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Stitch, progesterone or pessary: a randomised controlled trial

Submission date
29/07/2015

Recruitment status
No longer recruiting

Registration date
29/07/2015

Overall study status
Completed

Last Edited
17/07/2024

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Babies born very early are more likely to have health problems than babies born at the right time. Although many do survive, being born early may affect them throughout their life. Doctors have done a lot of work to try and stop babies being born too soon. They have identified that women who have a short cervix are at higher risk of having an early baby. There are three treatments which have been shown to reduce risk of premature birth in such women. A cervical stitch or 'cerclage' involves a minor operative procedure performed by an obstetrician. It is a suture, or stitch, which is placed around the cervix (the neck of the womb) and tied in order to prevent the cervix opening too early in pregnancy. This has been shown to reduce the likelihood of changes occurring to the cervix that can cause it to open too soon in women with a shortened cervix. A vaginal progesterone also reduce the risk of premature birth. Progesterone is a hormone, which mimics the natural hormone produced by the body during pregnancy. An arabin pessary is a ring made of silicon which is inserted into the vagina by a doctor. It sits under the cervix and provides support to the pregnancy. Although there is evidence to show that all three treatments reduce the risk of premature birth in women who have a short cervix it is not known which is best. This study is being undertaken to find out which of these treatments work best at preventing premature birth.

Who can participate?
Women pregnant with one baby with a short cervix.

What does the study involve?
Participants are randomly allocated into one of three groups. Those in group 1 are treated with a cervical stitch or 'cerclage'. It is inserted in the operating theatre through the vagina using a spinal anaesthetic (involving an injection in the back). The cerclage is removed by a doctor at 37 weeks' of pregnancy, or when the participant goes into labour. Those in group 2 are given a vaginal progesterone. The treatment dose is 200mg (one capsule) per day, inserted into the vagina every evening by the participant until 34 weeks' of pregnancy. Those in group 3 are given a arabin pessary, a ring made of silicon which is inserted into the vagina by a doctor. It sits under the cervix and provides support to the pregnancy. It is removed by a doctor at 37 weeks' or in

the event of labour. The treatments are then compared to see if one is better than the others. This includes, among other things, looking at the number of births occurring before 37 weeks of pregnancy, number of stillbirths and neonatal deaths and costs of each treatment.

What are the possible benefits and risks of participating?
Having a cervical stitch inserted is a relatively common procedure. The uncommon risks include tearing of the cervix or bladder (1 out of 1000), bleeding or infection (1 out of 100-1000). There is a very small risk that the patient's waters could break during the procedure (less than one in 300). The unlikely but possible side effects of a vaginal progesterone are: acne, flushing, rashes, fluid retention, weight changes, tummy upset, changes in libido, breast discomfort, migraine, tiredness and premenstrual symptoms. Patients with such side effects should contact their doctor or the study team. There may be some discomfort felt when the arabin pessary is inserted. Patients may also notice an increase in vaginal discharge, and there is a small risk of infection. Rarely, the pessary may become dislodged, and will need to be re-inserted by an obstetrician. If this happens, patients should seek care immediately from their local hospital, and inform the study team.

Where is the study run from?
St Thomas's Hospital (lead centre), Queen Charlotte's and Chelsea Hospital and St Mary's Maternity Unit, Poole Hospital (UK)

When is the study starting and how long is it expected to run for?
July 2015 to July 2018

Who is funding the study?
1, National Institute for Health Research (UK)
2. Tommy's Baby Charity (UK)

Who is the main contact?
Dr Natasha Hezelgrave
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2015-000456-15

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
19350

Study information

Scientific Title
The prevention of pre-term birth in women who develop a short cervix. A multicentre randomised controlled trial to compare three treatments; cervical cerclage, cervical pessary and vaginal progesterone.

Acronym
SuPPoRT

Study objectives
This study aims to compare the efficacy of three treatments, vaginal progesterone pessaries, cervical stitch and cervical arabin pessary, for preventing preterm birth in women who develop a short cervix.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London City & East, 19/5/2015, ref: 15/LO/0485

Study design
Randomised; Interventional; Design type: Prevention

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Prevention

Participant information sheet

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

Health condition(s) or problem(s) studied
Prevention of preterm birth in women with a short cervix

Interventions
1. Cervical cerclage:
The cerclage procedure will be booked at the time of recruitment. It will be performed (according to local practice and procedures) within 7 days of recruitment to the trial. A vaginal cerclage will be inserted in in the operating theatre by a clinician trained in the procedure, according to the technique preferred by the clinician. It is usually inserted under regional anaesthetic. Tocolysis, antibiotics and antenatal corticosteroids can be considered at the clinician's preference, but will be documented and considered in the analysis. The patient will usually go home the same day and will be followed up with two to four weekly transvaginal ultrasound scans (or more frequent if clinically indicated) according to local protocols. The suture is removed easily by exposing the cervix and cutting the knot, usually without the need for anaesthetic. This is done electively when a woman is 37 weeks' gestation, or if she presents in symptomatic preterm labour before labour becomes established, to avoid cervical trauma. The suture will also be removed if there is clinical evidence of chorioamnionitis.

