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Pregnancy and chronic hypertension; nifedipine or labetalol as anti-hypertensive treatment

Submission date
08/07/2014

Recruitment status
No longer recruiting

Registration date
10/09/2014

Overall study status
Completed

Last Edited
07/06/2018

Condition category
Circulatory System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Chronic hypertension is high blood pressure that usually needs to be treated with medication. It is important that high blood pressure is diagnosed and treated; without treatment it can cause damage to the heart, brain and kidneys, and complications such as a stroke. Around 3% of pregnant women have been diagnosed with high blood pressure before they become pregnant. A pre-existing high blood pressure puts pregnant women at an increased risk of complications in pregnancy such as pre-eclampsia and the baby not growing properly. The researchers want to find out which one of two different drugs works best at lowering blood pressure in pregnant women without any harmful effects for the mother or the baby. Both drugs are commonly used in pregnancy. Labetalol has a license for pregnancy which means that it has undergone clinical trials that have found it to be safe and effective for its use. Nifedipine is not licensed in pregnancy but can be used off-label (outside its license) if it is felt that the benefits of treatment are likely to outweigh the risks of harm to the mother or baby. These medications have been used by doctors in the UK for many years to treat pregnant women with high blood pressure and the medicines safety watchdog has reviewed this study and given its approval. As the choice of drug for high blood pressure outside of pregnancy depends partly on ethnic background, the study also looks at which treatment works best in pregnant women from different ethnic backgrounds.

Who can participate?
Women aged 18 and over, with chronic hypertension, between 12 and 28 weeks pregnant with one baby, and who need treatment for their blood pressure

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 are given labetalol. Those in group 2 are given nifedipine. Both participants and their doctors know which treatment they are getting to make sure they are taking the right dose. All participants are seen regularly by healthcare professionals and are asked to give extra blood and urine samples on five occasions during their pregnancy, usually at the same time that their routine blood tests are performed. These samples are used to measure substances in the blood and urine at the end of

the study to see if we can find out how each drug works. Participants are also asked for extra measurements of their blood pressure and to have a simple ultrasound (at the base of the neck) to check how the different drugs are working.

What are the possible benefits and risks of participating?
It is known that both treatments lower a woman's blood pressure, which helps avoid complications of high blood pressure in pregnancy. Each participant is seen regularly by the hospital doctors and midwives (as usual) and by the research team. The study will provide information to help improve the treatment of women with high blood pressure in pregnancy in the future. No serious side effects are expected from either drug. Both drugs are taken by many pregnant women worldwide and serious side effects are rare. A woman cannot take labetalol if she suffers from asthma or some heart conditions. Possible side effects do, however, include, feeling faint on standing, headache, rashes, scalp tingling, difficulty in passing urine, tummy pain, nausea, vomiting and liver damage. A woman cannot take nifedipine if she has certain heart conditions. Possible side effects include nausea, vomiting or diarrhoea, swelling of the legs, palpitations, headache and dizziness.

Where is the study run from?
The lead centre for the trial is Guy's and St Thomas Hospital, London. The maternity units in Manchester and Leicester are also taking part.

When is the study starting and how long is it expected to run for?
August 2014 to September 2015

Who is funding the study?
1. Tommy's Charity (UK)
2. Kings Health Partners Challenge Fund (UK)

Who is the main contact?
Dr Lucy Chappell
Lucy.chappell@kcl.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Lucy Chappell

Contact details
Womens Health Academic Centre
St Thomas Hospital
London
United Kingdom
SE1 7EH
+44 (0)20 7188 3639
lucy.chappell@kcl.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2013-003144-23

Protocol serial number
N/A

Study information

Scientific Title
Labetalol or nifedipine for treating chronic hypertension in pregnancy

Acronym
PANDA

Study objectives
Nifedipine is as effective as labetalol at controlling blood pressure in women with chronic hypertension in pregnancy, with greater efficacy in women of African/ Caribbean family origin

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. East of England Cambridge East Research Ethics Committee (REC), 03/02/2014, ref: 13/EE /0390
2. Medicines and Healthcare products Regulatory Agency (MHRA), 31/01/2014, ref: 14523/0251 /001-0002

Study design
Randomised controlled trial (feasibility study)

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic hypertension in pregnancy

Interventions
Women will be randomised to one of two treatments: labetalol or nifedipine, with the dose adjusted for blood pressure control.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)

Labetalol, nifedipine

Primary outcome(s)

As of 24/02/2016:
1. Primary clinical outcome measure: Highest systolic blood pressure (BP) between randomisation and delivery (highest of any recorded systolic BP measurement made between gestation at randomisation and gestation at delivery, excluding recordings made on the day of delivery and in addition average systolic BP during each pregnancy between randomisation and delivery will be calculated (using all available systolic BPs taken clinically using area under the curve by trapezium method)
2. Primary process outcome measure: Number of women enrolled per site per month (calculated at end of trial as total number of women enrolled per site divided by number of months of enrolment at that site)

Previous:
1. Primary clinical outcome measure: Highest systolic blood pressure between randomisation and delivery (highest of any recorded systolic blood pressure measurement made between gestation at randomisation and gestation at delivery, excluding recordings made in labour)
2. Primary process outcome measure: Number of women enrolled per site per month (calculated at end of trial as total number of women enrolled per site divided by number of months of enrolment at that site)

Key secondary outcome(s))

Clinical:
1. Maternal outcomes including:
1.1. Maternal morbidity or mortality (pre-eclampsia, eclampsia, intracranial haemorrhage or infarct, myocardial ischaemia/ infarction, intubation, pulmonary oedema, hepatic dysfunction, acute renal insufficiency, placental abruption, post-partum haemorrhage) (assessed on maternal discharge after delivery)
1.2. Gestation at delivery (assessed at delivery)
1.3. Mode of delivery (assessed at delivery)
1.4. Indication for delivery (assessed at delivery)
1.5. Number of episodes of systolic BP >=160mmHg, >=150mmHg (including home monitoring) (assessed between randomisation and delivery, excluding recordings made in labour)
1.6. Diastolic BP <80mmHg (assessed between randomisation and delivery, excluding recordings made in labour)
1.7. Need for additional oral or parenteral antihypertensive medication (assessed between randomisation and delivery)
2. Perinatal outcomes including:
2.1. Neonatal morbidity (admission to neonatal unit (length and place of stay), respiratory distress syndrome, need for ventilator support, intraventricular haemorrhage, confirmed infection, necrotising enterocolitis, seizures, encephalopathy, retinopathy of prematurity, other indications and main diagnoses related to neonatal unit admission) (assessed on discharge of infant)
2.2. Stillbirth (assessed at time of death)
2.3. Neonatal death (assessed at time of death)
2.4. Birth weight (assessed at delivery)
2.5. Birth weight centile (assessed at delivery)
2.6. Umbilical artery pH at birth (assessed at delivery)
3. Health resource use outcomes including:
3.1. Number of antenatal attendances (clinic and day unit) (assessed on maternal discharge)

3.2. Maternal admission nights (ward, delivery suite, intensive care) (assessed on maternal discharge)
3.3. Neonatal admission nights (including level of care) (assessed on discharge of infant)
4. Process:
4.1. Medication adherence (through self-report and pill count) (assessed as average of self-report and average of pill count checked at each visit between randomisation and delivery)
4.2. Side-effects of medication (assessed through direct questioning at each antenatal visit between randomisation and delivery)
4.3. Satisfaction with medication (assessed through postnatal questionnaire)

Completion date
31/05/2016

Eligibility

Key inclusion criteria
1. Chronic hypertension (defined as diastolic BP >=90mmHg present at booking or before 20 weeks' gestation, or requiring treatment outside pregnancy and/or at time of referral)
2. Gestation 12-28 weeks at recruitment
3. Singleton pregnancy
4. Able to provide informed consent
5. Age >=18 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Contraindication to labetalol (including asthma, uncontrolled heart failure, Prinzmetal's angina, marked bradycardia, hypotension, sick sinus syndrome, second- or third- degree AV block, cardiogenic shock, metabolic acidosis, severe peripheral arterial disease; phaeochromocytoma) or nifedipine (including cardiogenic shock; advanced aortic stenosis; within 1 month of myocardial infarction; unstable or acute attacks of angina)
2. Insufficient understanding of the trial

Date of first enrolment
14/08/2014

Date of final enrolment

30/09/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Womens Health Academic Centre, St Thomas Hospital
London
United Kingdom
SE1 7EH

Sponsor information

Organisation
King's College London, Guy's and St Thomas's NHS Foundation Trust (UK)

ROR
https://ror.org/00j161312

Funder(s)

Funder type
Charity

Funder Name
Tommy's Baby Charity

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
King's Health Partners

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

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?
Results article	results	01/11/2017		Yes	No
HRA research summary			28/06/2023	No	No