Significant Improvement In The Management Of Major Obstetric Haemorrhage With A Rotem Guided Algorithm Using Fibrinogen Concentrate

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Clinical Lead for Blood Transfusion
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Background
Largest maternity unit in the UK
(used to be – other units may have caught us up now!)

• Total number of women delivered in 2013 were 7983
• Total caesarean sections were 2060 (~25.8%)
  – Electives – 957
  – Emergencies - 1103

Univeristy of Liverpool
Liverpool Women's NHS Foundation Trust
Largest maternity unit in the UK

Handicapped by:

- On site haematology lab **only** available between
  - 0830 hrs and 2100 hrs Monday to Friday, and
  - 0830 to 1300 hrs on Saturday.

- Outside of these hours, our laboratory is at the Royal Liverpool University Hospital, 1.3 miles down the road.
Liverpool Women’s Hospital
‘Tweaks & fixes to cope’
And in April 2011…

We adopted the NWRTC recommendations for massive haemorrhages

• Requesting ‘shock packs’ with PRCs:FFP: platelets in a ratio of 4:4:1 at the start when a massive bleed is diagnosed

• Made it easy to order and obtain blood products for all cases of major obstetric haemorrhage
Also in April 2011,
Interim retrospective analysis

Looking at 64 patients who had already triggered MOH pathway i.e >1500 ml blood loss

![Pie chart showing 30 patients with MCF < 15 and 34 patients with MCF ≥ 15]
Haemostatic impairment in PPH

Varies in severity depending on the cause:

<table>
<thead>
<tr>
<th>Obstetric complication</th>
<th>Mechanism of haemostatic compromise</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dilutional</td>
</tr>
<tr>
<td>Trauma</td>
<td>+</td>
</tr>
<tr>
<td>Surgery</td>
<td>++</td>
</tr>
<tr>
<td>Atony</td>
<td>++</td>
</tr>
<tr>
<td>Placental abruption</td>
<td>+</td>
</tr>
<tr>
<td>Placenta praevia/accreta</td>
<td>++</td>
</tr>
<tr>
<td>Amniotic fluid embolus</td>
<td>+</td>
</tr>
</tbody>
</table>
Can FibTEM be relied on?

Mean [95% CI] number of units transfused

<table>
<thead>
<tr>
<th></th>
<th>Blood</th>
<th>FFP</th>
<th>Cryo</th>
<th>Platelets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MCF &lt; 15</strong></td>
<td>3.7***</td>
<td>2.6</td>
<td>0.9</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>[2.1 – 4.9]</td>
<td>[1.3-3.3]</td>
<td>[0.26-1.3]</td>
<td>[0-0.5]</td>
</tr>
<tr>
<td><strong>MCF ≥ 15</strong></td>
<td>0.8***</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>[0.2-1.1]</td>
<td>[0-0]</td>
<td>[0-0]</td>
<td>[0-0]</td>
</tr>
</tbody>
</table>

Statistics to show the difference between each group
*P<0.05  ** <0.01  ***<0.001
• However, it takes 30 to 40 minutes to get the MCF value!

• Until then, most algorithms involving ROTEM values used MCF values to guide decision making.
FibTEM A5 vs MCF

R=0.963, p<0.0001
Evaluation of practice at the end of one year in March 2012:

- **ROTEM (√)**
  - A reliable ‘point of care’ test for coagulopathy
  - Easily taught & performed even by trainees rotating every 3 months
  - Even better than expected because we could get reliable results in just over 5 minutes!

- **Shock packs (??)**
  - Still needed time for xmatch, defrosting and transport
  - Wastage when ROTEM indicated they were not needed
So we now had a rapid test to confirm coagulopathy!

The rate limiting factor now was the defrosting time for products
There was a ‘new kid on the block’!!

Was only licensed for use in congenital hypofibrinogenemia

Any other use has to be on a named patient basis.

Expensive at £340 per g
So by July 2012

‘We (too!) wanted it quick & we wanted it now!’

(apologies to Dr Jakob Stensballe or anyone else here from Copenhagen for having pinched your slogan!)
Transfusion Management of Massive Haemorrhage in Obstetrics

Activation Protocol:
- Call 2222
- Alert Emergency Response Team (including blood transfusion laboratory, portering/transport staff)
- Consultant involvement
- Resuscitate Airway Breathing Circulation
- Move patient to HDU when safe to do so
- Take bloods and send to lab:
  - XM, FBC, PT, APTT, fibrinogen, U+E, Ca²⁺
  - NPT: ABG, ROTEM
  - Order MHP 1
    - Red cells* 4 units
    - FFP 4 units
    - Platelets 1 dose (ATD)
    - (*Emergency O blood, group specific blood, XM blood depending on availability)
- Give MHP 1
- Reassess
  - Suspected continuing haemorrhage requiring further transfusion
  - Take bloods and send to lab:
    - FBC, PT, APTT, fibrinogen, U+E, Ca²⁺
    - NPT: ABG, ROTEM
- Order Products:
  - According to ROTEM or Order MHP 2
    - Red cells 4 units
    - FFP 4 units
    - Platelets 1 dose (ATD)
    - Request Cryoprecipitate 2 packs if fibrinogen <2
- Give MHP 2
- Once MHP 2 administered, repeat bloods:
  - FBC, PT, APTT, fibrinogen, U+E, NPT: ABG, TEG if available
  - To inform further blood component requesting

