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The Giant PANDA study: which blood pressure medication is best for pregnant women with high blood pressure?

Submission date
06/11/2020

Recruitment status
No longer recruiting

Registration date
18/11/2020

Overall study status
Completed

Last Edited
02/10/2025

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Around 10% of women in the UK have high blood pressure in pregnancy, which without treatment can cause serious complications for the woman and baby. We want to find out which of the two most commonly used medicines to treat high blood pressure in pregnancy (labetalol and nifedipine) in the NHS is best at treating high blood pressure without having troublesome side effects for the woman or baby. Both medications have been widely used in the UK for many years and are considered safe in pregnancy.
The study aims to find out which blood pressure medication is best at treating high blood pressure in pregnancy.
Study results will help to understand which medication best treats high blood pressure in pregnancy and is safe for the baby, helping doctors and women with high blood pressure decide which medication is best for each woman and their baby.

Who can participate?
Pregnant women with hypertension, aged 18 years or over

What does the study involve?
Over 2,300 pregnant women with high blood pressure from around 50 maternity units in the UK that need treatment for their blood pressure will be offered information about the study and decide if they would like to take part. Women will be asked for their consent to take part and to complete a short questionnaire about how they are feeling. Women will then be randomly allocated (by chance) to either labetalol or nifedipine using a computer. To ensure women are treated safely, women and their healthcare team will know which medication group they are in. All women will continue to have their usual antenatal care including adding and switching their blood pressure medication and changing dose as needed. Two weeks after joining the study women will be asked to complete a few short questionnaires about how they are finding their blood pressure medication. Women and their babies will be followed through the pregnancy until they leave the hospital after birth.

What are the possible benefits and risks of participating?
Taking part will help us to understand how best to treat women with high blood pressure in pregnancy. Because women were about to be prescribed one of these two medications to treat their high blood pressure, there is very little risk to taking part. The only possible disadvantage is the additional time spent with the study team. We will keep these contacts as brief as possible, and if it is easier for women the two-week check-in can be over the phone or by email.
The doctor or healthcare professional prescribing their medication will explain any side effects as they usually would, and they can ask them at any time if they are not sure. The commonest side-effect reported for both drugs in pregnancy is a headache. Some women also reported dizziness or breathlessness. All women will continue to receive their usual NHS care during pregnancy while in this study.

Where is the study run from?
The Birmingham Clinical Trials Unit is running the study with Kings College London (UK)

When is the study starting and how long is it expected to run for?
April 2020 to September 2025

Who is funding the study?
National Institute for Health Research (NIHR) Health Technology Assessment Programme (UK)

Who is the main contact?
Lisa Leighton, Giant-PANDA@trials.bham.ac.uk

Contact information

Type(s)
Scientific

Contact name
Mrs Lisa Leighton

Contact details
BCTU
Robert Aitken Institute
Birmingham University
Edgbaston
Birmingham
United Kingdom
B15 2TT
+44 (0)121 415 9110
Giant-PANDA@trials.bham.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2020-003410-12

Integrated Research Application System (IRAS)
284958

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 47078, IRAS 284958

Study information

Scientific Title
Pregnancy ANtihypertensive Drugs: which Agent is best?

Acronym
Giant PANDA

Study objectives
Nifedipine will be superior compared to labetalol with less women in this group with severe systolic blood pressure readings, but the co-primary perinatal outcome will be no worse for the nifedipine group (non-inferior) compared with the labetalol group

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/11/2020, London - South East Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8085; londonsoutheast.rec@hra.nhs.uk), ref: 20/LO/1110

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Oedema, proteinuria and hypertensive disorders in pregnancy, childbirth and the puerperium

Interventions
The trial is a pragmatic, open-label, multicentre, two-arm randomised controlled trial of a treatment strategy with nifedipine versus labetalol in women with pregnancy hypertension. We aim to recruit 2,300 pregnant women (less than 34 weeks' gestation), with pregnancy hypertension (chronic or gestational hypertension or pre-eclampsia), over 18 years, able to provide consent and where the decision has been made to initiate or continue use of anantihypertensive drug.

Women will be identified by referral letters and/or at antenatal clinics and approached by a member of the direct clinical care team or the local research team (part of the direct care team) and provided with information on the study and given appropriate time to make the decision to

participate. Following informed consent completion, women will be asked to complete a short questionnaire about how they feel. Women will then be randomised, by random allocation (1:1), to treatment with any preparation of modified release nifedipine, a calcium channel blocker, (intervention arm) or any preparation of labetalol, a mixed alpha/ beta blocker, (active control arm). Two weeks after randomisation women will be contacted by the research team and asked to complete a few short questionnaires about their blood pressure medication. Women and their babies will be in the study from consent until primary hospital discharge or 28 days post birth, whichever occurs sooner.

This study is open-label to ensure women are effectively and safely treated, with healthcare professionals and women aware of their treatment allocation. Dose titration, switching, or add to the randomised antihypertensive drug will occur as in usual clinical practice as clinically indicated throughout pregnancy.

If a woman declines randomisation to the trial then she will be offered participation in the Giant PANDA observational study, involving data collection only. All other aspects of antenatal and delivery care will follow usual clinical care pathways underpinned by NICE 2019 guidelines for pregnancy hypertension.

