MANAGEMENT OF COAGULOPATHY AFTER TRAUMA OR MAJOR SURGERY

19th ANNUAL CONTROVERSIES AND PROBLEMS IN SURGERY

Thabo Mothabeng
General Surgery: 1 Military Hospital

sa military health service
Department: Defence
REPUBLIC OF SOUTH AFRICA
ONE OF THE MOST FRUSTRATING SITUATIONS ever encountered by the operating surgeon is an open wound in a patient whose blood will not clot and cannot be made to clot. By far the most extreme example is a bleeding diathesis complicating laparotomy. This event is an all-too-common occurrence in the patient who has sustained a major intraabdominal injury or who has a disease process or operation which has been attended by a massive hemorrhage. The coagulopathy can seldom be reversed satisfactorily. Thus, the usual outcome is continued bleeding and thereby death through exsanguination.

Coagulopathy of Trauma

The blood loss is usually underestimated!
What is this Coagulopathy?

- Various terminology
  - Trauma Induced Coagulopathy (TIC)
  - Acute Coagulopathy of Trauma Shock (ACoTS)
  - Acute Traumatic Coagulopathy (ATC)

- Acute Coagulopathy
  - Bloods ability to clot is impaired
  - Increased fibrinolysis
  - There may be thrombotic states
  - Prolonged or excessive bleeding
Acute Coagulopathy of Trauma

- Complicates trauma and major surgery
  - Hypoperfusion is crucial
- Control of bleeding is difficult when coagulopathy is established
- Immediate/ Early Onset
  - One in four trauma patients
  - Four fold increase in mortality
Characteristics of Coagulopathy

- Immediate effect; before hemodilution
- Proportional to injury
- Hypoperfusion initiates
- Hypothermia and acidemia augment
- Clot strength reduced (Coagulopathy)
- Clot formation minimally delayed
- Fibrin polymerization impaired (Fibrinolysis)
- Platelet dysfunction augments (Delayed)
## Association with ISS

<table>
<thead>
<tr>
<th>Injury Severity Score</th>
<th>Incidence of ACoTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 - 29</td>
<td>21%</td>
</tr>
<tr>
<td>30 - 44</td>
<td>41%</td>
</tr>
<tr>
<td>45 - 59</td>
<td>59%</td>
</tr>
<tr>
<td>60 - 75</td>
<td>79%</td>
</tr>
</tbody>
</table>

May. J Trauma 2003; 54
Key Initiators

1. Tissue damage (Endothelial damage)
2. Hypoperfusion (Shock)
3. Hemodilution
4. Hypothermia
5. Acidosis
6. Inflammation
LETHAL TRIAD OF TRAUMA

Coagulopathy

Halt coagulation cascade

Lactic acidosis

Decreased myocardial performance

Hypothermia

Metabolic Acidosis
Hypothermia

- Reduced function of all factors
- Activity reduced by 50% at $T_0$ less than 33°C
- Impaired platelet aggregation

*Johnston. J Trauma 1994; 37*

- Fibrinolysis is stimulated.
- Rohrer et al found that aPTT

<table>
<thead>
<tr>
<th>37 Degrees</th>
<th>34 degrees</th>
<th>31 degree</th>
</tr>
</thead>
<tbody>
<tr>
<td>36 seconds</td>
<td>39</td>
<td>46</td>
</tr>
</tbody>
</table>

- Decreases activation of platelets
Acidosis

- Reduced activity and activation of coagulation factors
- Increased degradation of fibrinogen
- Impaired function of plasma proteases
- Corrected by administration of buffer solutions

✓ This does not correct coagulopathy

Meng. J Trauma 2003
Shock

- Prime driver of early coagulopathy
  - Direct tissue trauma
  - Systemic hypoperfusion
- Prolonged clotting times

<table>
<thead>
<tr>
<th>BASE DEFICIT</th>
<th>&lt;6MMOL/L</th>
<th>&gt;6MMOL/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>% PROLONGED CLOTTING TIMES</td>
<td>2%</td>
<td>20%</td>
</tr>
</tbody>
</table>
Hemodilution

- Direct loss of coagulation factors
- Haemorrhage quickly reduce
  - Fibrinogen (10g)
  - Platelets (15ml)
- Losses are then replaced with fluids
  - Crystalloids or colloids
  - Causing **dilutional coagulopathy**
- **Paradigm shift in resuscitation!**
THE “BLOODY VICIOUS CYCLE”

- Injury severity score > 25
- pH<7.10 + Systolic BP<70 mmHg
- Core temperature <34°C

WHEN ALL 3 PRESENT: INCIDENCE OF COAGULOPATHY = 98%
Underlying Diseases and Drugs

- Coagulation defects e.g. von Willebrand disease
- Liver disease
  - Thrombopoietin and haemostatic proteins
  - Reduced Vit K dependent coagulation factors (II, VII, IX and X)
  - Inhibited platelet aggregation.
- Renal disease
  - Impaired platelet function
- Oral anticoagulants
Vitamin K Antagonists

- Increased incidence of use: 2.3% (2002) to 12.8% (2006)
- Related to 50% mortality in young patients
- Prothrombin concentrate complex (PCC) & Vit K.
  - CA Dossett. Arch Surg 2011
  - GH Guyatt. Chest 2012
- High doses of PCC reverse rivaroxaban, not dabigatran
Pathophysiology
Fibrinolysis
Classical Coagulation Tests

- Platelet count
- Haematocrit
- INR
- Prothrombin time
- Activated partial thromboplastin time
- Fibrinogen
- Platelet function analysis
Classical Coagulation Tests

- No consensus on what values
- Test first 20 seconds of clot mechanism
- No correlation with bleeding or clotting factor activity
- Plasma based test not whole blood (in vivo)
- May not detect fibrinolysis
- Takes 45 to 75 minutes

“Closer to the Ideal”

- Thromboelastography (TEG)
- Rotational thromboelastography (ROTEM)
  - Replacing TEG
  - Information in 5 to 10 minutes
  - Measure of entire clotting mechanism (in vivo haemostasis)
  - 64% accuracy vs. 10% of CCT
  - Predict need for massive transfusion

Davenport R, 2011
Viscoelastic Haemostatic Assay
Viscoelastic Haemostatic Assay

- **Measures 5 parameters**

  - **R time:**
    - Coagulation factor activity
  
  - **K time:**
    - Speed of clot formation
  
  - **Alpha angle:**
    - Fibrin formation
  
  - **Maximal Amplitude (MA):**
    - Platelet function
  
  - **Whole blood lysis:**
Figure 4. Thromboeslastograph (TEG) tracing. The reaction time (R) represents the time to onset of clot formation. K time is a measure of the speed to reach a certain level of clot strength. $\alpha$ angle represents the rate of clot formation. The maximum amplitude (MA) measures the clot strength. Reprinted with permission from Kiraly, J Trauma 2006;61:57–64.
Management: Key Steps

- Permissive hypotension
- Blood and blood products
- Temperature control and Rewarming
- Correction of acidosis
- Calcium homeostasis
- Pharmacological treatment
  - Tranexamic acid
  - Antifibrinolytic
  - Prothrombin complex concentrate (PCC)
Predicting massive transfusion

- INR Greater than 1.2
- Base deficit Less than -6 mmol/L
- Systolic blood pressure Less than 90 mmHg
- Injury severity score Greater than 15
- Haemoglobin Less than 11 g/dL
- FAST exam Positive for haemorrhage
- Blood pH Less than 7.25
- Body temperature Less 35.5 celsius
- Heart rate Greater than 120 bpm
End points of resuscitation

- VHA directed management
- Give FFP, cryoprecipitate and platelets as indicated
- Massive Transfusion Protocol
- Targets
  - INR < 1.5
  - Fibrinogen > 1 gm/L
  - Platelets > 50 x 10⁹/L
Fibrinogen

- Affected early and most of all factors
- Depleted in many bleeding patients
- Poor outcome, reversed by administration

Rourke. J Thrombo Haemost 2012; 10

Tranexemetic Acid

Standard of care in most trauma units
Benefit when administered early

H Shakur. Lancet 2010; 376
# Recombinant Factor VIIa

- **Boffard K et al**

<table>
<thead>
<tr>
<th></th>
<th><strong>BLUNT</strong></th>
<th><strong>PENETRATING</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>NUMBER</td>
<td>143</td>
<td>134</td>
</tr>
<tr>
<td>PLACEBO</td>
<td>74</td>
<td>64</td>
</tr>
<tr>
<td>rFVIIa</td>
<td>69</td>
<td>70</td>
</tr>
<tr>
<td>REDUCTION RBC UNIT</td>
<td>REDUCED: 2.6UNIT</td>
<td>REDUCED: 1UNIT</td>
</tr>
<tr>
<td>MASSIVE TRANSFUSION</td>
<td>REDUCED BY 33%</td>
<td>REDUCED BY 19%</td>
</tr>
</tbody>
</table>
Recombinant FVIIa

- Binds directly to surface of activated platelets
- Enhances
  - Enhances thrombin generation
  - Fibrin clot formation
  - Producing a stable clot
Prothrombin Complex Concentrate

- PCC or a complex of factors II, VII, IX, X
- Off label use in trauma
- Reduce transfusion requirements
- Reversal of oral anticoagulants
Combination of fibrinogen and PCC:

- Fibrinogen levels are the first to decline during hemorrhage.
- Use of PCC can:
  - Reduce risk of TRALI.
  - Reduce risk of viral infections.
  - Reduce blood loss.
  - Shorten time to coagulation.
- Maintain fibrinogen level of > 1.5 g/L.

Leir. J Trauma 2008
Calcium homeostasis

- Necessary for fibrin clot stabilisation.
- Hypocalcaemia (< 0.9 mmol/L) should be treated.
- Hypocalcaemia is aggravated by rapid infusion of blood products.
- Chelation of calcium by the anticoagulant citrate.
- Low levels associated with higher mortality and increased need for blood transfusion.

Cherain, WJS 2014
Thank You!