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Statins to Ameliorate early onset Pre-eclampsia

Submission date
17/11/2008

Recruitment status
No longer recruiting

Registration date
08/05/2009

Overall study status
Completed

Last Edited
20/05/2019

Condition category
Pregnancy and Childbirth

[X] Prospectively registered

[_] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Pre-eclampsia is a serious condition of pregnancy, where the mother develops high blood pressure and high levels of protein in the urine (proteinuria). There are no effective drug treatments for pregnant women to reverse pre-eclampsia. Drugs can be given to help reduce blood pressure and prevent seizures. Doctors monitor the mothers blood pressure, blood tests and the babys wellbeing and then recommend birth of the baby if the mother or her babys health is threatened. However, if pre-eclampsia develops between 24-32 weeks and the baby is born prematurely, he or she will almost always need special care on a neonatal unit. Recent scientific research has identified that changes in some specific blood chemicals (biomarkers) can lead to pre-eclampsia. Initial studies on samples of placenta and blood vessels, as well as animal experiments, suggest that statins can reduce the level of these blood chemicals, and perhaps reduce or eliminate the effects and risks of pre-eclampsia. This study is the first step in determining if these same beneficial effects are seen in pregnant women.

Who can participate?
Pregnant women with severe pre-eclampsia.

What does the study involve?
Participants do not have to do anything extra if they take part in the study. The pre-eclampsia is managed carefully in the usual way by the same doctors who would normally look after the pregnancy. The only difference is the taking of an extra capsule each day until delivery, either pravastatin or an identical looking placebo (sugar) capsule. This is in addition to any other drugs that the doctors think is appropriate for the pre-eclampsia. Neither the woman nor her doctor can choose which treatment is given. The decision is made randomly by computer at the trial office. This is essential so that a fair comparison can be made between the two treatment groups. Clinical information about the mother and her baby's health is collected from their medical notes every day, including blood pressure, protein in the urine and side effects. Routine monitoring also involves taking regular blood and urine samples, which are also used to measure specific blood chemicals (biomarkers) thought to be important in pre-eclampsia. Permission is also sought to take a sample of blood from the umbilical cord and samples of the placenta following delivery. This is only done if the umbilical cord blood or placenta would otherwise be discarded. The blood samples are used to measure the level of treatment drug. The placenta samples are used to measure specific blood chemicals thought to be important in pre-eclampsia and also to measure the level of treatment drug that passes into the baby's bloodstream. Once

the participant has left hospital, she is asked to come back once or twice, until her baby is 6 weeks old, for check-ups, with further blood samples from the mother.

What are the possible benefits and risks of participating?
All drugs have side-effects, but we do not anticipate any side effects of the study drugs in the relatively short time that they are taken. Statins are taken by millions of non-pregnant people worldwide and side effects are rare. Participants are encouraged to tell their doctor if they feel ill in any way at all, so that the doctor can check to see whether the pre-eclampsia is worsening or if it is a side effect of the drug. Participants may not gain any individual benefit, as only half of the women taking part will receive pravastatin whilst the other half will receive a dummy (placebo) drug. It is hoped that pravastatin will help improve the symptoms and problems associated with pre-eclampsia, so some participants may feel better and their baby may not need to be born early. However, it is not known in advance whether this is the case - that is the reason for doing this study. The main benefit from this study will be that the information gained will help improve the treatment of women with pre-eclampsia in the future.

Where is the study run from?
Birmingham Clinical Trials Unit, University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
June 2011 to July 2014

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)

2009-012968-13

Protocol serial number
MRC ref: G0701824, MRCIES10215; Sponsor ref: UCLH08/0350

Study information

Scientific Title
A proof of principle, double-blind, randomised placebo-controlled, multicentre trial of pravastatin to ameliorate early onset pre-eclampsia

Acronym
StAmP

Study objectives
The aim of the trial is to establish whether a significant reduction of angiogenic markers by statins will alleviate the severity of early-onset pre-eclampsia (PE) in women. To test this hypothesis, we will ask the following questions:
1. Do statins, compared to placebo, inhibit anti-angiogenic factors in women with early-onset PE?
2. If this principle is established, how best can a substantive trial/health technology assessment be undertaken to develop guidance for routine use of statins in PE?
3. Are there any adverse effects to the mother or the baby?

Protocol can be found at: http://www.birmingham.ac.uk/Documents/college-mds/trials/bctu/stamp/Stamp-protocol-version-7-0-22-11-2013.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wales Research Ethics Committee, 03/09/2010, ref: 10/MRE09/10

Study design
Double-blind randomised placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Pre-eclampsia

Interventions
On 27/09/2010 the drug of treatment was changed to pravastatin; this was previously simvastatin.

Oral pravastatin, 40 mg, or placebo, once daily until delivery of the baby.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Simvastatin

Primary outcome(s)
Effect of statins on soluble fms-like tyrosine kinase 1 (sFlt-1) at 48 hours post-randomisation

Key secondary outcome(s))
Maternal:
1. Blood pressure and proteinuria at delivery
2. Use of anti-hypertensives during pregnancy and until 1 month post delivery
3. Severe morbidity (Haemolysis, Elevated Liver enzyme levels and a Low Platelet count [HELLP], cerebrovascular accident [CVA]). Duration of follow-up: until 1 month post-delivery.
4. Days in high dependency unit
5. Total hospital stay
6. Mortality (up to 42 days post delivery)
7. Drug adverse effects during pregnancy

Neonatal outcomes:
1. Apgar at 5 min
2. Birth weight
3. Complications of prematurity (retinopathy, necrotizing enterocolitis [NEC], intraventricular haemorrhage [IVH])
4. Days in special care dependency unit
5. Mortality up to 28 days old
6. Drug adverse effects apparent at delivery
7. Congenital anomalies

Completion date
31/07/2014

Eligibility

Key inclusion criteria
Current inclusion criteria as of 27/09/2010:
To be eligible for the StAmP Trial, the women must:
1. Be between 24+0 weeks' and 31+6 weeks' gestation
2. Have a singleton pregnancy
3. Have a diagnosis of early onset pre-eclampsia
4. Be considered capable of safely continuing the pregnancy for 48 hours or more, as determined by the attending clinician
5. Obstetrician and neonatologist believe the fetus is likely to be viable
6. No major anomalies evident on the 20-week anomaly scan. Any anomaly should be assessed by the Principal Investigator and discussed with the Chief Clinical Investigator, following classification of the anomaly according to the ICD-10 codes. All major anomalies will be excluded, but minor anomalies, subject to agreement between the PI and CI will be included

7. Be capable of understanding the information provided, with use of an interpreter if required
8. Give written informed consent

Previous inclusion criteria:
To be eligible for the StAmP Trial, the women must:
1. Be at least 24 weeks and less than 33 weeks' gestation (no age limits on participant)
2. Have a diagnosis of pre-eclampsia
3. Have a normal cardiotocograph
4. Be considered capable of safely continuing the pregnancy for 12 hours or more
5. Be capable of understanding the information provided, with use of interpreter if required
6. Give written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Total final enrolment
62

Key exclusion criteria
Current exclusion criteria as of 27/09/2010:
Any women, who at the point of randomisation, exhibit any of the following are not eligible for the trial:
1. Eclampsia
2. Current use of statins
3. Contraindications to statin use (other than pregnancy) including:
3.1. Hypersensitivity to pravastatin or any of its excipients
3.2. Active liver disease or elevation of serum transaminases not thought to be related to pre-eclampsia
3.3. Pre-pregnant renal insufficiency (creatine clearance less than 30 ml/min)
3.4. Concomitant administration of potent CYP3A4 inhibitors
4. Imminent transfer to a non-trial centre due to unavailability of neonatal cots
5. Participation in any other blinded, placebo-controlled trials of investigational medicinal products in pregnancy
6. Significant uncertainty regarding gestational age. Under 24 weeks' gestation, pregnancies are often not considered viable and therefore women with pre-eclampsia less than 24 weeks gestation will be excluded. Women with pre-eclampsia around 32 weeks' gestation are often delivered when the mother is stable and therefore we will exclude women who develop pre-eclampsia over 32 weeks' gestation. For this reason, if there is any uncertainty about the gestational age, the mother should not be approached for randomisation.

Previous exclusion criteria:
Any women, who at the point of randomisation, exhibits any of the following symptoms or

contraindications, are not eligible for the trial:
1. Eclampsia
2. Absent or reversed end-diastolic flow
3. Pre-pregnant or continuing use of statins
4. Contraindications to statin use (other than pregnancy)

Date of first enrolment
01/06/2011

Date of final enrolment
31/07/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Aston University
Birmingham
United Kingdom
B4 7ET

Sponsor information

Organisation
University College London Hospitals NHS Foundation Trust (UK)

ROR
https://ror.org/042fqyp44

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (UK) (ref: G0701824, MRCIES10215)

Alternative Name(s)

Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			20/05/2019	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes