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The CHIPS trial: Control of Hypertension In Pregnancy Study

Submission date
31/07/2008

Recruitment status
No longer recruiting

Registration date
31/07/2008

Overall study status
Completed

Last Edited
26/04/2018

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
High blood pressure (hypertension) in pregnancy is associated with risks to you and your baby. Experts agree that blood pressure medication should be given to women with persistent severe hypertension in pregnancy, to protect them from stroke. However, there is no agreement about whether blood pressure medication should be given for non-severe hypertension in pregnancy. Guidelines for doctors in Canada have suggested that blood pressure should be made normal, but guidelines in the USA suggest that blood pressure should be treated only when it reaches severe levels. Some doctors give blood pressure medication because they believe that normalising blood pressure is best for you, and may be better for your baby. However, you should know that it is safe for blood pressure to be mild to moderately elevated for months to years , even when you are not pregnant, as long as you do not have pre-pregnancy diabetes or certain other health problems (e.g., kidney disease). In pregnancy, it is also safe for blood pressure to be mild to moderately elevated, and giving blood pressure medication has not been shown to prevent pre-eclampsia (toxemia of pregnancy) . Also, many women would prefer not to take antihypertensive therapy or any other medication during pregnancy. Other doctors do not give blood pressure medication unless persistent severe hypertension develops, because some studies suggest that blood pressure medication may result in poorer growth and well-being of your baby. The problem is that these studies are not strong enough to be relied upon, and doctors remain very uncertain about how blood pressure medication may affect your baby. In summary, we do not know which approach to treatment of non-severe high blood pressure in pregnancy is better for women and babies. In this study, we aim to find out whether 'less tight' control (aiming for a diastolic blood pressure of 100 mmHg) , compared with 'tight' control (aiming for a diastolic blood pressure of 85 mmHg) , can decrease the risks of adverse baby outcomes without increasing the risk of problems for the mother . The diastolic blood pressure is the bottom number of the blood pressure reading, and is less influenced by what is going on around a woman.

Who can participate?
You are being invited to take part in this research study because you have non-severe hypertension (diagnosed before or during pregnancy) and are 14-33 weeks pregnant.

What does the study involve?
Participants will be randomly allocated to be treated in one of two ways: either 'less tight' control or 'tight' control of their hypertension. If you are in the 'less tight' control group, your doctor will allow your blood pressure to be higher than normal but within a range that is believed to be safe for you, aiming for a diastolic (lower number) blood pressure of 100 mmHg. If you are in the 'tight' control group, your doctor will prescribe an appropriate medication to keep your blood pressure as normal as possible, aiming for a diastolic blood pressure of 85 mmHg. Both groups will be given a small diary, which should be carried with you at all times. This diary will serve to remind you and everyone involved in your care about the blood pressure goal for you. If you need blood pressure medication, your doctor will decide which medication is best for you, although we are asking doctors to consider using labetalol, one of the most commonly used and widely studied drugs for high blood pressure in pregnancy . If you are already on blood pressure medication, you may remain on it as long as your blood pressure is at the appropriate level for your treatment group . Until your baby is born, you should record the following information in the diary: outpatient visits and your blood pressure measurement at them, when you are sent to the laboratory for bloodwork, and when you have a test(s) of fetal well-being (i. e., non-stress test for the baby's heart rate and pattern , or ultrasound). Whether you are in the 'less tight' or 'tight' control group, you will be followed throughout your pregnancy, at a frequency of visits determined by usual care and your doctor, and until hospital discharge. Within four weeks after enrolment, your blood pressure will be measured by your maternity care provider. Also, at up to five times in pregnancy (at 14-20, 21-28, 29-33 and 34-40 weeks of pregnancy, and after delivery) , our research co-ordinator will speak with you to review how your blood pressure has been, some aspects of your care since enrolment in the study (such as antenatal hospitalisations, use of home blood pressure monitoring and changes in your activity level), and whether or not you have had tests to monitor you or your baby. This contact may be in person or by telephone, and will take no longer than 15 minutes. Your doctor will make decisions about all other medication that he/she feels that you need for whatever reason; whether bed-rest or admission to hospital will be used to monitor or treat your hypertension; if and when you have tests for you (such as blood tests) or your baby (such as ultrasound); when and how your baby should be delivered; and whether blood pressure medication should be given after delivery. Following delivery, with your permission, information about you and your baby will be collected from your and your baby's medical records. Your baby will be followed until 28 days of life (or until hospital discharge, if this is later) . You will be followed until 6-12 weeks after the birth (or until 36 weeks corrected gestational age or your baby is discharged home from hospital) , when our research co-ordinator will ask you, using a questionnaire over the phone or in person, about any medical problems that may have occurred since discharge from hospital for you or your baby, and whether or not you were satisfied with your care during the study. You will not be asked to answer any questions that you are uncomfortable answering. If you are not available, we would like to follow-up with your maternity care provider about how you and your baby are doing. We would also like to maintain contact with you (every 6-12 months) as we are interested in applying for funding to follow-up children at the age of five years.

