ISRCTN88609453 https://doi.org/10.1186/ISRCTN88609453

Glycerine Trinitrate for Retained Placenta (GOT-IT Trial)

Submission date
07/03/2014

Recruitment status
No longer recruiting

Registration date
26/03/2014

Overall study status
Completed

Last Edited
22/10/2020

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
We want to find out whether glyceryl trinitrate (GTN) is effective in treating a stuck or retained placenta (RP) after a woman has had a vaginal delivery. RP occurs when the placenta is not delivered after a baby is born. If the placenta is not delivered, women can bleed heavily. In the UK, nearly 11,000 women every year experience RP after giving birth. The only treatment currently available for women with a RP is an operation called a Manual Removal of Placenta (MROP). This is an invasive procedure that requires an anaesthetic and skilled staff. The mother and newborn baby are also separated during the operation which could be traumatic and could delay mother-baby bonding. There is therefore a need for a new medical (non-surgical) treatment for RP. GTN relaxes muscles and when given sublingually (under the tongue) it is absorbed quickly and causes the womb and cervix to relax within 5 minutes. Small studies suggest that GTN may be very good at managing RP. However, these promising results have not been supported by a more recent larger study. It is also not clear whether women will be willing to take GTN and whether the costs of using GTN compare favourably (or not) with current surgical management. We are looking to see whether GTN reduces the need for women with a RP to have MROP. We plan to do this by comparing women who have GTN or a placebo (dummy drug that contains no treatment). The study will be carried out in two phases. The aim of the first phase is to test out and refine trial procedures in a small number of hospital sites. This first stage will help us see how many women are willing to take part in the research. Women who take part, those who decide not to take part and delivery suite staff who have worked on the trial will be invited to take part in in-depth interviews to talk about their experiences. This information will be used to improve the way we carry out the research if necessary. The second phase will be the main trial where recruitment will be extended to a larger number of hospitals (at least 20 delivery units in the UK) in order to determine whether GTN works (clinical effectiveness) and whether it reduces costs for the NHS (cost effectiveness).

Who can participate?
Any woman aged 16 or over who has a vaginal delivery and then develops the complication of RP.

What does the study involve?
After receiving information about the study and deciding to take part, women will be randomly allocated to receive either GTN spray or a placebo spray that looks and tastes the same as GTN.

The placebo spray will not contain any active drug and we would not expect a placebo to release a RP. We will randomly allocate women, meaning that study investigators cannot choose which spray to give to women, so that we can compare the two groups fairly. The woman will be asked to spray the study drug (either GTN or placebo) under her tongue. After 5 minutes, if her placenta has not delivered, the midwife (or doctor) looking after her will try and deliver the placenta by gently pulling on the umbilical cord. If the placenta remains undelivered 15 minutes after taking the study drug, we think that it is very unlikely that the placenta will deliver by itself. At that stage, the decision will be made to transfer the woman to theatre as soon a theatre and skilled staff are available to perform the operation. Women who take part in the study will be asked to complete a questionnaire about their experience prior to discharge from hospital and then 6 weeks after taking part in the study. This information will be used to assess their satisfaction with treatment, potential side effects of treatment and their health resource use since they had their baby. Some women, including those who declined to take part in the study, will be invited to participate in a interview study to find out more about their experience of being approached about or being involved in the research.

What are the possible benefits and risks of participating?
All medications can sometimes cause side effects. GTN is a drug widely used for the treatment of angina (a heart condition). It is a drug which relaxes your blood vessels and muscles to help with blood flow. Common side effects include headache, dizziness, flushing/feeling hot, a drop in blood pressure and a rise in heart rate (pulse). This drug does not stay in the body for very long so any side effects are often very short lived and painkillers can be given for headache. The possible benefit in participating in this trial is the placenta may be delivered without the need for an anaesthetic, transfer to the operating theatre and an operation.

Where is the study run from?
The trial will be managed by the established Centre for Healthcare Randomised Trials Unit in Aberdeen and by an experienced Trial Manager and Administrator based in Edinburgh.

When is the study starting and how long is expected to run for?
The study is due to start in July 2014 and is expected to run for 42 months.

Who is funding the study?
NIHR Health Technology Assessment Programme - HTA (UK)

Who is the main contact?
Dr Fiona Denison
Fiona.denison@ed.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Kathryn Carruthers

Contact details
Room W1.14
The Queen's Medical Research Institute
47 Little France Crescent

Edinburgh
United Kingdom
EH16 4TJ

Additional identifiers

EudraCT/CTIS number
2013-003810-42

IRAS number

ClinicalTrials.gov number
NCT02085213

Secondary identifying numbers
HTA 12/29/01

Study information

Scientific Title
Glycerine Trinitrate for Retained Placenta (GOT-IT Trial)

Acronym
Glycerine Trinitrate for Retained Placenta (GOT-IT Trial)

Study objectives
This study will try to prove the clinical and cost effectiveness of a known treatment for angina, glyceryl trinitrate (GTN), used to treat retained placenta (RP). We will compare GTN against a placebo (dummy treatment) in a randomised controlled blinded trial (GOT-IT).

