admission to NICU/ward and the relation of the urinary metabolites to the measurements of these molecules in maternal and fetal blood (umbilical cord blood).

Study description

Background summary

Fetal growth restriction (FGR) is caused by placental insufficiency and occurs in approximately 10% of all pregnancies. It is a major risk factor for short -and long-term morbidity and mortality. Consequences include increased incidence of various diseases, including hypertension and renal disease. Predisposition for disease development originates in utero when the environment programs the placenta and fetus by epigenetic mechanisms (Barker hypothesis). A major issue in fetal growth restriction is the diagnostic process. Children grown below a certain population based centile are either constitutionally small or growth restricted. Children grown above that centile may be growth restricted although their weight seems to be normal. If we use p10 as a cut off we know that 50% of babies indicated as FGR are in fact healthy small babies and we miss 50% of babies who are growth restricted and are grown above the p10 (Voskamp et al., 2014). Ultrasound with combined biometrical and Doppler measurements predict the occurrence of FGR and we can add functional (invasive) parameters as PlGF and sFLit (Conde-Agudelo, Papageorghiou, Kennedy, & Villar, 2013). These measurements are expensive and not widely available. There is need for early predictors for FGR that are easy to measure, inexpensive and, preferably, easy to sample. It is known that several gaseous

signaling molecules such as H2S, CO and NO play a role in the (compensatory) mechanism of FGR since they are involved in blood pressure regulation, inflammation and reactive oxygen (ROS) scavenging. These molecules and their metabolites are of our interest since recent work in renal transplant patients, heart failure patients, diabetic patients, healthy individuals and patients with placental insufficiency. It has shown that gaseous signaling molecules predict mortality and disease outcome. Whether H2S is a cause or a consequence of placental insufficiency is unknown. In this pilot study we aim to find a predictive marker for FGR that is easily available, non-invasive and inexpensive.

Study objective

Hypothesis: gaseous signaling molecules influence placental vasomotor activity to compensate for hypoxemia. Metabolites of these vasoactive molecules can be found in the blood and urine and can indicate whether this (compensatory) mechanism is used to enhance placental function.

Objective:
To measure urinary and blood metabolites of gaseous vasoactive molecules in complicated and uncomplicated pregnancy to define a novel biomarker for FGR.

Study design

Blood samples are taken the day after the urine collection when the patient brings the urine container to the outpatient clinic. In case the patient is hospitalised, also the blood sample is taken the day after the urine collection. Placental biopsies, placental bed biopsies (in case of caeserean section) and umbilical cord blood are all taken just after delivery.

Study burden and risks

Blood samples will not possess any risk. Urine samples will possess no risk either. Placenta: no risk, Placenta bed biopsies and placental biopsies: no risk. Umbilical cord blood samples are taken from the umbilical artery after birth of the placenta, which will otherwise be discarded: no risk for the patient.

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

Fetal growth restriction
hypertension

Exclusion criteria

o Congenital anomalies
o being unable to understand the study information either caused by language differences or low
IQ
o Ruptured membranes
o Diabetes Mellitus (defined as use of insulin)
o Auto-immune disease
o Renal disease
o Seropositive for HIV
o HELLP
o Multiple pregnancy

Study design

Design

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

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-02-2017
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	14-02-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO

Date:	16-05-2018
Application type:	Amendment
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	NL58790.042.16
Other	NTR code volgt

Study results

Date completed:	02-03-2019
Actual enrolment:	51