Aims for therapy:
- Aim for:
  - Hb: 8-10 g/dl
  - Platelets: >75 x 10⁹/l
  - PT ratio: < 1.5
  - APTT ratio: < 1.5
  - Fibrinogen: >2 g/l
  - Ca²⁺: >1 mmol/l
  - Temp: > 36°C
  - pH: > 7.35 (on ABG)
  - Monitor for hyperkalaemia

Prevent Hypothermia
- Consider Calcium Chloride
- Continuous cardiac monitoring

Stand Down
- Inform lab
- Return unused components
- Complete documentation
- Include audit proforma

Thromboprophylaxis should be considered when patient stable

ABG – Arterial Blood Gas
FFP – Fresh Frozen Plasma
PT – Prothrombin Time
APTT – Activated partial thromboplastin time
MHP – Massive Haemorrhage Pack
TEG/ROTEM – Thromboelastography
ATD – Adult Therapeutic Dose
NPT – Near Patient Testing
XM – Crossmatch

STOP THE BLEEDING

Haemorrhage Control
- Bimanual compression
- Ergometrine 500 micrograms IV
- Syntocinon 10 IU IV
- 40 IU infusion
- Check placenta and for trauma
- Carboprost IM
- EUT
- Tamponade
- Compression sutures
- Hysterectomy

Haemostatic Drugs
- Vit K and Prothrombin complex concentrate for warfarinised patients and other haemostatic agents: discuss with Consultant Haematologist

Cell salvage if available and appropriate
- Consider ratios of other components:
  - 1 unit of red cells = c.250 ml salvaged blood

Blood Courier
- 07717 516 171
- Consultant Haematologist
- Via RUH switchboard
Changes to Massive Haemorrhage Pathway at LWH

- Emergency O red cells
  - 6 units in blood fridge on DS
  - 2 units in Gynae theatre

Blood Courier 📞
07717 516 171
Consultant Haematologist 📞
Via RLUH switchboard

Call for help 2222
‘Massive Haemorrhage, Location, Specialty’
Alert emergency response team (including blood transfusion laboratory, portering/transport staff)
Consultant involvement essential
Move patient to HDU when safe to do so

ASSESS: Take bloods for:
XM, FBC, PT, APTT, fibrinogen, U+E, Ca²⁺
NPT: ROTEM, HEMOCUE, ABG

RESUSCITATE
Airway
Breathing
Circulation

STOP THE BLEEDING

Order
Red cells 4 units
Platelets 1 dose
Follow ROTEM pathway

Suspected or continuing haemorrhage requiring further transfusion: REASSESS consider arterial line, FBC, PT, APTT, fibrinogen, U+E, Ca²⁺
REPEAT ROTEM, HEMOCUE,
Discuss with HAEMATOLOGIST *

Aims for therapy
Aim for:
Hb: 8-10g/dl
Platelets: >75 x 10⁹/l
PT ratio: < 1.5
APTT ratio: < 1.5
Fibrinogen: >2g/l
Ca²⁺: >1 mmol/l
Temp: > 36°C
pH: > 7.35 (on ABG)
Monitor for hyperkalaemia
LWH Protocol for Massive Obstetric Haemorrhage guided by results from ROTEM

4 Units Red Cells Run FibTEM and ExTEM

CT ExTEM > 100 s YES

Active bleeding? YES

Order FFP (give when ready)

Wait 5 minutes for FibTEM and ExTEM results

FibTEM A5 < 7 AND ExTEM A5 < 47

Active/high risk of bleeding?

Fibrinogen Concentrate 3g

Recheck ROTEM in 10 minutes

Low ExTEM but normal FibTEM Or if 10 units of blood or more

Give Platelets

FibTEM A5 7-12 AND ExTEM A5 < 47

Recheck ROTEM within 1 hour

FibTEM A5 > 12 AND ExTEM A5 > 47

No Products required

*On agreement between Consultant Anaesthetist and Obstetrician
NB Always base treatment upon clinical scenario

July 2012
Comparison of 12 months of ‘shock pack’ use with 12 months of ‘fibrinogen’ concentrate use
## Outcomes measured during each phase

### Blood component requirements
- Total number of blood components
- Proportion of patients receiving fibrinogen replenishing products
- Units of Fresh Frozen Plasma
- Pooled bags of Cryoprecipitate
- Total quantity of fibrinogen*
- Number of units of red blood cells
- Number requiring ≥ 6 units of red blood cells

### Patient outcomes and complications of blood component transfusion
- Intensive care admissions
- Transfusion associated circulatory overload (TACO)
- Transfusion related acute lung injury (TRALI)
- Post-partum hysterectomies
- Death
Shock pack (n=42) vs Fibrinogen Concentrate (n=51)

- Patient demographics were similar between the 2 groups
  - Age & Parity
  - Estimated blood loss
  - Obstetric diagnoses
RESULTS
Blood product usage
Red Cell Usage

- Although there was no statistical difference in the median number of units of red blood cells given to each group.

