Regulation of vascular function in women with pregnancy disorders

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The primary objective of this study is to investigate how the vascular regulation is altered in the maternal as well as placental vasculature of women with pregnancy disorders (preeclampsia, pregnancy-induced hypertension, FGR, preterm birth,...

Ethical review	Approved WMO
Status	Pending
Health condition type	Pregnancy, labour, delivery and postpartum conditions
Study type	Observational invasive

Summary

ID

NL-OMON53670

Source
ToetsingOnline

Brief title
Vascular function in pregnancy disorders

Condition

- Pregnancy, labour, delivery and postpartum conditions
- Vascular hypertensive disorders

Synonym
pregnancy disease, Pregnancy 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

Intervention

Keyword: Blood vessel, Pregnancy, Therapy, Vascular reactivity

Outcome measures

Primary outcome

The vascular reactivity of arteries from omental tissue, subcutaneous fat and placental tissue will be studied using 1) wire myography to assess vascular contractions and relaxations to agonists, as well as the effects of antagonists on these contractions and relaxations, 2) pressure myography to assess vascular distensibility and flow-mediated vasodilation, 3) biomarker concentrations in maternal and umbilical cord blood, 4) molecular response of placental and vascular cell types.

Secondary outcome

- To determine if and how alterations in maternal vascular reactivity correlate with alterations in foetoplacental vascular reactivity.
- To examine whether (novel) therapeutics can restore this altered response.
- To determine if and how alterations in maternal and placental vascular reactivity correlate with biomarker concentrations in maternal blood an umbilical cord blood.
- To detect placental alterations at the tissue level and at the molecular level for different cell types contributing to the maternal-placental interface.

Study description

Background summary

Normal pregnancy necessitates a large increase in blood flow to the fetoplacental unit, which is achieved through tremendous adaptations of the maternal cardiovascular system. Abnormal maternal vascular adaptations and subsequent reduced placental perfusion in early gestation play a significant role in the development of maternal vascular complications of pregnancy, and can indirectly lead to chronic disease in later life.
Vascular changes have been observed in pregnant women with preeclampsia, fetal growth restriction (FGR), preterm birth, and diabetes mellitus. Placental and vascular function are thus crucial determinants for pregnancy outcome, fetal health and neonatal outcome. As the placenta is composed of a maternal and a fetal circulation, sufficient placental function is determined by adequate function of both vasculatures. However, many pregnancy disorders remain incurable to date as the exact mechanisms that contribute to the vascular changes in pregnancy disorders remain poorly understood.

The identification of such alterations and the underlying mechanisms is necessary to provide novel therapeutic insights for these pregnancy disorders. We therefore aim to examine how maternal and fetoplacental vascular reactivity are altered pregnant women that suffer from vascular dysfunction. By collecting small pieces of omental tissue and subcutaneous fat tissue, as well as the placenta from the same women that will undergo an elective (or emergency) caesarean section, we will be able to study vascular function in all these tissues. These experiments will provide a unique opportunity to study (patho)physiological processes with human tissues that have high translational value to the clinic and reduce the need for animal research, without exposing the women to significant risks.

The importance of this study is that it may identify new medications that could be used to treat pregnancy complications, and thereby improve the outcomes of pregnant women and their fetuses.

Study objective

The primary objective of this study is to investigate how the vascular regulation is altered in the maternal as well as placental vasculature of women with pregnancy disorders (preeclampsia, pregnancy-induced hypertension, FGR, preterm birth, obesity, dysbiotic microbiome, and diabetes). If alterations are identified, the secondary objectives are to examine whether novel therapeutics can restore this altered response and to determine how these alterations correlate with biomarker levels in maternal and umbilical cord blood, and placental alterations at molecular and cell level.

Study design

Cross-sectional ex vivo research, conducted at the Erasmus MC University Medical Center Rotterdam. As no intervention is involved, this study can be considered as an observational study with a minimally invasive one-off procedure for each patient.

Study burden and risks

We expect no (or minimal) risks associated with participation. For the placental and biomarker studies we will only use waste material (placenta, maternal blood and umbilical cord blood), so there is no additional risk in collecting it. For the maternal vascular studies, the removal of the pieces of subcutaneous fat tissue and omental tissue (of approximately 1.5 x 1.5 cm each) after incision will not be noticed by the subject, not in a negative sense nor in a positive sense. The only minor risk associated with the removal of a piece of omental tissue is bleeding in case the tissue is not tied off completely. Collection of the tissues will not complicate the care or recovery of the patients, and will not interfere with the delivery of the baby. Nor will it cause problems for further pregnancies.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

In order to be eligible to participate in this study, a control subject must meet all of the following criteria:
- Pregnant persons >= 18 years old
- Sufficient command of the Dutch or English language
- Willing to donate a small sample of subcutaneous fat tissue and omental tissue
- Willing to provide written informed consent
- Undergoing elective caesarean section
- Blood pressures in a relatively normal range, which is 90-140 (systolic)/60-90 (diastolic).

In order to be eligible to participate in this study, a study subject must meet all of the following criteria:
- Women >= 18 years old
- Sufficient command of the Dutch or English language
- Willing to donate a small sample of subcutaneous fat tissue and omental tissue
- Willing to provide written informed consent
- Undergoing elective or emergency caesarean section
- Clinically diagnosed with either one of the following conditions: preeclampsia, FGR, preterm birth, obesity, dysbiotic microbiome, and diabetes

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Admission to an Intensive Care Unit (ICU) for any reason
- Admission during an obstetric emergency (Control group only)
- A viral infection (SARS-CoV-2 only during the third trimester)
- Severe fetal congenital anomalies
- Placenta praevia, placenta accreta/increta.

Study design

Design

Study type:	Observational 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):	01-06-2023
Enrollment:	290
Type:	Anticipated

Ethics review

Approved WMO

Date:	07-08-2023
Application type:	First submission
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	NL82454.078.22