A randomized, placebo-controlled, double blind, 4-period, cross-over trial, to study blood pressure lowering effects of losartan, Moxonidine and Low sodium diet in former pre-eclamptic women

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

Summary

ID

NL-OMON44513

Source
ToetsingOnline

Brief title
PALM study

Condition

- Other condition
- Pregnancy, labour, delivery and postpartum conditions

Synonym
Preeclampsia, toxemia of pregnancy

Health condition

Hart- en vaatziekten

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: ZonMw,Nierstichting

Intervention

Keyword: hypertension, preeclampsia, RAAS, sympatic nerve system

Outcome measures

Primary outcome

To compare mean 24-hour, day- and night time SBP and DBP in patients with a history of PE after 8 weeks of treatment with placebo, losartan, moxonidine and low sodium diet.

Secondary outcome

To compare changes in the following parameters in women with a history of PE after 8 weeks of treatment with placebo, losartan, moxonidine and low sodium diet: RAAS-activity, SNS-activity, endothelial function, arterial stiffness, lipid metabolism, insulin sensitivity, oxidative stress and systemic inflammation.

Study description

Background summary

There is considerable concern about the link between preeclampsia (PE) and the subsequent risk for developing cardiovascular disease and renal disease later in life. The risk for end stage renal disease after PE 8-15 fold increased. A growing body of evidence suggest that shared metabolic, immunological and vascular pathways are responsible for PE as well as future cardiovascular risk of women. Possibly PE itself contributes to the risk as well. Mechanistic

studies have shown that marked changes in the renin-angiotensin aldosterone system (RAAS), sympathetic nerve system (SNS) and sodium sensitivity of blood pressure are present in women with a history of PE. All these pathways are known to contribute to development of cardiovascular and renal disease.

Study objective

We hypothesize that formerly pre-eclamptic women have persistently increased angiotensin II sensitivity, sodium sensitivity, insulin resistance and sympathetic nerve activity together initially leading to susceptibility for early renal disease and subsequently hypertension, chronic kidney disease and cardiovascular disease. Possibly early intervention in these systems can lower blood pressure effectively a give specific tools for primary prevention strategies.

Study design

A randomized, placebo-controlled, double blind, 4-period, cross-over trial.

Intervention

Once daily doses of losartan (100 mg), moxonidine (0,4 mg), low sodium diet (50 mmol NaCl/24 hour) and placebo following standardised 8-week treatment schedules. Participants receive all four interventions in a randomized and blinded (except from low sodium diet).

Study burden and risks

All study medication is registered for the treatment of hypertension and effects on blood pressure are minimal (5-10 mmHg lowering). Participants are asked to come a total of 6 study visits to the UMC Utrecht. Prior to 4 of these visits, patients need to have fasted for 13 hours. Most measurements are non invasive, but also some venous blood samples (45 mL during each of the visits 3-6) will be drawn.

Participants do not directly benefit from study participation. The scientific value, however, is considerable. After the study is ended (last participant, last measurement), participants can choose to receive an overview of some of their metabolic parameters, in order to optimize their future cardiovascular disease risk management.

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

1. Patient is a female between 18 and 45 years of age on the day of signing informed consent.
2. Have a recent history of preeclampsia that is defined as gestational hypertension and concomitant proteinuria in the second half of pregnancy. Gestational hypertension was defined according to the criteria of the International Society for the Study of Hypertension in Pregnancy (ISSHP) as diastolic blood pressure above 90 mmHg and/or systolic blood pressure above 140 mmHg, measured on two or more separate occasions at least 4 hours apart. Proteinuria was diagnosed with urinary protein was above 300 mg per 24 hour or above 2+ at dipstick urinalysis 17
3. All patients should fulfil the following diagnostic criterion:
- Off treatment SBP > 120 mmHg and/or DBP > 80 mmHg during both visits.
4. Blood pressure is assessed by office readings in accordance with current guidelines for hypertension diagnosis18. The patient needs to be seated some minutes before and during the measurement. The cuff size should be adjusted to the patients* arm circumference and needs to be on the same height level as the patients* sternum during the measurements. Blood pressure is determined to a 2-mmHg accuracy-level. Blood pressure is measured on

both arms during the first visit. If both measurements differ more than 10 mmHg, the highest value is taken. After at least 15 seconds, the measurement is repeated during the same visit. The highest mean of the two measurements on the same arm is considered as the actual blood pressure value.
5. Patient understands the study procedures, alternative treatments available, and risks involved with the study and voluntarily agrees to participate by giving written informed consent.

Exclusion criteria

1. SBP >180 mmHg and/or DBP >110 mmHg during one or more screening measurements.
2. Current pregnancy
3. Use of *recreational* or illicit drugs
4. Recent history (within the last year) of alcohol abuse or dependence.
5. Several medical conditions as depicted in the protocol

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-12-2015
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Losartan
Generic name:	Losartankalium Mylan
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Moxonidine
Generic name:	Moxonidine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	18-12-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-04-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-08-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-12-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-01-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	13-06-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO	

Date:	01-03-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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: 28431
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2014-002524-27-NL
CCMO	NL49102.041.14
OMON	NL-OMON28431