Use of Prothrombin Complex Concentrate to Reverse Coagulopathy

Rio Grande Trauma Conference

John A. Aucar, MD, MSHI, FACS, CPE
EmCare Acute Care Surgery
Del Sol Medical Center
Associate Professor, University of Illinois, Urbana-Champaign
Double Whammy....

• Diagnosis and Management of Traumatic Coagulopathy
  • Use of Thromboelastography in the Management of the Trauma Patient
  • Use of Prothrombin Complex Concentrate to Reverse Coagulopathy
    * Off label use
Review – Concerns in Injury

• Perfusion – Oxygen delivery
• Stop ongoing bleeding
• Consider physiologic reserves
Resuscitation

• Permissive hypotension
• Permissive anemia
• Permissive coagulopathy
Review - Conventions

• Massive transfusion = > 10 U PRBC

• Traumatic Coagulopathy
  • > 1.5 X normal PT/PTT
  • Prolonged ACT
  • TEG/TEM - Prolonged CT (initiation)
  • TEG/TEM - Decreased angle (dynamics)
  • TEG/TEM – Reduced amplitude, MCF (strength)
Transfusion tidbits

• Blood collected in CDAP prior to fractionation
• Citrate Toxicity
• FFP has platelets, but they are inactivated
Fresh Frozen Plasma

• Single donor product
• ABO compatible, AB is the universal donor
• No CMV or Graft vs. Host risk
• Contains all Factors, V and VIII decrease rapidly
Cryoprecipitate

• Prepared from plasma and contains fibrinogen, von Willebrand factor, factor VIII, factor XIII and fibronectin
  • Only useful source of Fibrinogen replacement
  • Should not be used for FVIII or FIX replacement (use concentrates)

• Dosage
  • 1 bag contains ~350 mg Fibrinogen
  • 6 bags (1pool) contains 2100 mg Fibrinogen
  • 6 bags raises Fibrinogen level about 45 – 50 mg/dl

• Type matching not needed except kids < 2 y/o
Platelet Strategies

- Threshold for transfusion based on platelet count is controversial
- Initial strategies based on wash out calculations
- Experimental studies showed higher than predicted platelet counts
rFVIIa

• Potent initiation of final common pathway in presence of tissue factor
• Rapid correction of INR and reduction of bleeding
• Generated exuberance in early experience
  • Dose response in trauma never studied
  • Randomization thwarted
• Fell out of favor based on case reports of thrombotic complications
Transfusion strategies

- FFP of no value in patient receiving less than 10 U PRBC


- PRBC : FFP ratio should approach 1 : 1

Prothrombin Complex Concentrate

• 4F-PCC (Kycentra)
• Factors II, VII, IX, X; + Proteins C and S (Heparin)
• **Indication:** Reversal of Vitamin K antagonist acquired factor deficiency in adults with acute major bleeding.
  • Not indicated for VKA reversal in absence of acute major bleeding
  • Single administration, repeat dosing not recommended

• **Precautions:**
  • Human product with risk of viral transmission
  • Heparin associated thrombocytopenia
  • VTE events
PCC Administration

- Lyophilized concentrate, single use vials
  - 20 – 31 FIX units/ml average 25 units/ml
  - Approx 500 FIX units per vial reconstitutes to 20 cc
  - Slow infusion (8-10 min)

<table>
<thead>
<tr>
<th>Pre-treatment INR</th>
<th>2 – &lt; 4</th>
<th>4 – 6</th>
<th>&gt; 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose* of Kcentra (units† of Factor IX) / kg body weight</td>
<td>25</td>
<td>35</td>
<td>50</td>
</tr>
<tr>
<td>Maximum dose‡ (units of Factor IX)</td>
<td>Not to exceed 2500</td>
<td>Not to exceed 3500</td>
<td>Not to exceed 5000</td>
</tr>
</tbody>
</table>
## Factor Half-lives