2. Vaginal progesterone:
Vaginal progesterone (Cyclogest, 200 mg once daily) will be prescribed at the time of recruitment. Patients will be informed to insert one pessary every day until 34 weeks' gestation (or delivery, whichever is soonest). The patient will usually be followed up with two to four weekly transvaginal ultrasound scans or more frequently if clinically indicated) according to local protocols. If the cervix shortens and membranes are visible, prior to 24 weeks' gestation, a rescue cerclage will be inserted, according to local protocols. Cyclogest 200 mg pessary will be stored (at 15˚ – 25˚ C) and dispensed by the hospital pharmacy.

3. Cervical pessary:
The appropriately sized (see appendix 1) pessary will be inserted within 7 days of recruitment by the attending clinician, who will be trained in the procedure. It will be removed by a trained clinician at 37 weeks' gestation (or in the event of established labour). The patient will be usually be followed up with two to 4 weekly transvaginal ultrasound scans (or more frequent if clinically indicated) according to local protocols. If the cervix shortens and membranes become visible prior to 24 weeks' gestation, a rescue cerclage will be inserted, according to local protocols.

Intervention Type
Mixed

Primary outcome measure
Preterm birth prior to 37 weeks; Timepoint(s): <37 weeks gestation

Secondary outcome measures
1. Adverse perinatal outcome, defined as a composite outcome of death (antepartum /intrapartum stillbirths plus neonatal deaths prior to discharge from neonatal services) or one (or more) of intraventricular hemorrhage, periventricular leukomalacia, hypoxic ischemic encephalopathy, necrotizing enterocolitis, bronchopulmonary dysplasia and sepsis
2. Delivery <30 & 34 completed weeks' gestation
3. Gestation at delivery

4. Time between intervention and delivery
5. Requirement for Rescue Cerclage (bulging fetal membranes)
6. Other maternal and fetal outcomes: clinical course, therapies administered, maternal and fetal morbidity and mortality data until discharge or 28 days post-natal (whichever soonest)
7. Participant and clinician's perceptions of treatment: questionnaires with a selection of participants at 0-2 weeks post procedure. Questionnaires at one year are planned if funding is obtained
8. Health costs at 28 days post-natal
9. Biochemical end-points (on available samples): cervical swabs will be taken to determine the presence of cervico-vaginal infection and concentrations of biomarkers of preterm birth, infection and inflammation. Saliva samples will be collected for salivary hormone levels, and blood samples taken for inflammatory markers and genetic analysis. Results will be correlated with maternal and fetal outcomes

Overall study start date
22/07/2015

Completion date
01/07/2021

Eligibility

Key inclusion criteria
Women with singleton pregnancies who are found to have cervical length <25 mm on transvaginal ultrasound between 14+0 weeks' gestation (dated by ultrasound or LMP and adjusted for ultrasound estimated date of delivery once ultrasound performed if no miscarriage prior to dating ultrasound) until 23+6 weeks' gestation and one or more of the following risk factors
1. Written informed consent to participate
2. History of:
2.1. Previous preterm premature rupture of the fetal membranes (= 37 weeks')
2.2 History of previous PTB/second trimester loss (= 16 weeks' or = 37 weeks' gestation)
2.3. Any cervical procedure to treat abnormal smears i.e. large loop excision, laser conisation, cold knife conisation or radical diathermy
3. Incidental finding of a short cervix on ultrasound scan (e.g. at the time of anomaly scan)
4. Women aged 18-50

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
50 Years

Sex

Female

Target number of participants
Planned Sample Size: 540; UK Sample Size: 540

Key exclusion criteria
1. Women with persistent fresh vaginal bleeding evident on speculum examination.
2. Women with visible membranes evident on speculum examination or open cervix on ultrasound scan.
3. Women with severe abdominal pain/evidence of sepsis (as judged by attending clinician).
4. Known significant congenital or structural or chromosomal fetal abnormality.
5. Suspected or proven rupture of the fetal membranes at the time of recruitment.
6. Women currently using progesterone pessaries or who have taken progesterone beyond 18 weeks gestation.
7. Women who have a cervical suture in situ.
8. Women who already have a cervical pessary in situ.
9. Insufficient understanding of the trial in the opinion of the Investigator
10. If the attending clinician feels that an individual woman is more suited to one treatment modality over another
11. Any contraindications or cautions to the investigational medicinal product including:
11.1. Known allergy or hypersensitivity to progesterone
11.2. Hepatic dysfunction
11.3. Undiagnosed vaginal bleeding
11.4. Mammary or genital tract carcinoma
11.5. Thrombophlebitis
11.6. Thromboembolic disorders
11.7. Cerebral haemorrhage
11.8. Porphyria

Date of first enrolment
22/07/2015

Date of final enrolment
01/03/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St Thomas's Hospital (lead centre)
249 Westminster Bridge Road
London
United Kingdom
SE1 7EH

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

Study participating centre
St Mary's Maternity Unit, Poole Hospital
St Mary's Road
Poole
United Kingdom
BH15 2BH

Sponsor information

Organisation
Guy's and St. Thomas' NHS Foundation trust

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00j161312

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

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

Results and Publications

Publication and dissemination plan
It is intended that the results of the study will be reported and disseminated at international conferences and in peer-reviewed scientific journals within 6 months of outcome data collected from the final participant (estimated April-July 2019).

Intention to publish date
01/07/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored anonymously in a non-publically available repository (medscinet.net). The data-sharing plans are unknown and will be made available at a later date.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Results article		16/07/2024	17/07/2024	Yes	No