Early cryoprecipitate in major trauma haemorrhage: CRYOSTAT-2

| Submission date 19/04/2017 | Recruitment status No longer recruiting | [X] Prospectively registered | | |
|-------------------------------|---|--------------------------------|--|--|
| | | [X] Protocol | | |
| Registration date 24/04/2017 | Overall study status Completed | [X] Statistical analysis plan | | |
| | | [X] Results | | |
| Last Edited 07/05/2025 | Condition category Injury, Occupational Diseases, Poisoning | [] Individual participant data | | |

Plain English summary of protocol

Background and study aims

Major trauma is damage caused to the body by an external source, such as a car accident or stabbing. It accounts for a significant number of deaths in the UK, and is one of the most frequent causes of death in people under the age of 45. One of the most common causes of death in trauma patients is uncontrolled bleeding. At present, standard treatment for severe bleeding involves giving patients blood transfusions. Until recently one out of every two people who received a massive blood transfusion (more than 10 pints) would die from their injuries. Two important studies involving bleeding trauma patients have been conducted in the last five years showing that early intervention is more effective after injury and may help save lives. Patients who have severe bleeding after injury develop a problem with their clotting system which means that they tend to bleed more. One of the main problems is due to low levels of fibrinogen, a clotting protein normally circulating in the bloodstream. Fibrinogen acts as the 'glue' which holds a blood clot together and at low levels, blood clots don't form properly and bleeding can continue. Cryoprecipitate is a frozen blood component prepared from plasma (the liquid part of blood) and rich in fibrinogen. By giving patients cryoprecipitate early on to raise fibrinogen levels in bleeding trauma patients it may be possible to make blood clots more stable and reduce bleeding. The aim of this study is to find out whether or not giving cryoprecipitate treatment reduces death rates in trauma patients with severe bleeding.

Who can participate?

Trauma patients with severe bleeding who are taken to a Major Trauma Centre

What does the study involve?

Participants are randomly allocated to one of two groups. Those in the first group receive standard care, which involves being treated with large blood transfusions through a drip. Those in the second group are treated with cryoprecipitate before they are given the blood transfusions. Participants in both groups are followed up for survival rates until study day 28 and then for up to one year using the Office for National Statistics. The Trauma Audit Research Network administers questionnaires to assess quality of life six months after injury.

What are the possible benefits and risks of participating? There is a small chance that patients receiving cryoprecipitate early may raise their blood fibrinogen level higher than those receiving standard care and this may increase the risk of clots such as deep vein thrombosis (DVT), clots in the lungs, heart attacks and strokes. However, in small trauma studies to date there has been no evidence of an increased risk of developing clots. There are no anticipated additional risks associated with participating in this trial.

Where is the study run from? 23 NHS hospitals with Major Trauma Centres in England (UK)

When is the study starting and how long is it expected to run for? February 2017 to June 2022

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

Who is the main contact? Professor Karim Brohi k.brohi@gmul.ac.uk

Study website

https://cryostat2.co.uk/

Contact information

Type(s)

Public

Contact name

Prof Karim Brohi

ORCID ID

http://orcid.org/0000-0003-0643-8866

Contact details

Centre for Trauma Sciences Blizard Institute 4 Newark Street London United Kingdom E1 2AT +44 (0)20 7882 6175 k.brohi@gmul.ac.uk

Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

210735

ClinicalTrials.gov number

NCT04704869

Secondary identifying numbers

CPMS 34303, IRAS 210735

Study information

Scientific Title

CRYOSTAT-2: A multi-centre, randomised, controlled trial evaluating the effects of early high-dose cryoprecipitate in adult patients with major trauma haemorrhage requiring major haemorrhage protocol (MHP) activation

Acronym

CRYOSTAT-2

Study objectives

The primary aim of this study is to test whether early high-dose fibrinogen supplementation with cryoprecipitate reduces all-cause mortality at 28 days in adult trauma patients with haemorrhagic shock and active bleeding.

