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Use of a nitric oxide (ISMN) for the PREVENTION and MANAGEMENT of pre-eclampsia (pilot study)

Submission date	Recruitment status	[ ] Prospectively registered
29/11/2006	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
21/12/2007	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
03/03/2009	Pregnancy and Childbirth	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
FMI-63194

Study information

Scientific Title
A pilot study to evaluate glyceryl trinitrate (GTN) as a novel therapeutic for the prevention and treatment of pre-eclampsia

Study objectives
CIHR Grant Submission Title: Pre-eclampsia: Fetal and Maternal Outcomes and Innovative Therapies

To determine if exogenous glyceryl trinitrate (GTN), compared to placebo, will be effective at preventing the development and/or progression of clinical pre-eclampsia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board, Kingston, Ontario (Canada) approved on the 20th September 2002 (ref: ANAT-017-02)

Study design
Randomised, multicentre, blinded, placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

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

Interventions
The study is a randomised blinded drug/placebo trial. The randomisation scheme was prepared by an independent statistician prior to initiation of the pilot study, and prepared in blocks for if and when Ottawa Hospital comes on board. The study investigators, associated staff, outcome assessor, data analyst and the study participants will all be blinded to the treatment allocation.

ISMN and placebo capsules will be prepared to have identical shape, size, color, smell and feel. No form of identification labeling will be visible on either intervention. When a suitable participant is identified, the research nurse coordinator will explain the details and potential risks and benefits of the study. If consent is granted, the research nurse coordinator will determine the treatment assignment for that subject by calling the research pharmacist who will provide the next code indicating the treatment for a given patient. Patients will then be provided with an appropriately labeled package of pills prepared by the hospital pharmacy.

Prevention Arm:
Experimental intervention: Daily dose of low dose Isosorbide-5-mononitrate (ISMN) (30 mg) beginning after 20 weeks gestation till delivery.
Control intervention: Matching placebo containing lactose. Patients randomly assigned to either receive low dose ISMN (30 mg) as stated above or placebo.

Management Arm:
Experimental intervention: Daily dose of low dose Isosorbide-5-mononitrate (ISMN) (30 mg) following diagnosis of pre-eclampsia after 24 weeks gestation till delivery.
Control intervention: Matching placebo containing lactose. Patients randomly assigned to either receive low dose ISMN (30 mg) as stated above or placebo.

In both arms of the study, patients will receive standard clinical care. Total duration of treatment in each arm is flexible and based on each individual participant. There is no follow-up after delivery.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Glyceryl trinitrate

Primary outcome measure
Prevention arm: incidence of pre-eclampsia in the ISMN/placebo groups, measured at delivery
Treatment arm: randomisation-to-delivery interval between ISMN/placebo groups, measured at delivery

Secondary outcome measures
1. Serial change in biochemical markers in treatment/no treatment groups in each of the studies, measured at routine obstetrical visits until delivery (generally every 2 weeks)
2. Incidence of any side effects (major or minor), measured at routine obstetrical visits until delivery (generally every 2 weeks)
3. Neonatal outcomes (composite of neonatal morbidity), measured at delivery

Overall study start date
01/01/2007

Completion date
31/12/2009

Eligibility

Key inclusion criteria
Women of childbearing years (approximately 18 - 42 years).

Prevention arm:
All women with a past obstetrical history of one or more cases of severe early onset pre-eclampsia or later onset severe pre-eclampsia associated with haemolysis, elevated liver enzymes, low blood levels of platelets (HELLP) syndrome.

Treatment arm:
All women that have been diagnosed with pre-eclampsia that are being followed clinically and that provide informed consent. For a diagnosis of pre-eclampsia a patient must meet all three criteria:
1. Systolic blood pressure greater than 140 mmHg or an increase of 30 mmHg from the participants baseline (with that increase present at two measurements taken 6 hours apart)
2. Diastolic blood pressure greater than 90 mmHg or an increase of 15 mmHg from the participants baseline (with that increase present at two measurements taken 6 hours apart)
3. Proteinuria greater than 0.3 g in 24 hour urine or 2+ on dipstick

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
80 women in total: prevention arm (40), treatment arm (40)

Key exclusion criteria
Potential women excluded are those:
1. That have a contraindication to use of isosorbide mononitrate (ISMN)
2. That have either a maternal or foetal indication for delivery
3. That have a diagnosis of severe pre-eclampsia (diastolic blood pressure greater than 100 mmHg; proteinuria greater than 1 g/d), eclampsia, or HELLP syndrome at time of recruitment

Date of first enrolment
01/01/2007

Date of final enrolment
31/12/2009

Locations

Countries of recruitment
Canada

Study participating centre
Clinical Research Centre
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Sponsor information

Organisation
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Sponsor type
University/education

Website
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ROR
https://ror.org/02y72wh86

Funder(s)

Funder type
Research organisation

Funder Name
Canadian Institutes of Health Research (CIHR) (Canada) - http://www.cihr-irsc.gc.ca (ref: FMI-63194)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration