Massive Blood Loss

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Royal Infirmary Of Edinburgh
What Is Massive Blood Loss?

Gavin Hamilton, National Gallery, the Mound, Edinburgh
What Is Massive Blood Loss?

- Arbitrarily defined
  
i. loss of 1 blood volume in 24 hours (Mollinson 1997)

ii. 50% blood volume loss within 3 hours

iii. rate of loss of 150ml/min (Fakhry & Sheldon, 1994)

iv. obstetrics : major APH > 300 ml

    major PPH > 1500 ml
What Is Massive Blood Loss?
What Is Massive Blood Loss?

What’s the link?

98 units
What Is Massive Blood Loss?

* Adult blood volume is proportional to body weight *
Scale of the Problem

- **Global**
  - leading cause of death in those < 36 yrs – trauma
  - 40% of all trauma deaths caused by haemorrhage

- **Maternal mortality**
  - 600,000 women die of pregnancy-related complications
  - (1% : 99% developed : developing)
  - 150,000 women die of haemorrhage
Putting it in Context

Military arena
ISS > 15  -  20% of all trauma admissions
Massive transfusion  -  10% of admissions

Civilian trauma centres
Massive transfusion : 1-3% of admissions

Does This Matter?
Massive Transfusion is not Good News ..........

1. …independently associated with ↑ likelihood of death
   (Como, Transfusion, 2004: 44:809-813)

2. ….associated with 20-50% mortality rate

3. … and it’s quick : majority of deaths within 6-12 hrs
   of hospital arrival
Why These Patients Die - Coagulopathy

24% of patients had a coagulopathy

Coagulopathy was associated with increased mortality, over and above that of injury severity

Why These Patients Die - Coagulopathy

- Initial PT and PTT independently predicted all-cause mortality.
- Elevated initial PT associated with a 35% increase in all-cause mortality
- Elevated initial PTT associated with a 326% increase in all-cause mortality
- Most deaths occur early in the hospital stay; probability of survival paralleling as time goes on.

Origins of the Coagulopathy

Traumatic coagulopathy -
- multifactorial
- interaction between fibrin activation/dysfunction, platelets and endothelium
- inhibition of stable clot formation
- ? dominant mechanism – dependent upon
  - tissue injuries
  - circulatory upset
  - medical intervention
Coagulopathy: Trauma and Shock

**Trauma**
- Injury severity is associated with degree of coagulopathy
- Crucial role of circulatory upset in development of coagulopathy
- Endothelial damage exposes collagen and TF
  \[
  \text{TF:FVIIa} \rightarrow \rightarrow \rightarrow \text{fibrin (‘clot’)}
  \]
- Tissue injury and shock $\rightarrow$ hyperfibrinolysis
- Localisation of clot propagation to site of vascular injury - lost

**Shock**
- severity of hypoperfusion $\alpha \uparrow$ PT, PTT
- platelet sparing
- shock $\rightarrow$ anticoagulant and hyperfibrinolytic haemostatic system
  (secondary to endothelial cell ‘perturbation’)
Damage Control Resuscitation

Goal is to stay out of trouble, instead of get out of trouble

Remember: only 3% civilian population require massive transfusion

Principles

• Rapid recognition of high risk for trauma-induced coagulopathy (massive transfusion prediction)
• Permissive hypotension
• Rapid definition/surgical control of bleeding
• Prevention/treatment of hypothermia, acidosis and hypocalcaemia
• Avoidance of haemodilution by minimising use of crystalloids
• Early transfusion of red blood cells: plasma : platelets in a 1:1:1 unit ratio
• Appropriate use of coagulation factor products (*rFVIIa) and fibrinogen containing products (fibrinogen concentrates, cryoprecipitate)

• * rFVIIa : recombinant activated factor VII
Rapid Recognition of High Risk for Trauma-Induced Coagulopathy (Massive Transfusion Prediction)

- Prediction tools for massive trauma: BP, P, base deficit, PT, Hb, ultrasound
- High specificities (80-90%)
- Cotton et al, J. Trauma 2008;64:1177-82
  - An increase in survival with earlier application of a predefined massive transfusion guideline

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<tbody>
<tr>
<td>MOF</td>
<td>20%</td>
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<td>9%</td>
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<tr>
<td>30 day survival</td>
<td>38%</td>
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<td>51%</td>
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Conclusion: difference caused by earlier and rapid transfusion of increased amounts of plasma and platelets
Early Transfusion of Red Blood Cells: Plasma: Platelets in a 1:1:1 Unit Ratio

**Platelets**
>240.10⁹/unit
~300 ml

**Whole Blood**
- **Platelets**: 150-350.10⁹/L
- **Hb**: 120-150 g/L
- **FVIIIc**: 1,000 iu/L
- **fibrinogen**: 1.5-4 g/L

**RCC**
- **Hb**: >40 g/unit
~300 ml

**FFP**
- FVIIIc > 0.70 iu/ml
 (>840 iu / therapeutic dose, ~1200ml)

**Cryoprecipitate**
- fibrinogen > 140 mg/unit
 (>1.4g / therapeutic dose, 300ml)

Holcomb et al, J.Trauma 2009;66:S69-76 : increased survival with warm, fresh whole blood compared with component therapy.
# Early Transfusion of Red Blood Cells: Plasma: Platelets in a 1:1:1 Unit Ratio

## Summary of Plasma (11)/Platelet (4) : RBC Ratios in Massive Transfusion Populations

<table>
<thead>
<tr>
<th>Author</th>
<th>Design</th>
<th>Single or Multicentre</th>
<th>No. of Patients</th>
<th>Predominant Mechanism of Injury</th>
<th>Time Ratio Measured</th>
<th>Main Results</th>
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+ high plasma/platelet : RBC ratio was assoc with survival

- high plasma / platelet :RBC ratio was not assoc with survival

Adj adjusted results with logistic regression

R : retrospective  P : prospective  R : retrospective with prospectively collected data  Multi: multicentre
Early Transfusion of Red Blood Cells: Plasma: Platelets in a 1:1:1 Unit Ratio

- Statistical limitations in the studies that find in favour of high ratios, …. and also those that find against.

- The preponderance of current literature indicates that patients in haemorrhagic shock at high risk of death or who require massive transfusion benefit from increased ratios of platelets and plasma to red cells.

- Conversely, DCR should not be performed in those not in haemorrhagic shock, or who are not at high risk of massive transfusion.
Appropriate Use of Coagulation Factor Products (rFVIIa) and Fibrinogen Containing Products (Fibrinogen Concentrates, Cryoprecipitate)

rFVIIa

- Should we or shouldn’t we….?
- Boffard et al, J.Trauma 2005;59:8-15
  - 2 randomised prospective trials
  - adult trauma
  - decreased use of red cells and ARDS
  - BUT – no improved survival

- on-going questions:
  1. what patient population may benefit?
  2. how to answer 1.?
  3. when to give it? Sooner or later?
Appropriate Use of Coagulation Factor Products (rFVIIa) and Fibrinogen Containing Products (Fibrinogen Concentrates, Cryoprecipitate)

Fibrinogen

- Should we or shouldn’t we…? 
- Does liberal use of fibrinogen improve survival? 
- Animal studies: early hyperfibrinolysis → decreased fibrinogen 
- Stinger et al, J. Trauma, 2008;64:S79-85: better survival with increased fibrinogen was ‘hinted’ at 
- Current teaching: replace when fibrinogen<1g/L - ? evidence base 

→ More studies required
Summary

- Worldwide, trauma is a common cause of death in people < 40 years.
- Haemorrhagic shock is the most common cause of preventable death.
- Our understanding of traumatic coagulopathy and ACoTS is improving.
- Patients with severe traumatic injury and life-threatening bleeding are uncommon, but they must be identified, and early.
- Principles of DCR applied to this group may improve survival.
- Other conditions with severe bleeding require similar attention.
Massive Blood Loss

Acknowledgements

Jilly Martin (and colleagues), Administrative Office, SEBTS, RIE.

Dr Dermot McKeown, Consultant Anaesthetist, RIE.