What are the possible benefits and risks of participating?
If you are in the 'less tight' control group, you have a lower chance of being prescribed blood-pressure medication in pregnancy and your baby's growth and health soon after birth may be improved. If you are in the 'tight' control group, you may have fewer visits to your doctor. However, it is possible that you may experience no benefit from participating in this study. There are no additional risks to women participating in this study over and above that of usual care of non-severe hypertension. The interventions of 'less tight' and 'tight' control of blood pressure are both used in current clinical practice and both are endorsed by international guidelines. T here may be some risks associated with either 'less tight' or 'tight' control, but that is what the

study is designed to address. For example, women receiving 'less tight' control of blood pressure are more likely to have severe hypertension ; however, this is common even among women having 'tight' blood pressure control (40% in our pilot study), and regardless of allocated group, all women with severe hypertension will be treated promptly with antihypertensive medication that lowers blood pressure . Babies of women in the 'tight' control group may be smaller than expected and may suffer more health problems, particularly soon after birth . Whether babies in the 'tight' control group will be worse off is not known with certainty, and this is the reason for this study.

Where is the study run from?
BC Women's Hospital and Health Centre (Canada)

When is the study starting and how long is it expected to run for?
April 2009 to March 2014

Who is funding the study?
Canadian Institutes of Health Research (CIHR) (Canada)

Who is the main contact?
Dr Laura Ann Magee
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Study website
http://www.utoronto.ca/cmicr/chips/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT01192412

Secondary identifying numbers
MCT-87522

Study information

Scientific Title
The CHIPS trial: Control of Hypertension In Pregnancy Study

Acronym
CHIPS

Study objectives
Primary research question:
For pregnant women with non-severe, non-proteinuric maternal hypertension at 14 - 33 weeks, will 'less tight' control (target diastolic blood pressure [dBP] of 100 mmHg) versus 'tight' control (target dBP of 85 mmHg) increase (or decrease) the likelihood of pregnancy loss or Neonatal Intensive Care Unit (NICU) admission for greater than 48 hours?

Secondary research question:
Will 'less tight' versus 'tight' control increase (or decrease) the likelihood of serious maternal complications?

Other research questions:
Will 'less tight' versus 'tight' control:
1. Increase (or decrease) the likelihood of serious perinatal complications?
2. Increase (or decrease) the likelihood of severe hypertension and pre-eclampsia?
3. Increase (or decrease) the likelihood of maternal satisfaction with care?
4. Result in significant changes in dBP or health care costs?

This is the resulting randomised trial from the pilot study registered under ISRCTN57277508.

Ethics approval required
Old ethics approval format

Ethics approval(s)
University of British Columbia Clinical Research Ethics Board (UBC CREB), 14/07/2008

Study design
Unblinded randomised parallel assignment trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)

Treatment

Participant information sheet
Patient information can be found at: http://www.utoronto.ca/cmicr/chips/

Health condition(s) or problem(s) studied
Non-proteinuric pre-existing or gestational hypertension in pregnancy

Interventions
Experimental group:
'Less tight' control. The dBP treatment goal is 100 mmHg. For safety, if dBP is greater than or equal to 105 mmHg, then antihypertensive medication must be started or increased in dose. The intervention will be applied until delivery.

