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Administering cryoprecipitate in obstetric bleeding at an earlier time

Submission date
15/01/2019

Recruitment status
No longer recruiting

Registration date
14/02/2019

Overall study status
Completed

Last Edited
05/05/2022

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
During childbirth it is normal to lose some blood; however, in very rare cases, the blood loss can be so severe that in order to stop the bleeding, blood transfusion is required. Bleeding that occurs within 24 hours of childbirth is called postpartum haemorrhage. During postpartum haemorrhage, levels of one important blood protein, called fibrinogen, reduce early. Fibrinogen is vital for clot formation and stopping the bleeding. During postpartum haemorrhage fibrinogen reduction is associated with poor outcomes for women. Therefore, it follows that if we replace fibrinogen early during postpartum haemorrhage, it is plausible that we could stop bleeding sooner and potentially improve outcomes for women. Replacement of fibrinogen can be achieved by administering blood transfusion with a blood product called cryoprecipitate. Currently, cryoprecipitate is given at a later stage of postpartum bleeding, and in some cases is not given at all. The aim of this study is to determine if it is feasible to administer cryoprecipitate early during postpartum haemorrhage, and also assess different aspects of the trial, with the view to informing the development of a large trial in the future.

Who can participate?
Pregnant women at over 24 weeks who are actively bleeding within 24 hours of childbirth, and for whom a blood transfusion is required to manage the active bleeding.

What does the study involve?
Four hospitals participate - two hospitals are randomly allocated to the intervention group and the other two to the control group. This means that all women who are delivering in hospitals that are part of the intervention group and who develop postpartum haemorrhage requiring blood transfusion will receive cryoprecipitate early, in addition to standard care. Women admitted to hospitals that are in the control group, and who develop postpartum haemorrhage that requires blood transfusion, will receive standard treatment, where cryoprecipitate is administered later in the course of bleeding, and in some cases not at all.

What are the possible benefits and risks of participating?
It is possible that participants receiving early cryoprecipitate might respond better, but at present it is not known if this will be the case. The information from this study will help improve and develop future studies, which in turn will help to improve the treatment of pregnant women

who experience PPH during childbirth in the future. No significant risks are expected with this study, as cryoprecipitate is already part of standard care.

Where is the study run from?
1. The Royal London University Hospital (UK)
2. Homerton University Hospital, London (UK)
3. Newham University Hospital, London (UK)
4. Whipps Cross University Hospital, London (UK)

When is the study starting and how long is it expected to run for?
July 2018 to April 2020

Who Is funding the study?
Barts Charity (UK)

Who is the main contact?
Dr Laura Green
ORCID ID: 0000-0003-4063-9768
Haematology Consultant,
The Royal London Hospital,
4th Floor Pathology and Pharmacy Building,
Newark St,
E1 2ES
Tel: +44 (0)2032460338
Email: Laura.green@bartshealth.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Dr Laura Green

ORCID ID
http://orcid.org/0000-0003-4063-9768

Contact details
Haematology Consultant
The Royal London Hospital
4th Floor Pathology and Pharmacy Building
Newark St
London
United Kingdom
E1 2ES
+44 (0)2032460338
Laura.green@bartshealth.nhs.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
39791

Study information

Scientific Title
The effect of early cryoprecipitate transfusion versus standard care in women who develop severe postpartum haemorrhage: a pilot cluster randomised trial

Acronym
ACROBAT

Study objectives
Can we deliver a large interventional trial in the future that will evaluate early fibrinogen replacement therapy in severe postpartum haemorrhage?

This pilot study will answer the above question by identifying barriers to recruitment, assessing feasibility and acceptability of the treatment, and fine-tune study procedures (such as data collection and administration of study treatment) for the definitive trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - Brighton & Sussex Research Ethics Committee, Health Research Authority, Ground Floor, Skipton House, 80 London Road, London, SE1 6LH, Tel: +44 (0)2071048129, Email: NRESCommittee.SECoast-BrightonandSussex@nhs.net, 15/01/2019, REC ref: 18/LO/2062

Study design
Randomised; Both; Design type: Treatment, Management of Care, Qualitative

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 to request a patient information sheet

Health condition(s) or problem(s) studied
Postpartum haemorrhage

Interventions
The study is a non-blinded, cluster randomised controlled pilot study where four hospitals will participate – two sites will be randomised to the intervention group and two to the standard group.

Intervention arm: Hospitals randomised to the intervention arm will administer two pools of cryoprecipitate to any woman who develops primary postpartum haemorrhage and for whom at least one unit of red cell transfusion has been started to manage the bleeding. These two pools of cryoprecipitate will be administered in addition to standard major haemorrhage protocol.

Control arm: Hospitals randomised to the control arm will administer standard transfusion therapy, where cryoprecipitate is administered in accordance with national guidelines. In practice, the average time to cryoprecipitate transfusion is >90 minutes.

Intervention Type
Procedure/Surgery

Primary outcome measure
Proportion of women who were administered cryoprecipitate within 90 minutes of major haemorrhage protocol (MHP) activation, or request of the first unit of RBC transfusion (whichever is earlier)

Secondary outcome measures
1. Local rates of massive obstetric haemorrhage, measured as number of cases per week
2. Proportion of women who were recruited to the trial, and for whom complete outcomes were obtained
3. Proportion of women who were approached and did not consent to the trial
4. Proportion of women who were approached and agreed to routine data collection
5. Proportion of women where there was a study protocol violation
6. Time (in minutes) to first administration of cryoprecipitate from activation of MHP or request of first unit of RBC transfusion (whichever is earlier)
7. Preliminary clinical outcome data collected by accessing medical records between recruitment and hospital discharge (or until 28 days after recruitment, whichever is sooner); clinical outcome data that will be collected include: mortality (all cause), hysterectomy, surgical interventions to stop haemorrhage within 24 hrs, total transfusion requirements within 24 hours of first RBC unit issued to treat PPH, and until hospital discharge, transfusion-related reactions, length of stay (days) in high dependency unit, intensive care units and hospital, requirement for mechanical ventilation, any organ failure, symptomatic thrombotic events, which include: venous thromboembolism (i.e. pulmonary embolism, and/or deep vein thrombosis) and arterial thrombotic events (e.g. myocardial infarction or stroke).
8. Symptomatic thrombotic events (arterial or venous) up to 3 months after receiving the intervention
9. Mortality (all cause) up to 3 months after receiving the intervention
10. Maternal fatigue as measured by the Multidimensional Fatigue Inventory (MFI) questionnaire, completed between recruitment and discharge

11. Views of women on participation in a cluster randomised trial without advance consent, and of the intervention, through qualitative research interviews performed 3 months after discharge
12. Views of healthcare professionals involved in delivering the study interventions and overall study processes through qualitative research interviews taken during the recruitment period
13. The optimal infrastructure pathway and personnel for delivering the intervention, and identifying and recruiting patients within and outside working hours (i.e. transfusion laboratory or clinical areas) using thematic analysis from qualitative research
14. Haemostasis evaluated through the assessment of clotting factors and thrombin generation on blood samples collected as part of routine care between onset of bleeding and discharge

Overall study start date
01/07/2018

Completion date
10/04/2020

Eligibility

Key inclusion criteria
Pregnant women at >24 weeks gestation, who are actively bleeding within 24 hours of delivery, and for whom at least one unit of RBC has been started or transfused to stem active bleeding

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
Planned Sample Size: 200; UK Sample Size: 200

Total final enrolment
200

Key exclusion criteria
1. Women who decline blood transfusion in advance
2. Women with inherited Factor XIII
3. Women with inherited fibrinogen deficiency

Date of first enrolment
01/03/2019

Date of final enrolment
10/01/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
The Royal London Hospital
Whitechapel Rd
London
United Kingdom
E1 1BB

Study participating centre
Homerton University Hospital
Homerton Row
London
United Kingdom
E9 6SR

Study participating centre
Whipps Cross University Hospital
Whipps Cross Road
Leytonstone
London
United Kingdom
E11 1NR

Study participating centre
Newham University Hospital
Glen Road
Plaistow
London
United Kingdom
E13 8SL

Sponsor information

Organisation
Queen Mary University of London

Sponsor details
c/o Dr Mays Jawad
R&D Governance Operations Manager
Joint Research Management Office
5 Walden Street
London
England
United Kingdom
E1 2EF

Sponsor type
University/education

ROR
https://ror.org/026zzn846

Funder(s)

Funder type
Charity

Funder Name
Barts and the London Charity and Related Charities; Grant Code: MGU0371

Funder Name
Labcold Ltd

Results and Publications

Publication and dissemination plan
The trialists plan to publish the protocol in a peer reviewed journal. There are no plans to make available additional documents at this time. Planned publication of the results in a peer reviewed journal within 1 year after the trial end date. The trialists will also disseminate the findings to local pregnancy support groups via their patient and public involvement advisory group, Katie's Team and in different obstetric, haematology, and anaesthetic national and international annual conferences.

Intention to publish date
01/08/2021

Individual participant data (IPD) sharing plan
The datasets generated during the current study are available upon request from the chief investigator Dr Laura Green (laura.green@bartshealth.nhs.uk).

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	21/06/2020	06/01/2021	Yes	No
Results article		20/10/2021	11/11/2021	Yes	No
Other publications	qualitative interview findings on deferred consent	04/05/2022	05/05/2022	Yes	No
HRA research summary			28/06/2023	No	No