Potential effect of proton-pump inhibitor on angiogenic markers in preeclampsia

Published: 03-05-2018
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To evaluate the potential effect of PPI administration in women with confirmed preeclampsia on sFlt-1 levels until delivery.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Pregnancy, labour, delivery and postpartum conditions
Study type	Interventional

Summary

ID

NL-OMON50177

Source
ToetsingOnline

Brief title
The PPI Study

Condition

- Pregnancy, labour, delivery and postpartum conditions

Synonym
Toxemia 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: Pre-eclampsia, Proton pump inhibitor, sFlt-1

Outcome measures

Primary outcome

The difference in sFlt-1 levels in women who have received PPI, in comparison to women who have not received PPI.

Secondary outcome

The difference in PlGF levels as well as sEndoglin and ET-1 levels in women who have received PPI, in comparison to women who have not received PPI.

The difference in cord blood PlGF levels as well as sEndoglin and ET-1 levels, in women who have received PPI in comparison to women who have not received PPI.

Blood pressure regulation and the need for blood pressure medication between PPI group and non-PPI group.

Days until delivery between PPI group and non-PPI group.

Difference in preeclampsia-related complications between PPI group and non-PPI group as defined by maternal complications and/or fetal/neonatal complications (as described in the research protocol)

Study description

Background summary

Preeclampsia (PE) is a devastating complication of pregnancy. The pathogenesis of PE is unknown. Recent data suggest an angiogenic imbalance characterized by elevated placenta-derived soluble Fms-like tyrosine kinase-1 (sFlt-1) and decreased placental growth factor (PlGF) levels in the maternal circulation. As a consequence, novel therapies now focus on sFlt-1 removal or PlGF supplementation. Given the fact that heme-oxygenase-1 negatively regulates sFlt-1 secretion, a role for proton pump inhibitors (PPIs) that upregulate heme oxygenase-1, has been suggested as potential treatment for preeclampsia. Indeed, Onda et al. observed that PPIs decreased sFlt-1 secretion from trophoblasts and reduced blood pressure in a transgenic PE mouse model with placental sFlt-1 overexpression. Recently, we reported that women with suspected/confirmed PE using PPIs, displayed about 60% lower levels of sFlt-1 in comparison to women not using PPIs.

Study objective

To evaluate the potential effect of PPI administration in women with confirmed preeclampsia on sFlt-1 levels until delivery.

Study design

A multi-centre, randomized, intervention proof-of-concept study. The study will be performed at the Erasmus MC-Sophia in Rotterdam.

Intervention

The PPI group will receive omeprazole, 40mg, once daily. The non-PPI group will receive no medication. In both groups, blood will be drawn at several time points, until delivery.

Study burden and risks

This study evaluates the effect of PPI use in patients with preeclampsia on sFlt-1 levels. A potential benefit of participation in this study is that lowering of sFlt-1, mitigates the severity of PE, leading to a prolongation of days until delivery. A potential burden of participation in this study is that in both groups, blood is drawn repeatedly. Furthermore, in the PPI group, patients need to take (additional) daily medication.

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

Women (>=18 years) with a singleton pregnancy diagnosed with PE with a gestational age between >= 20 weeks and <35 weeks admitted to the obstetric department who give written informed consent, will be included.

Exclusion criteria

- Multiple pregnancies , - Not willing to give written informed consent., - Other reasons than (suspected) PE requiring hospitalization, - The use of PPI at time of randomization, - Contraindications or hypersensitivity to PPI use, - The use of medication affected by PPI , - Fetal death at time of inclusion, - Signs of fetal distress at time of inclusion, - Expected delivery of <= 2 days

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	19-12-2018
Enrollment:	44
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Prilosec, Losec
Generic name:	Omeprazol
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	03-05-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-09-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-12-2018

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-12-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-01-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-03-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-11-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-12-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-02-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-04-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	15-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-07-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-09-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-09-2020
Application type:	Amendment
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
EudraCT	EUCTR2018-000283-28-NL
CCMO	NL64821.078.18