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A study comparing pre-hospital administration of packed red blood cells and freeze-dried plasma with administration of normal saline in patients with low blood pressure after major injuries

Submission date
11/07/2016

Recruitment status
No longer recruiting

Registration date
11/07/2016

Overall study status
Completed

Last Edited
02/09/2024

Condition category
Injury, Occupational Diseases, Poisoning

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

Plain English summary of protocol

Background and study aims
Major trauma accounts for a significant number of deaths worldwide, and is one of the most frequent causes of death in people under the age of 40. A large number of these deaths are caused by major bleeding as a result of the trauma (traumatic haemorrhage). Patients with traumatic heamorrhage are currently given clear fluids but military and civilian research suggests that survival increases if hospital patients receive blood products (red blood cells and freeze-dried plasma) instead. The best treatment for bleeding patients before reaching hospital is uncertain. Giving too much fluid to improve blood pressure can increase bleeding. Therefore only small amounts of clear fluid are given. Some pre-hospital doctors now give red blood cells instead. Animal research suggests that this is better than clear fluids, and that adding plasma is better still. Some studies in humans support this however other research has found no benefit. There is currently no good quality evidence exists to show whether giving blood products before hospital, saves lives. The aim of this study is to find out whether giving blood products to badly injured adult patients, before reaching hospital improves their clinical condition and survival.

Who can participate?
Patients believed to be over the age of 16 who have sustained a serious injury leading to major blood loss.

What does the study involve?
Participants are randomly allocated to one of two groups at the scene of the emergency. Those in the first group receive fluids through a drip, with up to four bags of normal saline (salt water). Those in the second group receive two units of concentrated red blood cells and two units of freeze dried plasma (straw like fluid that makes up the liquid part of blood). Participants in both groups are followed up for 30 days to find out if any patients died (of their injuries or otherwise), as well as the speed they are able to clear lactic acid from their tissues (indicator of good blood

flow). Blood pressure, heart rate, blood clotting and whether patients need organ support are also monitored while they are on intensive care.

What are the possible benefits and risks of participating?
There are no guaranteed direct benefits involved with participating in this study however the blood product treatment could be shown to be more effective than standard treatment. There are no notable risks involves for those participating in this study.

Where is the study run from?
Pre-hospital emergency medicine and major trauma centres in the West Midlands, Dorset & Somerset and in the East of England (UK)

When is the study starting and how long is it expected to run for?
October 2015 to April 2020

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

Who is the main contact?
Miss Gemma Slinn, rephill@trials.bham.ac.uk

Contact information

Type(s)
Public

Contact name
Miss Gemma Slinn

Contact details
Birmingham Clinical Trials Unit
University of Birmingham
Birmingham
United Kingdom
B15 2TT
+44 121 415 9100
rephill@trials.bham.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2015-001401-13

Protocol serial number
31157

Study information

Scientific Title

A multi-centre randomised controlled trial of pre-hospital blood product administration versus standard care for traumatic haemorrhage

Acronym
RePHILL

Study objectives
The aim of this study is to investigate whether giving blood products (red blood cells and freeze-dried plasma) to badly injured adult patients, before reaching hospital improves their clinical condition and survival.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central - Oxford C Research Ethics Committee, 15/12/2015, ref: 15/SC/0691

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Treatment, Drug

Study type(s)
Treatment

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

Interventions
Participants are randomised in a 1:1 ratio to receive:

Crystalloid resuscitation: Consisting of up to 4 x 250 mL bags of 0.9% sodium chloride (normal saline). These will be administered as boluses of 250 mL to maintain a radial pulse

Pre-Hospital Blood Products (BHBP) resuscitation: Consisting of up to 2 units of PRBC and 2 units of LyoPlas. These will be administered as boluses consisting of a single unit of blood product, given in the sequence: PHBP, LyoPlas, PHBP, LyoPlas.
LyoPlas N-w is a freeze dried plasma product derived from a single donation and is licenced for use in the same indication as fresh frozen plasma. LyoPlas N-w is licensed for use in Germany as a medicinal product under the Marketing Authorisation Number PEI.H.03075.01.1.
PRBC are a concentrated preparation of red blood cells that is obtained from whole blood by removing the plasma (as by centrifugation). The PRBC used in RePHILL will be blood group O, RhD negative, Kell negative from NHS Blood and Transplant national stocks supplied by the blood banks that are supporting this trial.

Patients receive the trial interventions on-scene, because of the emergency nature of this trial, patients are considered randomised when the transport box containing the interventions is opened. Follow-up will comprise of standard care follow-up for patients that have a traumatic injury, no further trial-specific procedures will be undertaken after the delivery of the

interventions but we will collect data pertaining to the RePHILL outcome measures for up to 30 days post-injury.

Intervention Type
Other

Phase
Phase III

Primary outcome(s)
1. 1. Episode mortality is measured by whether or not the patient is still alive up to 30 days post injury up to 30 days post injury
2. Lactate clearance is measured by obtaining a lactate measurement at randomisation and a repeat measurement two hours post-randomisation

Key secondary outcome(s)
1. All-cause mortality rate is measured by whether or not the patient is still alive within 3 hours of randomisation
2. Pre-hospital time and type and volume of fluid is measured by the pre-hospital emergency medical team at on-scene.
3. Vital signs (systolic blood pressure, heart rate, capillary oxygen saturation) are measured at scene, on arrival at ED and at 2, 6, 12 and 24 hours after arrival at ED
4. Venous lactate concentration is measured by the receiving hospital medical team on arrival at ED and at 2 hours after arrival at ED
5. Trauma-induced coagulopathy (defined as International Normalised Ratio (INR) >1.5) is measured by measuring clotting factors on arrival at ED and at 2 and 6 hours after arrival at ED
6. Coagulation is measured using viscoelastically by rotational thromboelastometry on arrival at ED
7. Platelet function is measured using multiple electrode impedence aggregometery on arrival at ED
8. 8. Total blood product receipt is measured by recording fluids given to the patient at 6, 12 and 24 hours after arrival at ED
9. Acute respiratory distress syndrome (ARDS) is measured by the presence of clinical symptoms within the first 7 days after injury
10. Transfusion-related complications are measured by the presence of clinical symptoms up to 30 days post injury
11. Organ failure-free days are measured using the Sepsis-related Organ Failure Assessment (SOFA) score up to 30 days post injury

Completion date
31/05/2021

Eligibility

Key inclusion criteria
1. Traumatic injury
2. Pre-Hospital Emergency Medical team attend
3. Hypotension (SBP <90mmHg or absence of palpable radial pulse) believed to be due to traumatic haemorrhage

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
432

Key exclusion criteria
1. Children (known or apparently aged <16 years)
2. Refusal of blood product administration; known Jehovah's Witness
3. Pregnancy (known or apparent)
4. Isolated head injury

Date of first enrolment
01/10/2016

Date of final enrolment
31/12/2020

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Birmingham
United Kingdom
B15 2WB

Study participating centre
West Midlands Ambulance Service NHS Foundation Trust
Trust Headquarters
Millennium Point
Waterfront Business Park
Waterfront Way

Brierley Hill
United Kingdom
DY5 1LX

Study participating centre
West Midlands Air Ambulance/ MERIT
Midlands Air Ambulance Charity
Hawthorn House
Dudley Road
Stourbridge
United Kingdom
DY9 8BQ

Study participating centre
Warwickshire and Northamptonshire Air Ambulance
The Air Ambulance Service
Hazell House
Burnthurst Lane
Princethorpe
United Kingdom
CV23 9QA

Study participating centre
Yorkshire Ambulance Service
Headquarters, Springhill
Brindley Way
Wakefield 41 Business Park
Wakefield
United Kingdom
WF2 0XQ

Study participating centre
Yorkshire Air Ambulance
Cayley House
10 South Lane
Elland
United Kingdom
HX5 0HQ

Study participating centre

East of England Ambulance Service NHS Trust
East of England Ambulance Service NHS Trust Headquarters
Whiting Way
Melbourn
Melbourn
United Kingdom
SG8 6EN

Study participating centre
MAGPAS
Centenary House
St. Mary's Street
Huntingdon
United Kingdom
PE29 3PE

Study participating centre
East Anglian Air Ambulance
Hangar E
Gambling Close
Norwich Airport
Norwich
United Kingdom
NR6 6EG

Study participating centre
Essex & Herts Air Ambulance
Essex and Herts Air Ambulance Trust
Flight House
Earls Colne Business Centre
Earls Colne Business Park
Earls Colne
Colchester
United Kingdom
CO6 2NS

Study participating centre
East Midlands Ambulance Service NHS Trust
Trust Headquarters
1 Horizon Place
Mellors Way
Nottingham Business Park
Nottingham

United Kingdom
NG8 6PY

Study participating centre
Derbyshire, Leicestershire and Rutland Air Ambulance
35 King Street
Belper
United Kingdom
DE56 1PX

Study participating centre
Warwickshire and Northamptonshire Air Ambulance
The Air Ambulance Service
Hazell House
Burnthurst Lane
Princethorpe
United Kingdom
CV23 9QA

Study participating centre
University Hospitals Coventry and Warwickshire NHS Trust
University Hospital
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Study participating centre
University Hospitals of North Midlands NHS Trust
Royal Stoke University Hospital
Newcastle Road
Stoke-on-Trent
United Kingdom
ST4 6QG

Study participating centre
North Bristol NHS Foundation Trust
Southmead Hospital
Southmead Road
Westbury-on-Trym
Bristol

United Kingdom
BS10 5NB

Study participating centre
The Leeds Teaching Hospital NHS Trust
Leeds General Infirmary
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
South Tees Hospital NHS Foundation Trust
James Cook Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
Hull and East Yorkshire Hospitals NHS Trust
Hull Royal Infirmary
Anlaby Road
Hull
United Kingdom
HU3 2JZ

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Northern General Hospital
Herries Road
Sheffield
United Kingdom
S5 7AU

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Addenbrooke's Hospital
Cambridge Biomedical Campus
Hills Road
Cambridge

United Kingdom
CB2 0QQ

Study participating centre
Norfolk & Norwich University Hospitals NHS Foundation Trust
Norfolk and Norwich University Hospital
Colney Lane
Norwich
United Kingdom
NR4 7UY

Study participating centre
Nottingham University Hospitals NHS Trust
Queen's Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Sponsor information

Organisation
University Hospitals Birmingham NHS Foundation Trust

ROR
https://ror.org/014ja3n03

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

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available

Previous participant exclusion criteria:
Planned publication in a high-impact peer reviewed journal. A protocol paper will be published within the next six months.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		04/03/2022	11/03/2022	Yes	No
Results article		01/01/2024	02/09/2024	Yes	No
Protocol article	protocol	01/10/2018	06/03/2020	Yes	No
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes