Response to angiotensin II in formerly preeclamptic women. RETAP study.

Published: 08-02-2011
Last updated: 19-03-2025

Primary Objective: Primary endpoints will be renal (ERPF, GFR and FF) response to angiotensin II after low and high sodium diet in formerly preeclamptic patients compared to healthy controls. Secondary Objectives: Secondary endpoint will be systemic…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON36569

Source
ToetsingOnline

Brief title
RETAP-study

Condition

- Other condition
- Renal disorders (excl nephropathies)

Synonym
kidney disease, preeclampsia

Health condition

preeclampsie, zwangerschap

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: Angiotensin II, Preeclampsia, Renal function, Sodium diet

Outcome measures

Primary outcome

The main study endpoint of this study is the renal response (GFR, ERPF and FF)

to angiotensin II in formerly preeclamptic women compared to healthy controls.

Secondary outcome

To evaluate the difference in systemic response (blood pressure) to angiotensin

II

To evaluate the difference in response to sodium intake in relation to blood

pressure and renal function

To evaluate absolute renal function determined as GFR, ERPF and FF.

To evaluate the difference in response to sodium intake on plasma values of

markers of renin-angiotensin system activity, including angiotensin II,

aldosteron, angiotensin converting enzyme activity and plasma renin activity.

To evaluate the gender differences in renal and blood pressure response to

different sodium intakes and angiotensin II infusion.

Study description

Background summary

Preeclampsia (PE) is characterized by hypertension and proteinuria in the

second half of pregnancy and complicates about 5% of pregnancies. In the Netherlands (pre)eclampsia represents the number one cause of maternal mortality. Moreover, recent data show that pregnancy complicated by PE is also a risk factor for long-term cardiovascular, cerebrovascular and renal disease. The pathogenesis of PE is unknown but it is likely to be multifactorial. Its pathophysiology involves activation of the inflammatory response including endothelial cell activation and dysfunction, immune mechanisms and altered activity of the renin angiotensin aldosterone system (RAAS). During PE there is an increased sensitivity for angiotensin II. This maladaptation of the renin angiotensin aldosteron system is one of the main factors altered during PE. This increased sensitivity for angiotensin II might be involved in the increased cardiovascular and renal risk after PE.

Study objective

Primary Objective:
Primary endpoints will be renal (ERPF, GFR and FF) response to angiotensin II after low and high sodium diet in formerly preeclamptic patients compared to healthy controls.

Secondary Objectives:
Secondary endpoint will be systemic respons (blood pressure) to angiotensin II after low and hogh sodium diet in formerly preeclamptic patients compared to healthy controls.
Secondary endpoints will be renal function after preeclampsia, expressed as glomerular filtration rate (GFR), effective renal plasma flow (ERPF), filtration fraction (FF) and extracellular volume (ECV) and changes in RAAS-parameters (plasma renine activity, aldosteron, angiotensins, ACE-activity) in relation to sodiumintake, in formely preeclamptic patients compared to healthy controls.

Gender specific differences in renal hemodynamics and bloodpressure in response to dietary sodium intake and angiotensin II infusion will be analysed using our previous studies. The exact same protocol is performed in healthy young male subjects. This will allow us to perform analysis on gender differences.

Study design

The study design of this study is a patient-control, cross over study, with a study day after a week of low sodium intake and a week of high sodium intake, with four weeks in between. There will be one visit for inclusion before the first dietary period with the investigator, including a physical examination and explanation of the dietary sodium diets. During their mid follicular phase women will use a low sodium diet during one week (50 mmol sodium/day, 1.2 gram) followed by a week of high sodium diet (200 mmol sodium/day, 4.8 gram), with four weeks in between. On day 3 and day 6 of each dietary period subjects will

collect 24-hour urine to assess dietary compliance and achievement of stable sodium balance. At the end of each week a day of renal function measurements will follow. Baseline blood pressure and renal function will be measured. GFR, ERPF, FF and ECV will be measured by constant infusion of radioactive-labelled tracers: 125-I-iothalamate and 131-I-hippurate. Blood samples will be drawn for the measurement of RAAS parameters (plasma renine activity, angiotensins, ACE-activity). In the afternoon angiotensine II will be infused at a rate of 0.3, 1 and 3 ng/kg/hour all during one hour. Both blood pressure and renal hemodynamics will be measured during angiotensin II infusion.

Intervention

During one week women will use a low sodium diet (50 mmol sodium/day, 1.2 gram). This will be followed by a week of high sodium diet (200 mmol sodium/day, 4.8 gram) (with four weeks in between). On day 3 and day 6 of each dietary period subjects will collect 24-hour urine to assess dietary compliance and achievement of stable sodium balance.

At the end of both the low and the high sodium diet week, a day of renal function measurements will follow. Baseline blood pressure and renal function will be measured. GFR, ERPF, FF and ECV will be measured by constant infusion of radioactive-labelled tracers: 125-I-iothalamate and 131-I-hippurate. In the afternoon ang II will be infused at a rate of 0.3, 1 and 3 ng/kg/min all during one hour. Both blood pressure and renal hemodynamics will be measured during ang II infusion

Study burden and risks

The subject has to come three times to the clinic, one short visit for intake and two eight hours visits for renal function measurements and angiotensin II infusion. In total, during the entire study, a maximum of 250 ml of blood samples will be drawn. The subjects will follow one week of low sodium diet and one week of high sodium diet, with in total four times 24-hour urine collection. This study can only be conducted in healthy women and women with a history of preeclampsia to answer the research questions. During the study days radioactive tracers (in total 0,2 mSv) and angiotensin II will be infused. All substances are safe; and our research group has extensive experience with similar experiments in healthy subjects and patients with diabetes mellitus using similar study designs.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
9700 RB
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
9700 RB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Healthy females with history of normotensive pregnancy, with a range of one to five years after their pregnancy.
- Females with a history of severe preeclampsia, with a range of one to five years after their pregnancy

Exclusion criteria

Diabetes mellitus
Diabetes gravidarum
BMI >= 30
Oral contraceptive pill use which can*t be temporally stopped
Participants with renal diseases
Participants with cardiovascular diseases
Treatment with anti-hypertensive drug
Blood pressure: systolic > 150, diastolic > 100 mmHg
Pregnant or lactating women
Any surgical or medical condition that in the opinion of the investigator would jeopardize the

evaluation of efficacy or safety

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-03-2011
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO

Date:	08-02-2011
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

ID: 26813
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL34387.042.11
OMON	NL-OMON26813