Control group:
'Tight' control. The dBP treatment goal is 85 mmHg. For safety, if dBP is less than or equal to 80 mmHg, then antihypertensive medication must be decreased in dose or discontinued. The intervention will be applied until delivery.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
Pregnancy loss or NICU admission for greater than 48 hours, as recorded in the maternal and infant medical records immediately following the birth (or pregnancy loss), and then again after the mothers' and infants' discharge home. Supplemental information, about potential post-discharge maternal or neonatal morbidities in the 6 weeks following birth for the mother, or 28 days of life for the baby, will be obtained by contacting women at 6 weeks postpartum and/or from medical records.

Secondary outcome measures
Serious maternal complications measured up to 6 weeks postpartum. Death or one or more life-threatening maternal complications:
1. Adverse neurological complications (stroke, eclampsia, and/or blindness), and/or
2. End-organ failure (uncontrolled hypertension, inotropic support, pulmonary oedema, respiratory failure, myocardial ischaemia/infarction, renal failure, coagulopathy, and/or transfusion)

Overall study start date
01/04/2009

Completion date
31/03/2014

Eligibility

Key inclusion criteria

1. Pre-existing or gestational hypertension (pre-existing hypertension is dBP greater than or equal to 90 mmHg before pregnancy or 20 weeks' gestation; gestational hypertension is dBP greater than or equal to 90 mmHg that develops after 20 weeks)
2. dBP of 90 - 105 mmHg if NOT TAKING antihypertensive therapy, or dBP of 85 - 105 mmHg if TAKING antihypertensive therapy
3. Live foetus (confirmed by Doptone assessment of foetal heart tones within one week before randomisation)
4. Gestational age 14 - 33+6 weeks (as measured by last menstrual period or dating ultrasound)

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
1028

Key exclusion criteria
Amendments as of 15/03/2010:
Please note that as of the above date, this record has been updated to include a protocol amendment (approved 17/03/2009) to point 3 of the exclusion criteria below. This should now read as follows:
3. Use of an angiotensin converting enzyme (ACE) inhibitor at greater than or equal to 14+0 weeks' gestation

Initial exclusion criteria at time of registration:
1. Severe systolic hypertension (defined as a systolic blood pressure [sBP] greater than or equal to 160 mmHg at randomisation)
2. Proteinuria (defined as greater than or equal to 0.3 g/d by 24 hour urine collection, or if a 24 hour urine collection is not available, by a urinary protein:creatinine ratio of greater than or equal to 30 mg/mmol or urinary dipstick of greater than or equal to 2+)
3. Use of an angiotensin converting enzyme (ACE) inhibitor at any time in the pregnancy
4. Contraindication to either arm of the trial or to pregnancy prolongation
5. Known multiple gestation
6. Known lethal or major foetal anomaly
7. Plan to terminate pregnancy
8. Prior participation in CHIPS

Date of first enrolment
01/04/2009

Date of final enrolment
31/03/2014

Locations

Countries of recruitment

Argentina

Australia

Brazil

Canada

Chile

Colombia

Estonia

Hungary

Israel

Jordan

Netherlands

New Zealand

Poland

United Kingdom

United States of America

Study participating centre
BC Women's Hospital and Health Centre
Vancouver
Canada
V6H 3N1

Sponsor information

Organisation
University of British Columbia (Canada)

Sponsor details
c/o Dean Kuusela
102-6190 Agronomy Road
Vancouver
Canada
V6T 1Z4

Sponsor type
University/education

Website
http://www.ubc.ca/

ROR
https://ror.org/03rmrcq20

Funder(s)

Funder type
Research organisation

Funder Name
Canadian Institutes of Health Research

Alternative Name(s)
Instituts de Recherche en Santé du Canada, Canadian Institutes of Health Research (CIHR), CIHR_IRSC, Canadian Institutes of Health Research | Ottawa ON, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	29/01/2015		Yes	No
Results article	results	01/06/2016		Yes	No
Results article	results	01/06/2016		Yes	No
Results article	results	01/11/2016		Yes	No
Other publications	secondary analysis	01/06/2018		Yes	No