The GOT-IT Trial will be conducted in two phases. The first phase will involve an internal pilot study where the aim will be to test out and refine trial procedures in a small number of hospital sites. The second phase will be the main trial where recruitment will be extended to a larger number of hospitals in order to determine clinical and cost effectiveness.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/122901
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0018/112464/PRO-12-29-01.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
13/NE/0339; First MREC approval date 18/12/2013

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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

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

Interventions
Participants will be randomly allocated to receive either two doses of sublingual GTN spray (800 mcg total) or a placebo spray (single time point of administration). There will be a 6-week postnatal follow-up.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Glyceryl trinitrate

Primary outcome measure
Primary outcomes will be measured over four interrelated domains: clinical, safety, patient-sided and economic.
1. Clinical: need for MROP, defined as the placenta remaining undelivered 15 minutes post study treatment and/or being required within 15 minutes of treatment due to safety concerns
2. Safety: measured blood loss between administration of treatment and transfer to the postnatal ward or other clinical area (e.g., labour ward high dependency) - up to 24 hours
3. Patient-sided: satisfaction with treatment and side effect profile assessed by postal questionnaire at 6 weeks postnatal
4. Economic: net incremental costs (or cost savings) to the National Health Service of using GTN versus standard practice. Costs will include GTN (dose and time to administer drug, monitor woman and deliver the placenta if effective), MROP, and further health service resource use as measured by the 6-week postnatal questionnaire

Secondary outcome measures
1. Clinical outcomes:
1.1. Fall in haemoglobin of more than 15% between recruitment and the first postnatal day (approximately 24 hours since the birth)
1.2. Time from randomisation to delivery of placenta (approximately 2 hours)

1.3. MROP in theatre (approximately 2 hours)
1.4. Need for earlier than planned MROP on the basis of the clinical condition (approximately 2 hours)
1.5. Fall in systolic or diastolic blood pressure of more than 15 mmHg and/or increase in pulse of more than 20 beats/minute between baseline and 5 and 15 minutes post-administration of active /placebo treatment (up to 15 minutes post-treatment)
1.6. Need for blood transfusion between time of delivery and discharge from hospital (up to 7 days)
1.7. Need for general anaesthesia (approximately 2 hours)
1.8. Maternal pyrexia (one or more temperature reading of more than 38°C (within 72 hours of delivery or discharge from hospital if discharge occurs sooner)
1.9. Sustained uterine relaxation after removal of placenta requiring uterotonics (within 24 hours of the time of delivery of the placenta)
2. Costs: the mean costs will be summarised by treatment allocation group, and the incremental cost (cost saving) associated with the use of GTN will be estimated using an appropriately specified general linear model. The cost data will be presented alongside the primary and secondary outcome data in a cost-consequence balance sheet, indicating which strategy each outcome favours (6-week postnatal questionnaire)

Overall study start date
01/04/2014

Completion date
01/10/2017

Eligibility

Key inclusion criteria
1. Women with retained placenta
2. Women aged 16 or over
3. Women with vaginal delivery (including women with a previous caesarean section)
4. Haemodynamically stable (systolic blood pressure more than 100mg Hg and pulse less than 110 beats per min).
5. > 14 weeks gestation

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
Planned Sample Size: 1100; UK Sample Size: 1100

Total final enrolment
1107

Key exclusion criteria
1. Unable to give informed consent
2. Suspected placenta accreta/increta/percreta
3. Multiple pregnancy
4. Women having an instrumental vaginal delivery in theatre
5. Allergy or hypersensitivity to nitrates or any other constituent of the formulation
6. Taken alcohol in the last 24 hours
7. Concomitant use with phosphodiesterase inhibitors (such as sildenafil, tadalafil,or vardenafil).
8. Contra-indication due to one of the following: Severe anaemia, constrictive pericarditis, extreme bradycardia, incipient glaucoma, Glucose-6-phosphatedehydrogenase-deficiency, cerebral haemorrhage and brain trauma,
aortic and / or mitral stenosis and angina caused by hypertrophic obstructive cardiomyopathy. Circulatory collapse, cardiogenic shock and toxic pulmonary oedema
9. Currently participating in another CTIMP

Date of first enrolment
01/09/2014

Date of final enrolment
01/10/2017

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
The Queen's Medical Research Institute
Room W1.14
47 Little France Crescent
Edinburgh
United Kingdom
EH16 4TJ

Sponsor information

Organisation
University of Edinburgh (UK)

Sponsor details
QMRI, 51 Little France Crescent
Edinburgh
Scotland

United Kingdom
EH16 4SA

Sponsor type
University/education

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

ROR
https://ror.org/01nrxwf90

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
01/07/2018

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	11/04/2016		Yes	No
Results article	results	01/06/2016		Yes	No
Results article	qualitative study results	24/05/2017		Yes	No
Results article	results	30/12/2019	31/12/2019	Yes	No
Results article	HTA report in	01/12/2019	09/01/2020	Yes	No
Results article	results	01/12/2019	22/10/2020	Yes	No
HRA research summary			28/06/2023	No	No