The starting dose will be left to the discretion of the responsible healthcare professional, guided by blood pressure on the day, previous antihypertensive dose (where applicable) and any other relevant factors. The usual starting dose for the study drugs are:
Labetalol - Oral - 100mg twice a day, increased to a maximum of 2,400mg total daily dose
Nifedipine - Oral - 10mg twice a day, increased to a maximum of 40mg twice daily

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Labetalol, nifedipine

Primary outcome(s)
1. Maternal: Blood pressure measured using a sphygmomanometer daily between randomisation and birth
2. Fetal/neonatal: Composite of fetal loss before birth or known neonatal death, or neonatal unit admission between randomisation up to primary hospital discharge or 28 days post-birth, whichever occurs sooner (with no double counting of outcomes)

Key secondary outcome(s))
Measured using patient records:
Up to birth:
1. Severe hypertension (defined as any episode of severe maternal hypertension (systolic blood pressure ≥160 mmHg between randomisation and birth))
2. Mean antenatal systolic blood pressure (using highest systolic blood pressure per day as collected for the primary outcome)
3. New diagnosis of pre-eclampsia
4. Severe maternal morbidity (fullPIERS consensus definition (von Dadelszen, Payne et al. 2011))
5. Discontinued allocated antihypertensive drug

6. Undesirable effects of allocated (and other) antihypertensive drug(s) (number of women and number of undesirable effects)
At delivery/birth:
1. Indicated delivery (induction of labour or prelabour rupture of membranes (PROM) with stimulation of labour or pre-labour Caesarean section)
Between birth and primary hospital discharge or 28 days post-birth, whichever occurs sooner:
1. Neonatal unit admission (separation of baby from mother)
2. Major congenital abnormality as defined by EUROCAT
3. Mode of birth (spontaneous vaginal, assisted vaginal, Caesarean section)
4. Gestational age at birth
5. Birthweight centile
6. Need for treatment for neonatal hypoglycaemia (in those having blood glucose monitoring)

Completion date
30/09/2025

Eligibility

Key inclusion criteria
1. Pregnancy 11+0 and 34+6 weeks' gestation inclusive
2. Diagnosis of pregnancy hypertension (chronic/gestational hypertension or pre-eclampsia)
3. Clinician decision to initiate or continue use of antihypertensive drugs
4. Aged 18 years or over
5. Able to give informed consent

For observational study:
6. Women will be eligible to participate in the observational study at any gestational age up to and including 34+6 weeks. Women are able to take part in the observational study prior to 11+0 weeks gestation where the use of any antihypertensive drugs prescribed in clinical care will be recorded but will not form part of the interventional trial

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Total final enrolment
2254

Key exclusion criteria

1. Contraindication to either labetalol or nifedipine
2. Already taking both labetalol and nifedipine, and not able to be randomised to a single drug

For observational study:
3. Neither exclusion criterion for the trial are relevant for the observational study. Women contraindicated to either labetalol or nifedipine and/or women already taking both labetalol and nifedipine and not able to be randomised to a single drug, are eligible for the observational study

Date of first enrolment
08/06/2021

Date of final enrolment
17/01/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St Thomas' Hospital
Guy's and St Thomas' NHS Foundation Trust
Westminster Bridge Road
London
United Kingdom
SE1 7EH

Study participating centre
Manchester University Hospitals NHS Foundation Trust
Cobbett House
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Liverpool Women’s Hospital
Liverpool Women's NHS Foundation Trust
Crown Street
Liverpool
United Kingdom
L8 7SS

Study participating centre
St James University Hospital
Leeds Teaching Hospitals NHS Trust
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Leicester Royal Infirmary
University Hospitals of Leicester NHS Trust
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Birmingham Women's and Children's NHS Foundation Trust
Steelhouse Lane
Birmingham
United Kingdom
B4 6NH

Study participating centre
Queen's Medical Centre
Nottingham University Hospitals NHS Trust
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Bristol Royal Infirmary
University Hospitals Bristol and Weston NHS Foudnation Trust
Marlborough Street
Bristol
United Kingdom
BS1 3NU

Study participating centre
Bradford Royal Infirmary
Bradford Teaching Hospitals NHS Foundation Trust
Duckworth Lane
Bradford
United Kingdom
BD9 6RJ

Study participating centre
Royal United Hospital
Combe Park
Bath
United Kingdom
BA1 3NG

Study participating centre
Colchester Dist General Hospital
East Suffolk and North Essex NHS Foundation Trust
Turner Road
Colchester
United Kingdom
CO4 5JL

Study participating centre
New Cross Hospital
Royal Wolverhampton NHS Trust
Wolverhampton Road
Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
Chelsea and Westminster Hospital
369 Fulham Road
London
United Kingdom
SW10 9NH

Study participating centre
Kingston Hospital NHS Foundation Trust
Galsworthy Road

Kingston upon Thames
United Kingdom
KT2 7QB

Study participating centre
St George's Hospital
St George's University Hospitals NHS Foundation Trust
Blackshaw Road
Tooting
London
United Kingdom
ST17 0QT

Study participating centre
John Radcliffe Hospital
Oxford University Hospitals NHS Foundation Trust
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Southampton General Hospital
University Hospital Southampton NHS Foundation Trust
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Homerton University Hospital NHS Foundation Trust
Homerton Row
London
United Kingdom
E9 6SR

Sponsor information

Organisation

University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR128721

Funder Name
National Institute for Health Research (NIHR) (UK)

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request. Requests for the final dataset can be made through the chief investigator in accordance with the data-sharing policies of King's College London and Birmingham Clinical Trials Unit, with input from the co-investigator group where applicable.

IPD sharing plan summary
Available on request

Study outputs

	Date	Date	Peer	Patient-

Output type	Details	created	added	reviewed?	facing?
Protocol article		12/09/2023	14/09/2023	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	Inclusion of people with multiple long-term conditions in pregnancy research: patient, public and stakeholder involvement and engagement in a randomised controlled trial	07/10/2024	08/10/2024	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 1.2	18/08/2023	25/04/2024	No	No
Statistical Analysis Plan	version 1.0		25/04/2024	No	No