Ethics approval required

Old ethics approval format

Ethics approval(s)

South Central REC C - Oxford, 12/04/2017, ref: 17/SC/0164

Study design

Randomized controlled trial

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

Major trauma haemorrhage

Interventions

Adult Trauma patients admitting to recruiting Major Trauma Centres, who are eligible for the trial, will be entered into the trial using an emergency waiver of consent. Patients on arrival will be incapacitated as a result of their injuries and ongoing bleeding and therefore will be unable to provide informed consent. Professional consultees (physicians who are not part of the study team) will provide approval for the patient to continue in the study until such time it is possible to speak with the patient and/or their next of kin.

Participants will be randomised to one of two groups using opaque sealed randomisation envelopes to enable rapid access and timely recruitment in the emergency setting.

Control group: Participants receive care using the tandard major haemorrhage protocol only. This involves administering red blood cells, fresh frozen plasma and platelets following a major haemorrhage protocol (MHP) as part of a balanced resuscitation.

Intervention group: Participants receive early cryoprecipitate – 3 pools (equivalent to 15 single units cryoprecipitate or 6g fibrinogen supplementation), infused as rapidly as possible, within 90 minutes of admission in addition to the standard (local) major haemorrhage

Patients will be followed up for death up until study day 28 and for up to 1 year post admission with the Office for National Statistics. Follow up for quality of life will be undertaken at 6 months post injury via the Trauma Audit Research Network.

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Cryoprecipitate

Primary outcome measure

All-cause mortality at 28 days as documented and confirmed in the patients medical notes by attending physicians. The primary cause of death will be documented and if possible categorised according to the following clinical causes:

- 1. Uncontrolled bleeding
- 2. Vascular occlusion (myocardial infarction, stroke)
- 3. Pulmonary embolism
- 4. Multi-organ failure
- 5. Traumatic brain injury
- 6. Multiple injury
- 7. Sepsis
- 8. Other (reason)

Secondary outcome measures

- 1. All-cause mortality (including death from bleeding) at 6 hours, 24 hours, 6 months and 12 months from admission as record in the patients medical notes during their admission and captured by the Office for National Statistics for up to 1 year post admission
- 2. Death from bleeding at 6 hours and 24 hours as recorded in the patients medical notes
- 3. Transfusion requirements, in numbers of units, for RBC, platelets, FFP & cryoprecipitate at 24 hours from admission, including pre-hospital transfusion as recorded in the patients medical

notes

- 4. Destination of participant at time of discharge from hospital as recorded by the research team
- 5. Quality of life measures: EQ5D-5L and Glasgow Outcome Score at discharge and 6 months after injury captured by patient questionnaires administrated by the Trauma Audit Research Network
- 6. Hospital resource use up to discharge or day 28, including blood transfusions, surgical procedures, ventilator days, hours spent in critical care and in-patient stays measured by clinical data captured by the research teams in the Case Report Forms

Overall study start date

07/02/2017

Completion date

30/06/2022

Eligibility

Key inclusion criteria

- 1. The participant is judged to be an adult (according to local practice, e.g. 16 years or older in UK) and has sustained severe traumatic injury
- 2. Deemed by the attending clinician to have on-going active haemorrhage
- 3. Requires activation of the local major haemorrhage protocol for management of severe blood loss
- 4. Has started or received at least one unit of any blood component

Participant type(s)

Patient

Age group

Adult

Sex

Both

Target number of participants

Planned Sample Size: 1600

Total final enrolment

1604

Key exclusion criteria

- 1. The participant has been transferred from another hospital
- 2. The trauma team leader deems the patient inappropriate for the trial i.e. injuries deemed to be incompatible with life
- 3. More than 3 hours have elapsed from the time of injury

