On the Role of The (Pro)Renin-Angiotensin System in Preeclampsia

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Maternal complications of pregnancy
Study type	Observational invasive

Summary

ID

NL-OMON32502

Source
ToetsingOnline

Brief title
RAS in preeclampsia

Condition

- Maternal complications of pregnancy

Synonym
preeclampsia, toxicosis of pregnancy

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: (pro)renine-receptor, preeclampsia, prorenin, renin

Outcome measures

Primary outcome

To assess whether concentrations of renin and prorenin in the circulation and amniotic fluid change during preeclampsia and whether circulating and amniotic fluid concentrations are inversely related.

To assess whether concentrations of renin and prorenin are infuenced by diabetes mellitus.

To assess the gene expression of components of the RAS, including the (pro)renin-receptor in the maternal and foetal part of the placenta and the influence of preeclampsia and diabetes mellitus.

To assess the functional role of (pro)renin-receptors in the endometrium.

To assess the influence of pregnancy and preeclampsia on the role of the angiotensin II, subtype 2 receptor.

Secondary outcome

Not applicable

Study description

Background summary

Preeclampsia is a disorder of gestation characterized by hypertension and proteinuria and an important cause of maternal and neonatal morbidity and mortality. The cause of preeclampsia is unknown but several lines of evidence indicate involvement of the renin-angiotensin system (RAS). In preeclampsia the vasoconstrictor sensitivity of resistance arteries to angiotensin II is increased. In amniotic fluid high concentrations of prorenin, the precursor of

renin, have been reported. Mating of transgenic female mice or rats with overexpression of human angiotensinogen with transgenic male mice or rats with overexpression of renin leads to preeclampsia-like syndrome in pregnant animals. In women with preeclampsia antibodies that are agonistic for the angiotensin II, subtype 1 receptor have been reported. Finally in subjects with diabetes mellitus the concentration of prorenine is increased and this increased concentration is a predictor of and associated with microvascular disease.
One hypothesis is that in preeclampsia the local placental RAS is activated, and that this local activated system influences the maternal circulating RAS. This could explain why the circulating RAS is less active in preeclampsia than it is in normal pregnancy.

Study objective

The primary objective of our study is get more insight in the role of the RAS in preeclampsia. For this purpose concentrations of RAS components in the maternal circulation and amniotic fluid and the expression of RAS genes in the maternal and foetal part of the placenta are measured. In resistance vessels, isolated from subcutaneous fat biopsies, the change in function of the angiotensin II, type receptor during normotensive pregnancy and preeclampsia is evaluated and in a human endometrial cell-line the function of the recently discovered (pro)renin-receptor is evaluated.

Study design

For this study blood, amniotic fluid, placental tissue and abdominal subcutaneous fat tissue for isolation of resistance arteries is sampled from healthy and preeclamptic women who are subjected to a caesarian section. The above mentioned material is also sampled from pregnant women with diabetes mellitus with or without preeclampsia who are subjected to a caesarian section. In non-pregnant women < 50 years who undergo and abdominal gynaecological operation blood and subcutaneous fat tissue is sampled as well.
Different methods, ranging from functional vessel research, gene expression and biochemical measurements will be appied to address the objectives.

Study burden and risks

The burden to participate in this study is minimal. Participation will extend the surgical procedure by maximal 5 minutes. Participation in this study is not associated with risks.

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

pregnant women who undergo a caesarian section.
women with and without preeclampsia and with or withour preexistent or gestational diabetes mellitus are included.
Non-pregnant women who undergo abdominal gynaecological surgery

Exclusion criteria

Not willing to give informed consent
Use of antihypertensive medication

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:	Recruiting
Start date (anticipated):	15-03-2010
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO Date:	26-11-2009
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	NL29595.078.09