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PRISM: Progesterone in spontaneous miscarriage

Submission date
11/02/2015

Recruitment status
No longer recruiting

Registration date
11/02/2015

Overall study status
Completed

Last Edited
02/07/2020

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
One in five pregnancies miscarry, and the loss of an unborn baby has the potential to cause both physical harm and psychological distress. A recently launched NICE guideline has urged that a large and robust randomised controlled clinical trial should be done to clarify whether progesterone treatment for women with bleeding in early pregnancy reduces the risk of miscarriage.

Who can participate?
Women between the ages of 18-39 who have experienced bleeding during the last 4 days in early pregnancy (up to 12 weeks).

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 are given progesterone capsules to place into their vagina twice a day to up to 16 weeks of pregnancy. Those in group 2 are given placebo capsules to be administered in the same way. The main outcome of the study is live birth beyond 34 weeks of pregnancy. A number of other key outcome measures, including gestation at birth, miscarriage rates and the condition of the baby at 28 days of life, are also collected and analysed and we gather resource-use outcomes to perform a health economic evaluation.

What are the possible benefits and risks of participating?
We do not know whether each participant will benefit personally from taking part in this study, but the knowledge gained thanks to their help will inform future treatment and potentially lead to improved antenatal care and pregnancy outcomes for women in the future. Previous studies using progesterone treatment during pregnancy have found very little evidence of risks for the mother or the baby. However, some women may experience swollen hands or feet, bloating, headache, sleeplessness, diarrhoea or jaundice.

Where is the study run from?
48 NHS hospitals in the UK

When is the study starting and how long is it expected to run for?
October 2014 to June 2018

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Professor Arri Coomarasamy

Contact information

Type(s)
Scientific

Contact name
Dr Adam Devall

Contact details
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Additional identifiers

EudraCT/CTIS number
2014-002348-42

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
18314

Study information

Scientific Title
Effectiveness of progesterone to prevent miscarriage in women with early pregnancy bleeding: A randomised placebo-controlled trial (PRISM Trial: PRogesterone In Spontaneous Miscarriage Trial)

Acronym
PRISM

Study objectives

The aim of this trial is to clarify the evidence that progesterone treatment for women with bleeding in early pregnancy can reduce the risk of miscarriage.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee South Central – Oxford C, 26/11/2014, ref: 14-SC-1345

Study design
Randomised; Interventional; Design type: Not specified, Prevention

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Community

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Topic: Reproductive health and childbirth; Subtopic: Reproductive Health and Childb (all Subtopics); Disease: Reproductive Health & Childbirth

Interventions
1. Placebo: The placebo will be a vaginal capsule, encapsulated in the same form as the IMP, and identical in colour, shape and weight
2. Progesterone: The Investigational Medicinal Product (IMP) is progesterone at a dose of 400mg to be taken as vaginal pessaries twice daily from confirmation of an intrauterine gestation sac visible on ultrasonography until 16 completed weeks of pregnancy or until miscarriage is confirmed

Intervention Type
Drug

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

Primary outcome measure
Live birth beyond 34 completed weeks of gestation is assessed using medical record review at pregnancy end.

Secondary outcome measures

Secondary outcome measures as of 01/02/2017:
1. Time from conception to pregnancy end (any reason) is assessed using medical record review at pregnancy end. Conception date will be estimated using the patient's booking scan if available or, if not, the date of last menstrual period or, failing that, the date from the ultrasound scan.
2. Ongoing pregnancy at 12 weeks (range 11 to 14 weeks) of gestation is assessed using medical record review at 11-14 weeks gestation
3. Miscarriage rate (defined as delivery before 24 weeks of gestation) is assessed using medical record review at pregnancy end
4. Other pregnancy end outcomes: live birth <34 weeks, ectopic pregnancy, termination, stillbirth, molar pregnancy, resolved pregnancy of unknown location (PUL), failed PUL, twin live births, gestational age at miscarriage is assessed using medical record review at pregnancy end
5. Where live birth ≥24 weeks: time from conception to delivery (gestational age), gestational age <28/<32/<37 weeks, mode of delivery (unassisted vaginal, instrumental vaginal, elective c-section, emergency c-section, vaginal breech delivery, other), birth weight, arterial and venous cord pH, APGAR scores, base excess is assessed using medical record review at pregnancy end
6. Antenatal complications: pregnancy-induced hypertension, pre-eclampsia, obstetric cholestasis, cervical cerclarge, preterm (<37 weeks) pre-labour rupture of membranes, gestational diabetes (other complications will be tabulated but not formally analysed) (medical record review)
7. Intrapartum complications: chorioamnionitis, intrauterine growth restriction (IUGR), macrosomia (other complications will be tabulated but not formally analysed) is assessed using medical record review at pregnancy end
8. Post-partum complications: haemorrhage (other complications will be tabulated but not formally analysed) is assessed using medical record review at pregnancy end
9. Maternal complications: admission to high dependency unit (HDU), admission to intensive therapy unit (ITU), (other complications will be tabulated but not formally analysed) is assessed using medical record review up to 28 days after pregnancy end
10. Neonatal complications: discharge to hospital, early infection, retinopathy of prematurity, necrotising enterocolitis, intraventricular haemorrhage, congenital and chromosomal abnormalities, respiratory distress syndrome, ventilation or oxygen support (other complications will be tabulated but not formally analysed is assessed using medical record review up to 28 days after live birth
11. Survival at 28 days of neonatal life is assessed using medical record review up to 28 days after live birth
12. Maternal adverse events (tabulated but not formally analysed) is assessed using medical record review throughout pregnancy and up to 28 days of neonatal life
13. Serious adverse events are assessed using medical record review throughout pregnancy and up to 28 days of neonatal life

Original secondary outcome measures:
1. Adverse events; Timepoint(s): Throughout pregnancy and up to 28 days of neonatal life
2. Antenatal complications; Timepoint(s): Until pregnancy end
3. APGAR score; Timepoint(s): Pregnancy end beyond 24 weeks
4. Arterial cord pH; Timepoint(s): Pregnancy end beyond 24 weeks
5. Birthweight; Timepoint(s): Pregnancy end beyond 24 weeks
6. Chromosomal and congenital abnormalities; Timepoint(s): Pregnancy end
7. Gestation at delivery; Timepoint(s): Pregnancy end
8. Miscarriage; Timepoint(s): Up to 24 weeks of gestation
9. Mode of delivery; Timepoint(s): Pregnancy end beyond 24 weeks
10. Neonatal complications; Timepoint(s): Live birth
11. Neonatal survival; Timepoint(s): 28 days of neonatal life

12. Ongoing pregnancy at 12 weeks of gestation; Timepoint(s): 11-13 weeks of gestation
13. Requirements for resuscitation; Timepoint(s): Pregnancy end beyond 24 weeks
14. Resource use; Timepoint(s): Throughout pregnancy and up to 28 days of neonatal life
15. Surfactant use; Timepoint(s): Live birth
16. Venous cord pH; Timepoint(s): Pregnancy end beyond 24 weeks
17. Ventilation support; Timepoint(s): Live birth

Overall study start date
01/10/2014

Completion date
30/06/2018

Eligibility

Key inclusion criteria
Correct as of 01/02/2017
1. Women presenting with with early pregnancy vaginal bleeding that has occurred within the last 4 days and is in the first 12 weeks of pregnancy
2. Upper Age Limit 39 years
3. Lower Age Limit 18 years

Previous inclusion criterion:
1. Women presenting with vaginal bleeding in the first 12 weeks of pregnancy with an intrauterine gestation sac visible on ultrasonography

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Planned Sample Size: 4150; UK Sample Size: 4150

Total final enrolment
4153

Key exclusion criteria
1. Women of age less than 18 years or more than 40
2. Women with life-threatening bleeding
3. Women already taking progesterone supplementation therapy
4. Women with contraindications to progesterone use

Date of first enrolment
01/03/2015

Date of final enrolment
28/07/2017

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Birmingham Women's Hospital
Metchley Park Road
Edgbaston
Birmingham
United Kingdom
B15 2TG

Study participating centre
Queen Charlotte's and Chelsea Hospital
London
United Kingdom
W12 0HS

Study participating centre
Royal Infirmary of Edinburgh
Edinburgh
United Kingdom
EH16 4SA

Study participating centre
Liverpool Women's Hospital
Liverpool
United Kingdom
L8 7SS

Study participating centre
Birmingham Heartlands Hospital
Birmingham
United Kingdom
B9 5SS

Study participating centre
University College London Hospital
London
United Kingdom
NW1 2BU

Study participating centre
Chelsea and Westminster Hospital
London
United Kingdom
SW15 2QJ

Study participating centre
St Michael’s University Hospital
Bristol
United Kingdom
BS2 8UG

Study participating centre
Queen's Medical Centre
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Sunderland Royal Hospital
Sunderland
United Kingdom
SR4 7TP

Study participating centre
Princess Royal Hospital
Glasgow

United Kingdom
G31 2ER

Study participating centre
University Hospital Coventry
Coventry
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CV2 2DX

Sponsor information

Organisation
University of Birmingham

Sponsor details
Edgbaston
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Sponsor type
University/education

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

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

Publication and dissemination plan
A meeting will be held after the end of the study to allow discussion of the main results among the collaborators prior to publication in an open access journal.

Intention to publish date
30/06/2019

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	09/05/2019	09/05/2019	Yes	No
Other publications	cost-effectiveness analysis	01/05/2020		Yes	No
Results article	results	01/06/2020	02/07/2020	Yes	No