- Patients receiving ≥ 6 units of packed red cells
  - Shock Pack - 12/42 (29%)
  - Fibrinogen – 5/51 (10%) \( (p=0.0299) \)
## Patient outcomes & complications

<table>
<thead>
<tr>
<th></th>
<th>Shock Pack (n=42)</th>
<th>Fibrinogen (n=51)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TACO</td>
<td>4 (9%)</td>
<td>0 (0%)</td>
<td>0.0367</td>
</tr>
<tr>
<td>ICU admission</td>
<td>4 (9%)</td>
<td>1 (2%)</td>
<td>NS</td>
</tr>
<tr>
<td>TRALI</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Post Partum Hysterectomy</td>
<td>6 (14%)</td>
<td>3 (6%)</td>
<td>NS</td>
</tr>
</tbody>
</table>
In summary:

- Reduction in post partum hysterectomies not statistically significant but of clinical importance!

- Significant reduction in blood product usage

- Significant reduction (perhaps elimination) of Transfusion Associated Circulatory Overload (TACO) and need for ITU admission
With Fibrinogen Concentrate in MOH

- Do a ‘ROTEM’ ASAP – reading in 6 – 7 mins
- Recognise presence of coagulopathy
- Decide if Fibrinogen Concentrate is required
- Immediately available for reconstitution – few mins
- Given to the patient over a few minutes
- Recheck ROTEM after a few minutes
- More Fibrinogen Concentrate if indicated

Total time for all of this ~ 30 minutes!!
With FFP or Cryoprecipitate

- Need to ring the lab to order it
- Requires defrosting – may take 30 mins on a good day!! Frequently longer!
- ABO matching
- Transportation to the clinical area – staffing issues
- Time for checking blood groups
- Larger volumes take longer to get into patient
But fibrinogen concentrate is more expensive!! Or is it??

<table>
<thead>
<tr>
<th></th>
<th>Shock pack n=42</th>
<th>Fibrinogen n=51</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>unit price</td>
<td>total no used</td>
</tr>
<tr>
<td>PRCs</td>
<td>121.85</td>
<td>179</td>
</tr>
<tr>
<td>FFP</td>
<td>28.46</td>
<td>151</td>
</tr>
<tr>
<td>cryoprecipitate</td>
<td>180.54</td>
<td>66</td>
</tr>
<tr>
<td>platelets</td>
<td>196.96</td>
<td>28</td>
</tr>
<tr>
<td>fibrinogen concentrate</td>
<td>340</td>
<td>2</td>
</tr>
</tbody>
</table>

Total spend on blood & blood products: 44219.1
Cost per patient: 1052.84

Total spend on blood & blood products: 45119.45
Cost per patient: 884.7
Costs in each group

**Shock Pack**
- RBC (units): 49%
- FFP (units): 10%
- Cryo (units): 27%
- Fibrinogen concentrate (G): 2%
- Platelets (ATDs): 12%

**Fibrinogen**
- RBC (units): 44%
- FFP (units): 3%
- Cryo (units): 0%
- Platelets (ATDs): 4%
- Fibrinogen concentrate (G): 49%

Average cost: £1052.84
Average cost: £884.52
Difference: £168.32
With a little help from my friends!

- Dr Philip Barclay, Consultant Anaesthetist
- Dr Clint Chevannes, Consultant Anaesthetist
- Dr Anil Bhalla, SpR Anaesthesia
- Dr Iestyn Harrod, Spr Anaesthesia
- Mr Stephen Longman, Haematology Lab manager
- Ms Cristina Dragomir, Transfusion Practitioner
Thank You all for listening!!!
## Average costs per patient

<table>
<thead>
<tr>
<th></th>
<th>Shock pack</th>
<th></th>
<th>Fibrinogen</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Units</td>
<td>Costs</td>
<td>Units</td>
<td>Costs</td>
</tr>
<tr>
<td>RBC</td>
<td>4.26</td>
<td>£519.31</td>
<td>3.16</td>
<td>£384.66</td>
</tr>
<tr>
<td>FFP</td>
<td>3.60</td>
<td>£102.32</td>
<td>0.98</td>
<td>£27.90</td>
</tr>
<tr>
<td>Cryo</td>
<td>1.57</td>
<td>£283.71</td>
<td>0.00</td>
<td>£-</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>0.05</td>
<td>£16.19</td>
<td>1.27</td>
<td>£433.33</td>
</tr>
<tr>
<td>Platelets</td>
<td>0.67</td>
<td>£131.31</td>
<td>0.20</td>
<td>£38.62</td>
</tr>
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</table>