Massive Transfusion in Paediatric Trauma

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Clinical Scenario…
Overview

• Benefits of Damage Control Resuscitation
• The role of the Massive Transfusion Protocols in improving trauma outcomes
• Massive Transfusion Controversies / Conundrums
  • Role of Fibrinogen?
  • Role for Tranexamic Acid / Factor VIIa?
  • What is the right Blood Product Ratio?
Arrival in ED

During transport - haemodynamically unstable

➤ Ongoing haemorrhage despite packing of right foot

➤ Hypotensive and tachycardic

➤ Significant fluid resuscitation
  - 2 litres crystalloid given at scene
  - 3 Units of O-ve Packed Cells during transport

Mechanism of Injury!
Initial Assessment in ED

- Alert, maintaining airway
- HR 120
- Systolic BP 100
- Central Cap refill = 3 sec
- Blood pooling around packed right foot
Initial Management in ED

- High flow $O_2$
- Peripheral Access confirmed
  - 16G both Cubital Fossae
- Bloods sent with Venous Blood Gas
- CXR and FAST performed
- Foot re-packed, but unable to control bleeding
  - Tourniquet placed around right thigh whilst theatre prepared
Progress

- Bleeding controlled
- CXR & FAST NAD
- Increasing pain in right leg
- On transfer to OT tourniquet failed and significant haemorrhage
  - Became hypotensive and tachycardic
  - Hb dropped
- THEATRE PICTURES…
Wounds to right foot debrided, packed and re-dressed
Further 5 units of packed cells given
# Laboratory Results

<table>
<thead>
<tr>
<th>Time</th>
<th>2000 (ED)</th>
<th>2230 (OT)</th>
<th>2400 (ICU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>INR (NR 0.9-1.2)</td>
<td>1.3</td>
<td>1.8</td>
<td>1.5</td>
</tr>
<tr>
<td>PT (12-15)</td>
<td>17</td>
<td>22</td>
<td>19</td>
</tr>
<tr>
<td>APTT (26-41)</td>
<td>31</td>
<td>42</td>
<td>36</td>
</tr>
<tr>
<td>Fib (2.0-4.5)</td>
<td>1.8</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Plat (150-400)</td>
<td>257</td>
<td>112</td>
<td>100</td>
</tr>
<tr>
<td>Hb (135-175)</td>
<td>152</td>
<td>99</td>
<td>107</td>
</tr>
<tr>
<td>pH (7.35-7.45)</td>
<td>7.12</td>
<td>7.21</td>
<td>7.31</td>
</tr>
</tbody>
</table>
Blood Product Use

3 Units Packed Cells pre-hospital
5 Units Packed Cells used in OT
Nil other blood products in OT

Total of 8 Units RCC given since injury – no plasma or platelets

FFP given in Paediatric ICU

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Damage Control Resuscitation

Tenets... Proactive rather than Reactive
1. Aggressive control of bleeding
2. Aggressive maintenance of normal coagulation
3. Avoid hypothermia
4. If penetrating trauma → Permissive Hypotension

Requires...
Early diagnosis of at risk patients
Maintaining a Low Ratio of PRBC to FFP & Platelets
Minimisation of Crystalloid use
Risk Factors for Massive Transfusion (> 40ml/kg of blood products in 12hrs)

Acidosis (Base Deficit > 6)
Coagulopathy (INR > 1.5)
Hypotension (SBP < 90 (adult))
Haemoglobin (< 110 in a young adult)
Temperature (< 35.5)

Patients with these features have improved outcome with Damage Control Resuscitation approach
Blood Product Ratios to Achieve Normal Coagulation

Studies performed primarily by US military in Iraq / Afghanistan (eg. Borgman, Spinella et al J Trauma 2007)

Markedly improved survival if blood products given in a ~1:1 ratio compared with > 8:1

Civilian adult studies have also demonstrated improved survival (eg. Holcomb, Wade & Michalek Ann Surg 2008)

1 PRBC: 1 FFP: ¼ Pooled Platelet Unit = Reconstituted whole blood
Massive Transfusion Protocols

However... trauma cases requiring a damage control resuscitation / massive transfusion are:

- **rare** in paediatric practice
- **hectic** and **stressful** environments

Packed RBCs are remembered, but other blood products tend to be forgotten.
Massive Transfusion Protocols

Solution?

➢ Pre-existing protocol for the timely delivery of an appropriate mix of products from Blood Bank to the Clinical Area
  - Improves communication
➢ Studies have shown improved outcome by having a protocol (Cotton et al J Trauma 2008)
Activation of MTP if massive bleeding is occurring or patient is at risk

Aiming to give equal volumes of PRBCs & FFP Platelets and Cryoprecipitate every 80mls/kg
Case Outcome

- Massive Transfusion Protocol was activated in PICU
- Normal Coagulation rapidly achieved
- Foot was saved with good functional outcome
Massive Transfusion - Conundrums

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Coagulopathy of trauma is complex and dynamic
Several areas of controversy

Including:

- Fibrinogen replacement
- Role of antifibrinolytics
- Role of Recombinant VIIa
- Ratios FFP:RCC:Platelets
- Use of POCT
Fibrinogen – why is it important

Fibrinogen cleavage (forming fibrin / platelet clot) is the final common denominator of clotting cascade

**If low fibrinogen - rest of clotting process becomes ineffective**

Fibrinogen is a significant issue in massive bleeding in trauma consumption, dilution and hyperfibrinolysis

- Often reaches “critical” levels before other clotting factors / platelets
  - Consensus lacking on what “critical” fibrinogen level is
  - Better question: what level are we aiming for - ? normal

