Prediction of short-term outcome in pregnant women with suspected preeclampsia study

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Primary objectives:• To demonstrate that low ratios of sFlt-1/PlGF predict absence of PE / eclampsia / HELLP (according to diagnostic criteria) within one week after start visit (= Visit 1).• To demonstrate that high ratios of sFlt-1/PlGF predict PE...

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

Summary

ID

NL-OMON38312

Source
ToetsingOnline

Brief title
PROGNOSIS

Condition

- Pregnancy, labour, delivery and postpartum conditions

Synonym
preeclampsia

Research involving
Human

Sponsors and support

Primary sponsor: Roche Diagnostics GmbH
Source(s) of monetary or material Support: Roche Diagnostics

Intervention

Keyword: PlGF (Placental Growth Factor), Prediction, Preeclampsia, sFlt-1 (Soluble Fms-like tyrosine kinase 1)

Outcome measures

Primary outcome

Value of the sFlt-1/PlGF ratio at Visit 1 to predict PE / eclampsia / HELLP

(according to diagnostic criteria) within one and four weeks from Visit 1.

Secondary outcome

NA

Study description

Background summary

Hypertensive disorders are the most common medical problem encountered in pregnancy, affecting up to 15% of pregnancies and accounting for approximately 25% of antenatal admissions. Notably preeclampsia (PE) is a major cause of maternal and fetal or neonatal mortality and morbidity. To date no treatment is available to prevent PE or hinder at least progression of the disease. The only causal therapy of PE is delivery. The etiology of this disease has not yet been completely understood. Nevertheless, changes in circulating placental angiogenic factors appear to play a key role in the pathogenesis of PE. Two such angiogenic factors are sFlt-1 (Soluble Fms-like tyrosine kinase 1) and PlGF (Placental Growth Factor). In patients with PE levels of sFlt-1 are increased, wherease levels of PlGF are decreased. This results in a net anti-angiogenic state causing endothelial dysfunction. Of note, sFlt-1 concentrations are high 5-6 weeks prior to onset of PE. Concentrations of PlGF are also found to be low several weeks prior to clinical manifestation. Increased levels of sFlt-1 and reduced levels of PlGF herald the onset of PE, whereas the ratio of sFlt-1/PlGF, an index reflecting changes in both biomarkers, is a better predictor of PE than either measure alone.

Study objective

Primary objectives:
• To demonstrate that low ratios of sFlt-1/PlGF predict absence of PE / eclampsia / HELLP (according to diagnostic criteria) within one week after

start visit (= Visit 1).
• To demonstrate that high ratios of sFlt-1/PlGF predict PE / eclampsia / HELLP (according to diagnostic criteria) within four weeks after start visit (= Visit 1).

Secondary objectives:
• To collect evidence that low ratios of sFlt-1/PlGF correlate with absence of PE-related adverse outcomes (other than PE / eclampsia / HELLP being part of the primary objective) of the mother within one week after the start visit (= Visit 1) as follows: maternal death, pulmonary edema, acute renal failure, cerebral hemorrhage, cerebral thrombosis, DIC.
• To collect evidence that low ratios of sFlt-1/PlGF correlate with absence of PE-related adverse outcomes of the fetus within one week after the start visit (= Visit 1) as follows: perinatal/fetal death, delivery <34 weeks, IUGR, placental abruption, respiratory distress, necrotizing enterocolitis, intraventricular hemorrhage.
• To collect evidence that high ratios of sFlt-1/PlGF correlate with the mother*s PE-related adverse outcomes (other than PE / eclampsia / HELLP being part of the primary objective) within four weeks after start visit (= Visit 1) as follows: maternal death, pulmonary edema, acute renal failure, cerebral hemorrhage, cerebral thrombosis, DIC.
• To collect evidence that high ratios of sFlt-1/PlGF correlate with the fetus* PE-related adverse outcomes within four weeks after start visit (= Visit 1) as follows: perinatal/fetal death, delivery <34 weeks, IUGR, placental abruption, respiratory distress, necrotizing enterocolitis, intraventricular hemorrhage.
• To evaluate sFlt-1 and PlGF values and the sFlt-1/PlGF ratio in diagnosed cases of PE / eclampsia / HELLP in comparison to the corresponding parameters in gestational age-matched controls.
• To collect evidence that an increase of the sFlt-1/PlGF ratio within one week (Visit 1 to Visit 2; Visit 2 to Visit 3; Visit 3 to Visit 4; Visit 4 to Visit 5; including unscheduled visits) correlates with diagnosis of PE / eclampsia / HELLP within four weeks after start visit.
• To correlate severity of PE with incremental changes of sFlt-1 and PlGF values and sFlt-1/PlGF ratio, respectively, per time interval between visits (sFlt-1/PlGF time course) within four weeks after start visit (= Visit 1).
• To correlate severity of PE with absolute values of sFlt-1, PlGF and sFlt-1/PlGF ratio at diagnosis of PE.
• To collect evidence that high ratios of sFlt-1/PlGF correlate with preterm delivery.
• To collect evidence that ratios of sFlt-1/PlGF correlate with time to delivery.
• To investigate the economical benefit of considering the sFlt-1/PlGF ratio for decision on the length of hospitalization of women with clinical suspicion of PE and of the newborn.