<table>
<thead>
<tr>
<th>Factor</th>
<th>Terminal half-life (h)</th>
<th>Protein C</th>
<th>Protein S</th>
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<tbody>
<tr>
<td>Factor IX</td>
<td>16.7 (14.2-67.7)</td>
<td>47.2 (9.3-121.7)</td>
<td>49.1 (33.1-83.3)</td>
</tr>
<tr>
<td>Factor II</td>
<td>59.7 (45.5-65.9)</td>
<td></td>
<td></td>
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<tr>
<td>Factor VII</td>
<td>4.2 (3.9-6.6)</td>
<td></td>
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<tr>
<td>Factor X</td>
<td>30.7 (23.7-41.4)</td>
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In randomized, plasma-controlled study in acute major bleeding,

**Mean duration of infusion**
Kcentra 24 min (±32 min)  
Plasma was 169 min (±143 min)  

**Mean infusion volume**
Kcentra was 105 mL ±37 mL  
Plasma was 865 mL ±269 mL.
PCC for traumatic coagulopathy

- Standard doses
- Lower volume
- (Lower transfusion risks)
- (Thrombotic risk and effect on DIC)

- Limited observational data available
Prospective cohort study
144 patients, major abdominal trauma (ISS>15) Innsbruck, Austria

- Fibrinogen concentrate + PCC alone (CF group n= 66)
- FFP (+/- factors) (FFP group n= 78)

- Trends toward lower ICU and total LOS, NS
- Mortality and VTE events almost identical

<table>
<thead>
<tr>
<th></th>
<th>CF group</th>
<th>FFP group</th>
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<tbody>
<tr>
<td>RBC</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Platelets</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>MOF</td>
<td>18.2%</td>
<td>37.2%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>16.9%</td>
<td>35.9%</td>
</tr>
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Retrospective single hospital vs. national registry  
Fibrinogen/PCC vs. FFP (no F/PCC)  Salzberg, Austria

- F/PCC n = 80 (ISS 35.2 ± 12.5)  FFP n = 601 (ISS 35.5 ± 10.5)

- **RBC transfusion avoided** in 29% of patients in fibrinogen-PCC group vs. only 3% in the FFP group (P < 0.001).

- **Transfusion of platelet concentrate was avoided** in 91% of patients in the fibrinogen-PCC group vs. 56% in the FFP group (P < 0.001).

- **Mortality was comparable**: 7.5% in the fibrinogen-PCC group and 10.0% in the FFP group (P = 0.69).

Transfusion in trauma: thromboelastometry-guided coagulation factor concentrate-based therapy versus standard fresh frozen plasma-based therapy  
Schöchl et al. Critical Care 2011, 15:R83
Retrospective review PCC vs. rFVIIa in TBI

<table>
<thead>
<tr>
<th></th>
<th>PCC n = 64</th>
<th>rFVIIa n = 21</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coumadin use</td>
<td>44 %</td>
<td>14 %</td>
<td>0.001</td>
</tr>
<tr>
<td>Craniotomy rate</td>
<td>28 %</td>
<td>10 %</td>
<td>0.1</td>
</tr>
<tr>
<td>Mortality</td>
<td>47 %</td>
<td>67 %</td>
<td>0.02</td>
</tr>
<tr>
<td>Mean Cost/pt</td>
<td>$1,007</td>
<td>$5,757</td>
<td>&lt;0.01</td>
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There was a significant decline in packed red blood cell transfusion and fresh frozen plasma after PCC administration (p < 0.01).

Retrospective review of 25 geriatric trauma patients (age >55 years) Tx w/ either FFP or PCC

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<tr>
<th></th>
<th>PCC n = 15</th>
<th>FFP n = 10</th>
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<tbody>
<tr>
<td>Mean age</td>
<td>77</td>
<td>80</td>
</tr>
<tr>
<td>ISS</td>
<td>19.1</td>
<td>19.2</td>
</tr>
<tr>
<td>Hospital LOS</td>
<td>7.7</td>
<td>9.5</td>
</tr>
<tr>
<td>ICU LOS</td>
<td>4.4</td>
<td>7.1</td>
</tr>
<tr>
<td>FFP used</td>
<td>1.6</td>
<td>2.7</td>
</tr>
<tr>
<td>Decrease in INR</td>
<td>51 %</td>
<td>43%</td>
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Six patients (40%) in the prothrombin complex concentrate group avoided fresh frozen plasma transfusion altogether.
