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Early cryoprecipitate in major trauma haemorrhage: CRYOSTAT-2

Submission date	Recruitment status
19/04/2017	No longer recruiting
Registration date	**Overall study status**
24/04/2017	Completed
Last Edited	**Condition category**
07/05/2025	Injury, Occupational Diseases, Poisoning

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] 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@qmul.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@qmul.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

03/11/2021

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

Study participating centre
University of Texas Health Science Center, Houston
7000 Fannin Street
Houston
United States of America
77030

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	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	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			13/10/2023	No	No
Results article		12/10/2023	16/10/2023	Yes	No
Results article		01/11/2024	07/05/2025	Yes	No