Study design

PROGNOSIS is a Diagnostic Utility Study which is a multicenter, prospective, double-blind, non-interventional study evaluating the short-term prediction of preeclampsia / eclampsia / HELLP in pregnant women with suspected preeclampsia.

Study burden and risks

Risks Analysis:
Participation in the study is not afflicted with any risks, apart from the general risks that arise when a blood sample is taken. Blood sampling will be only performed with CE labeled sample collection devices. In rare cases complications like extended bleeding, damage to nerves/arteries or infections can happen. Urine-sample collection may give the patient a slight feeling of discomfort.
The study is a non-interventional trial, medical care for the pregnant women will be performed on the usual high medical standard at the study centre and won*t be influenced by their study participation. Since the study design is double-blind (neither the medical practitioner nor the study patient won*t learn the results of the preeclampsia assay measurements) no medical decision will be taken based on the diagnostics result of the preeclampsia assays. The entire medical supervision and medical decisions remain in the responsibility of the medical practitioner at the study site.

Benefits:
Even though there is no immediate clinical benefit for the study participants from the scientific investigation, the scientific results gained from this project will expand medical knowledge and will possibly contribute to improve and to facilitate judgment about diagnosis and short-term prediction of preeclampsia in the future.

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 >=18 years
• Gestational week 24+0 days - 36+6 days
• Signed written informed consent
• Suspicion of clinical diagnosis of PE based on one or more of the following criteria:
- New onset of elevated blood pressure (BP)
- Aggravation of preexisting hypertension
- New onset of protein in urine
- Aggravation of preexisting proteinuria
- One or more other reason(s) for clinical suspicion of PE:
• PE-related symptoms: epigastric pain, excessive edema, severe swelling (face, hands, feet), headache, visual disturbances, sudden weight gain (>1 kg/week)
• PE-related findings: low platelets, elevated liver transaminases, IUGR (Intra-uterine growth restriction) or abnormal uterine perfusion detected by Doppler sonography with mean PI > 95th percentile in second trimester and/or bilateral notch
Note: percentage of women with suspected PE due to abnormal uterine perfusion at each site shall not exceed 25%.

Exclusion criteria

• Proteinuria >=2+ (dipstick) (or in case available >=0.3 g protein/24 hours or >=30 mg/dL protein in spot urine or spot urine protein/creatinine ratio >=30 mg protein/mmol creatinine) AND elevated BP (>=140 mmHg systolic and/or >=90 mmHg diastolic, reproducible on two occasions)
• Proteinuria >=2+ (dipstick) (or in case available >=0.3 g protein/24 hours or >=30 mg/dL protein in spot urine or spot urine protein/creatinine ratio >=30 mg protein/mmol creatinine) AND current anti hypertensive treatment
• Confirmed diagnosis of HELLP syndrome

• Concomitant participation in another clinical study (with exception of existing Biobanks as site pecifically agreed upon with RD)
• Investigational medicinal product received in the past 3 months (90 days)
• Employee at the investigational site, or relative or spouse of the investigator

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-09-2011
Enrollment:	125
Type:	Actual

Ethics review

Approved WMO Date:	23-05-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-06-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

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	NL34759.068.10