Possibilities to resolve this

- Prevent / reduce fibrinolysis (Tranexamic Acid)
- Give fibrinogen earlier / in larger dose
CRASH-2: 20211 pts, randomised Tranexamic Acid (TXA) vs placebo

OUTCOMES with TXA

- All cause mortality reduced (RR 0.9)
  - Most related to reduced risk of death from bleeding or MI
- No difference
  - surgical intervention / blood transfusion / DVT / CVA or PE

- TXA is inexpensive, easy to use, safe and seemed to save lives
  - works best if given within 1 hour of injury
    - beyond 3 hours confers worse outcome
    - ? give at primary treatment site / pre hospital
  - works best in traumatic bleeding (vs other without hyperfibrinolysis)
    - Need to think about scenario
  - Note: most of data from low income countries + limited blood product availability
    - is it as useful if give FFP / cryoprecipitate early and adequately
Fibrinogen / Cryoppt - optimal replacement?

Evidence suggests:
- Higher fibrinogen:RCC ratios improve survival and result in lower deaths from haemorrhage in military population - Stinger HK et al J Trauma. 2008 Feb;64(2 Suppl):S79-85
- Large FFP loads associated with increased MOD / mortality
- Cryoprecipitate administration associated with reduced MOD (civilians)
- Fibrinogen concentrate results in dose dependent improvement in clotting and safe (animal models / haemodilution coagulopathy)
- Use of fibrinogen concentrate in hypofibrinogenemia due to massive haemorrhage (most not trauma pts) safe, reduced bleeding, reduced need for red cells, FFP and platelets (human trials)

Upshot:
- Earlier / more intense replacement may merit consideration
  – Especially in states with hyperfibrinolysis (eg trauma, obstetric bleeding)
  – FFP alone will not adequately replace in this setting
  – Cryoprecipitate typically given relatively late
  – Catch up is harder if fibrinogen very low
Recombinant VIIa

Included in most protocols
Retrospective case series, case reports and registry data suggest potential benefit
Prospective RCT (multicentre / multinational)
  – no difference in blood use at 48 hours or overall mortality

**Jury is still out - but use overall in this setting is less than in past**
**Utility remains unclear**
  - Doesn’t work well if acidotic, hypothermic or if “substrate – platelets / fibrinogen” lacking
  - When to give / what dose / which patients
  - Consider on case by case basis – current recommendation to use when other replacement optimised as much as possible and still bleeding

Expensive (90mcg/kg dose - ~$7000 for a 70kg adult)
Thrombosis risks
Ratios – what’s best

Best “cocktail” / ratio probably still uncertain
   Most centres aim for 1:1:1 ratio
   Realistically in most centres we are not giving this
       Patients typically receive no plasma containing components initially
   Logistics of supply of blood products (XM, thawing, transport etc) contributes

1:1:1 ratio is based largely on data from healthy young (mostly male) patients (military)
   Does this apply to all bleeding scenarios and patients?
       - some data shows high ratios in non trauma patients increases mortality
       - Is a 1:1.5 or 1:2 or even 1:3 ratio reasonable / appropriate in different critical
         bleeding scenarios (eg surgical bleeding)

Other factors probably important
   Timing of product in relation to injury / bleeding
       - ? earlier intervention / correction better
       - rate of bleeding vs transfusion / replacement
   Age / co-morbidities
   Severity / extent / type of injury (may preclude benefit of any intervention)
Large volumes of blood are not risk free!

Product related issues
- Hypothermia
- Electrolytes
  - Hyperkalemia
  - hypocalcaemia
- Acid base / acidosis
- Citrate toxicity
- Transfusion related lung injury
- ARDS / Multiorgan dysfunction (MOD)

Resource related issues
- Availability of components
- Cost
- Appropriate use of blood
MTP – what is it?

IT IS NOT A BLOOD PRODUCT PRESCRIPTION

It is a process pathway which should define:

Initiation of Protocol
  Who can initiate
  Personnel to involve
What blood product to immediate release
  Should some be stored near operating rooms or Emergency Department?
What Laboratory Tests to utilize
  How will these be communicated?
  Dedicated person to draw blood test
  Dedicated person to run laboratory tests
Transportation of blood and blood samples between laboratory and patient
Mechanism for monitoring outcomes of MTP and implementing modifications
Take Home Messages

Damage control resuscitation
TXA – Probably useful early in trauma
Factor VIIa – limited applicability
  ? Redundant if product replacement is early / “optimal”
Ratios – Area of ongoing investigation.
  “Optimal” ratio may depend on condition being treated
Have to find balance between good and harm
MTP is not a prescription, but a logistics pathway!

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Queensland Government
Further reading

Fibrinogen / plasma ratios

➤ Critical Care. 2010, 14:154-155. Is fibrinogen the answer to coagulopathy after massive transfusions. Tisherman S.


Review / guidelines


Recombinant VIIa


CRASH-2

Cochrane library 2011, issue 1. Roberts I, Shakur H et al.
Point of care testing

Real time assessment of coagulopathy and treatment response is an issue in critical bleeding

Standard lab tests take time
  - transport to lab / need to centrifuge sample to separate plasma can take 20 – 30 mins+ for results

Potential role for POCT testing
  - Technologies best studied in this setting are TEG / ROTEM
  - Cochrane review (9 studies)
    - reduced bleeding but no effect on any other outcomes
TEG / ROTEM – role undefined

Pros
  ➢ Results within 5-10 mins
  ➢ Measures fibrinolysis (takes a bit longer)

Cons
  ➢ Fresh blood (no anticoagulant), run immediately
  ➢ Interpretation of curves
  ➢ Cost / QA / Maintenance (who takes responsibility)
  ➢ Monitoring / recording information to retain with medical record