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Royal London Major Trauma Centre
Bart’s Health NHS Trust

www.c4ts.qmul.ac.uk
iTACTIC
Implementing Treatment Algorithms for the Correction of Trauma Induced Coagulopathy
## iTACTIC
Implementing Treatment Algorithms for the Correction of Trauma Induced Coagulopathy

| FIBRINOGEN | If FIBTEM CA5 < 10mm  
Give additional 4g equivalent of fibrinogen  
*(As Cryoprecipitate or Concentrate)* |
|---|---|
| PLATELETS | If (EXTEM CA5 - FIBTEM CA5) < 30mm  
Give 1 additional pool of platelets |
| PLASMA | If EXTEM CA5 >40mm **AND** EXTEM CT >80s  
Give 4 additional units of plasma |
| TRANEXAMIC ACID | If EXTEM LI30 <85%  
Give additional 1g IV bolus of tranexamic acid |
PREHOSPITAL FEASIBILITY STUDY

LONDON'S AIR AMBULANCE

NHS
Barts Health
NHS Trust

London Major Trauma System

NHS
Blood and Transplant
LEUCO-DEPLETED RED CELLS IN PLASMA

Male donor

Blood group O RhD negative, and Kell negative

High Titre negative for anti-A and anti-B antibodies

Collected in CPD and stored at 4 ±2°C

14 day shelf life
RC & PLASMA STUDY

PRIMARY objective = feasibility & wastage (n=140)

Day 10-14 recycled into ED

SECONDARY objectives

✓ 2015-2018 (LAA patients with RBC only)
✓ RBC + FFP in prehospital
  • Resuscitative effect (base excess, lactate) & coagulation
  • Haemolysis
  • Patient outcomes – transfusion, mortality, length of stay

→ NHSBT logistics, future demand?
RC & PLASMA PATIENTS

Nov 2018 – May 2019

64 patients have received RC&P

PLE at scene 12
RLH 31
SMH 13
KCH 5
SGH 3

Comparator sites = 53 patients
CRYO-STAT-2
EARLY CRYOPRECIPITATE IN TRAUMA
EVERY MTC

Major Trauma Centres in England
October 2016

Adult & Children’s MTCs
1: Addenbrooke’s Hospital Cambridge
2: James Cook University Hospital Middlesborough
3: John Radcliffe Hospital Oxford
4: St Mary’s Hospital London
5: St George’s Hospital London
6: Royal London Hospital
7: King’s College Hospital London
8: Leeds General Infirmary
9: Queen’s Medical Centre Nottingham
10: Royal Victoria Infirmary Newcastle
11: Southampton General Hospital

Adult MTCs
12: Southmead Hospital Bristol
13: Aintree University Hospital Liverpool
14: Derriford Hospital Plymouth
15: Hull Royal Infirmary
16: Northern General Hospital Sheffield
17: Queen Elizabeth Hospital Birmingham
18: Royal Preston Hospital Lancashire
19: Royal Sussex County Hospital Brighton
20: University Hospital Coventry
21: University Hospital of North Staffordshire Stoke on Trent
22: Salford Royal Hospital and Manchester Royal Infirmary (Collaborative)
Coagulopathy, cryoprecipitate and CRYOSTAT-2: realising the potential of a nationwide trauma system for a national clinical trial

M. Marsden, J. Benger, K. Brohi, N. Curry, C. Foley, L. Green, J. Lucas, A. Rossetto, S. Stanworth, H. Thomas, R. Davenport on behalf of the CRYOSTAT-2 investigators

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*Corresponding author. E-mail: max.marsden@nhs.net
584 patients!!!

>50% of UK recruitment (1142 patients)

= 37% of overall recruitment (1568 patients)
CRYOSTAT Mortality

Standard: 6/21 : 28%
Early CRYO: 2/20 : 10%
STUDY DESIGN

Randomised, un-blinded, controlled trial

Study groups
  – 3 pools of cryoprecipitate (~6g fibrinogen) plus MHP
  – Standard MHP alone

1568 patients in UK and USA

PRIMARY OUTCOME = 28 day mortality
INCLUSION CRITERIA

Adult trauma patients

On-going active haemorrhage

and requires

Activation of the local MHP

and has started

At least one unit of any blood component
LMTS = 41%
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

About the trial

Worldwide, it is estimated that 5.8 million people die annually from trauma with most of those who die under the age of 45. For the same age group that is more than cancer, HIV/AIDS and heart disease

Twitter @CRYOSTAT_2
Email CRYOSTAT2@nhsbt.nhs.uk
Website www.cryostat2.co.uk
Interim analysis

- Interim analysis for DMC (data to 31 January 2019)
- First site opened July 2017 (SGH)
- 419 patients randomised
- 338 patients analysed (CRF available)
- 185 patients with primary outcome (28 day mortality) data available
- HTA UK target: 496 patients (enrolled = 85% of UK predicted)
Allocated to: Early Cryoprecipitate (3 pools) within 90 minutes of admission plus standard major haemorrhage therapy (n=175)
- Received allocated intervention (n=117)
  - Did not receive allocated intervention
    - Cryoprecipitate given beyond 90m (n=21)
    - No active bleeding (n=16)
    - Less than 3 pools (n=4)
    - Patient died (n=5)
    - Other reason cryo not given (n=11)
    - Reason unavailable (n=1)

