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Does progesterone prophylaxis to prevent preterm labour improve outcome?: a randomised, double-blind, placebo-controlled trial

Submission date
29/08/2008

Recruitment status
No longer recruiting

Registration date
21/11/2008

Overall study status
Completed

Last Edited
28/06/2018

Condition category
Pregnancy and Childbirth

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
A preterm birth is a birth that takes place more than three weeks before the baby is due (i.e., a birth before the start of the 37th week of pregnancy). There is now good evidence that the hormone progesterone prevents preterm birth in women at high risk. However, there is no evidence that preventing preterm birth with progesterone has any long-term beneficial effect on the baby. Given that we know that preterm birth is associated with intrauterine infection (infection within the womb) and inflammation, which itself is associated with brain damage for the newborn, it is possible that keeping the baby “in utero” (in the womb) when it would otherwise have been born preterm is harmful. The purpose of this study is to see if progesterone is beneficial to babies - we think it will be but this study is needed to check. The aim is to determine whether progesterone improves outcomes in women at high risk of preterm delivery. The outcomes we are interested in are those of women at delivery and babies from birth to the age of two.

Who can participate?
Women with risk factors for preterm birth (e.g., history of previous preterm birth).

What does the study involve?
Women with risk factors for preterm birth are invited to have a fetal fibronectin test (a test for detecting premature labor). All those with a positive test result and women with selected risk factors but a negative test results are then randomly allocated to be treated with either progesterone or a placebo (dummy) treatment. Participants are followed up until after delivery, and their babies are followed up until the age of 2 years. Those just screened but not treated are also followed up until delivery.

What are the possible benefits and risks of participating?
Not provided at time of registration.

Where is the study run from?
University of Edinburgh (UK).

When is the study starting and how long is it expected to run for?
October 2008 to December 2015.

Who is funding the study?
Medical Research Council (UK).

Who is the main contact?
1. Sonia Whyte (Sonia.Whyte@ed.ac.uk)
2. Lorraine Adamson (L.D.Adamson@ed.ac.uk)

Study website
http://www.opptimum.org.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
MRC ref: G0700452

Study information

Scientific Title
Does progesterone prophylaxis to prevent preterm labour improve outcome?: a randomised, double-blind, placebo-controlled trial

Acronym
OPPTIMUM

Study objectives
Primary objective: In women at high risk of preterm labour, does prophylactic vaginal natural progesterone, 200 mg daily from 22-34 weeks gestation, compared to placebo:
1. Improve obstetric outcome by lengthening pregnancy and thus reducing the incidence of preterm delivery (before 34 weeks gestation)?
2. Improve neonatal outcome by reducing a composite of death and major morbidity?
3. Lead to improved childhood cognitive and neurosensory outcomes at two years?
4. Represent cost effective management for women at high risk of preterm delivery?

More details can be found at: http://www.mrc.ac.uk/ResearchPortfolio/Grant/Record.htm?GrantRef=G0700452&CaseId=9676

Ethics approval required
Old ethics approval format

Ethics approval(s)
Scotland MREC A, 19/02/2008, ref: 08/MRE00/6

Study design
Randomised double-blind placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Patient information sheet can be found at: http://www.opptimum.org.uk/general-information.aspx

Health condition(s) or problem(s) studied
Preterm labour

Interventions

Prophylactic vaginal natural progesterone, 200 mg daily from 22-24 weeks gestation until 34 weeks gestation vs placebo.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
1. Primary obstetric outcome of the treatment phase is delivery <34 weeks of gestation (Yes/No)
2. Primary neonatal outcome is a composite of death or two markers of neonatal morbidity
3. Primary childhood outcome is developmental status at two years
4. Formal economic evaluation

Secondary outcome measures
1. Gestational age at delivery
2. Death after trial entry or severe disability at two years of age
3. Incidence of the individual components of the primary neonatal outcome
4. Incidence of other major neonatal complications: need for and duration of respiratory support, surfactant administration, duration of oxygen therapy, necrotising enterocolitis, number of discrete episodes of infection (e.g., positive blood culture, cerebrospinal fluid [CSF] culture), daily level of care
5. Composite outcome of death or neurodevelopmental impairment at two years of age, the latter defined as one or more of:
5.1. Disabling cerebral palsy, defined as a score of 2 or higher on the Gross Motor Function Classification System, or 3 or higher on the Manual Ability Classification System, plus classified using the SCPE system
5.2. Developmental impairment (Cognitive standardised score <70)
5.3. Severe visual loss (legally certifiable as blind or partially sighted)
5.4. Profound/severe deafness (requiring hearing aids). Disability will be classified into domains according to professional consensus.
5.5. Brief Infant Toddler Social Emotional Assessment (BITSEA)
5.6. Women's perceptions of treatment
5.7. Maternal and child adverse events (e.g., operative delivery)

Overall study start date
01/10/2008

Completion date
31/12/2015

Eligibility

Key inclusion criteria
Screening Study:
High risk for preterm birth as indicated by at least one of the following:

1. History of previous preterm birth (PTB)/second trimester loss
2. Previous preterm premature rupture of the foetal membranes
3. Short cervical length (<25 mm) on ultrasound at 18-22 weeks gestation
4. All women will have gestation established by scan at ¡Ü 16 weeks to ensure that the estimated date of delivery is accurate
5. Signed consent form

Main Study:
All women fulfilling the above inclusion criteria and who have a positive screening (fFN) test at 22 weeks will be eligible for the main (treatment) phase of the study. Further consent must be obtained.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Planned sample size (randomised): 1125

Key exclusion criteria
1. Known significant structural or chromosomal foetal anomaly
2. Known sensitivity, contraindication or intolerance to progesterone (including peanut allergy)
3. Suspected or proven rupture of the foetal membranes at the time of recruitment
4. Multiple pregnancy
5. Prescription or ingestion of medications known to interact with progesterone (e.g., ketoconazole and ciclosporin)

Date of first enrolment
03/12/2008

Date of final enrolment
31/03/2013

Locations

Countries of recruitment
Sweden

United Kingdom

Study participating centre

66 centres in the UK and Sweden
United Kingdom
-

Sponsor information

Organisation
University of Edinburgh (UK)

Sponsor details
Edinburgh Clinical Trials Unit
The Queen's Medical Research Institute
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Sponsor type
University/education

Website
http://www.ed.ac.uk

ROR
https://ror.org/01nrxwf90

Funder(s)

Funder type
Government

Funder Name
Medical Research Council (UK) (grant ref: G0700452)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype

National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
To be confirmed at a later date
Participant level data may be available on request from the CI (Jane Norman) after publication of papers arising from the study

Intention to publish date

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	questionnaire results	01/08/2010		Yes	No
Protocol article	protocol	06/08/2012		Yes	No
Results article	results	21/05/2016		Yes	No
Results article	results	01/06/2018		Yes	No