Date of first enrolment

01/07/2017

Date of final enrolment

Locations

Countries of recruitment

England

Northern Ireland

United Kingdom

United States of America

Wales

Study participating centre Royal London Hospital

Whitechapel London United Kingdom E1 1BB

Study participating centre John Radcliffe Hospital

Headley Way Oxford United Kingdom OX3 9UD

Study participating centre Southampton Hospital

Tremona Road Southampton United Kingdom SO16 6YD

Study participating centre St George's Hospital

Blackshaw Road London United Kingdom SW17 0QT

Study participating centre St Mary's Hospital

Praed Street London United Kingdom W2 1NY

Study participating centre Derriford Hospital

Derriford Road Plymouth United Kingdom PL6 8DH

Study participating centre Addenbrooke's Hospital

Hills Road Cambridge United Kingdom CB2 0QQ

Study participating centre Southmead Hospital

Southmead Road Bristol United Kingdom BS10 5NB

Study participating centre James Cook University Hospital

Marton Road Middlesbrough United Kingdom TS4 3BW

Study participating centre Leeds General Infirmary

Great George St Leeds United Kingdom LS1 3EX

Study participating centre Queen's Medical Centre

Derby Road Nottingham United Kingdom NG7 2UH

Study participating centre Royal Victoria Infirmary

Queen Victoria Road Newcastle-upon-Tyne United Kingdom NE1 4LP

Study participating centre Hull Royal Infirmary

Anlaby Road Hull United Kingdom HU3 2JZ

Study participating centre Northern General Hospital

Herries Road Sheffield United Kingdom S5 7AU

Study participating centre Queen Elizabeth Hospital

Mindelsohn Way Birmingham United Kingdom B15 2TH

Study participating centre

Royal Preston Hospital

Sharoe Green Lane Preston United Kingdom PR2 9HT

Study participating centre Royal Sussex County Hospital

Eastern Road Brighton United Kingdom BN2N 5BE

Study participating centre University Hospital

Clifford Bridge Road Coventry United Kingdom CV2 2DX

Study participating centre University Hospital of North Staffordshire

Newcastle Road Stoke on Trent United Kingdom ST4 6QG

Study participating centre Salford Royal Hospital

Scott Lane Manchester United Kingdom M6 8HD

Study participating centre Manchester Royal Infirmary

Oxford Road Manchester United Kingdom M13 9WL

Study participating centre University Hospital Aintree

Lower Lane Liverpool United Kingdom L9 7AL

Study participating centre Kings College Hospital

Mapother House De Crespigny Park Denmark Hill London United Kingdom SE5 8AB

Study participating centre Royal Victoria Hospital

274 Grosvenor Rd Belfast United Kingdom BT12 6BA

Study participating centre University Hospital of Wales

Heath Park Cardiff United Kingdom CF14 4XW

77030

Study participating centre University of Texas Health Science Center, Houston 7000 Fannin Street Houston United States of America

Sponsor information

Organisation

Queen Mary University of London

Sponsor details

JRMO
QMUL Innovation Department
5 Walden Street
London
England
United Kingdom
E1 2EF
+44 20 7882 7265
sponsorsresp@bartshealth.nhs.uk

Sponsor type

University/education

ROR

https://ror.org/026zzn846

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

Planned publication in a high-impact peer reviewed journal in 2022

Intention to publish date

31/12/2023

Individual participant data (IPD) sharing plan

The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

| Output type HRA research summary | Details | Date created | Date added 28/06/2023 | Peer reviewed? No | Patient-facing? No |
|---|-------------|--------------------------|--|-----------------------------|-----------------------|
| Protocol file | version 4.0 | 15/02/2022 | 11/10/2023 | No | No |
| Statistical Analysis Plan | version 2.0 | 20/05/2022 | 11/10/2023 | No | No |
| Basic results Results article Results article | | 12/10/2023 01/11/2024 | 13/10/2023 16/10/2023 07/05/2025 | No Yes Yes | No No No |