Allocated to: Standard Major Haemorrhage Therapy Alone† (n=163)
- Received allocated intervention (n=163)

Follow-Up
- Lost to follow-up (n=3)
  - Not reached time point yet (n=1)
  - Completed study before day 24 (n=69)
  - No follow-up information (n=1)
  - Withdrawn (n=6)

Analysis
- 28-day outcome analysis (n=95)

Follow-Up
- Lost to follow-up (n=5)
  - Not reached time point yet (n=1)
  - Completed study before day 24 (n=64)
  - No follow-up information (n=1)
  - Withdrawn (n=2)

Analysis
- 28-day outcome analysis (n=90)
Patients

<table>
<thead>
<tr>
<th>Subjects</th>
<th>(n=338)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>261 (77)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>42 (27-56)</td>
</tr>
<tr>
<td>Time from injury to admission (mins)</td>
<td>78 (60-103)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Injuries and physiology at admission</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Blunt trauma</td>
<td>229 (68)</td>
</tr>
<tr>
<td>Injury Severity Score</td>
<td>29 (17-42)</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>98 (81-125)</td>
</tr>
<tr>
<td>Heart rate (per min)</td>
<td>106 (84-126)</td>
</tr>
<tr>
<td>Glasgow Coma Score</td>
<td>14 (3-15)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pre admission</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC (units)</td>
<td>0 (0-1)</td>
</tr>
<tr>
<td>FFP (units)</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Crystalloids (ml)</td>
<td>0 (0-300)</td>
</tr>
<tr>
<td>TXA administered</td>
<td>252 (75)</td>
</tr>
</tbody>
</table>
# Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 hour mortality rate (%)</td>
<td>31 (9)</td>
</tr>
<tr>
<td>24 hour mortality rate (%)</td>
<td>39 (12)</td>
</tr>
<tr>
<td>~28 day mortality (%)</td>
<td>90 (26)</td>
</tr>
<tr>
<td>Hospital stay</td>
<td>14 days</td>
</tr>
<tr>
<td>Blood product use in first 24 hours</td>
<td></td>
</tr>
<tr>
<td>RBC</td>
<td>4 (3-8)</td>
</tr>
<tr>
<td>FFP</td>
<td>4 (2-6)</td>
</tr>
<tr>
<td>Platelets</td>
<td>0 (0-1)</td>
</tr>
<tr>
<td>Cryoprecipitate</td>
<td>2 (0-3)</td>
</tr>
<tr>
<td>Number of SAEs (n)</td>
<td>122</td>
</tr>
<tr>
<td>Number of patients &gt;1 SAE</td>
<td>118</td>
</tr>
<tr>
<td>Average number of SAEs per patient (n)</td>
<td>0.30</td>
</tr>
</tbody>
</table>

~43% deaths occurred in first 24 hours
## Cause of death

<table>
<thead>
<tr>
<th>Cause</th>
<th>N (%)</th>
<th>(n=338)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multi-organ failure</td>
<td>7 (2)</td>
<td>90 (26)</td>
</tr>
<tr>
<td>Multiple injury</td>
<td>16 (5)</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (&lt;1)</td>
<td></td>
</tr>
<tr>
<td>Traumatic brain injury</td>
<td>30 (9)</td>
<td></td>
</tr>
<tr>
<td>Uncontrolled bleeding</td>
<td>23 (7)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>13 (4)</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>90 (26)</td>
</tr>
</tbody>
</table>
# Thromboembolic Events

<table>
<thead>
<tr>
<th>Event</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT</td>
<td>10</td>
</tr>
<tr>
<td>Ischaemic Stroke</td>
<td>3</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary embolus</td>
<td>14</td>
</tr>
<tr>
<td>Other occlusion of any other artery</td>
<td>4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>32 (9%)</strong></td>
</tr>
</tbody>
</table>

(n=338)
CRYOSTAT-2 Recruitment by site to 07/05/2019

- St. George’s: 22
- St. Mary’s Southampton: 20
- Sheffield: 18
- Oxford: 18
- Birmingham: 17
- Coventry: 17
- King’s College: 16
- Plymouth: 14
- Newcastle: 14
- Cambridge: 13
- Bristol: 12
- Middlesbrough: 11
- Hull: 10
- Nottingham Royal London: 9
- Brighton: 8
- Preston: 7
- Leeds: 6
- Salford: 5
- Stoke: 3
- Liverpool: 3
- Manchester: 0
Time to intervention

• Trial protocol (3 pools cryoprecipitate with first started 90 minutes after arrival in hospital)

• Received first pool of cryoprecipitate within 90 minutes of arrival at hospital = 69%

• Real world vs clinical trial

• Focus efforts on modifiable areas we can improve
USA update

• 4 sites will **FINALLY** come on board Summer/Autumn 2019
  – UT Health, Houston
  – Ben Taub, Houston
  – Shock Trauma, Baltimore
  – LA County

• Predicted recruitment to be >5 per site per month = 240/year

• Currently 193 patients behind target (no sites open to date)
  → likely 6+ month trial extension
#CRYOSTAT-2 is the most BIGGEST clinical trial for major haemorrhage EVER done in trauma ...ANYWHERE!!! YOU are THE BEST. #makeCRYOGreatAgain