Whole Blood for resuscitation

Barbara A. Gaines, MD
UPMC Children’s Hospital of Pittsburgh
University of Pittsburgh School of Medicine
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• I have nothing to disclose
The Problem

- Shock is poorly recognized in children
- hypotension ≠ shock
Pre-hospital

• Few children receive blood prior to arrival at a pediatric center
  – 17 year period; 64 children received blood prior to arrival (701 transfused after arrival)
  – 89% of those transfused were transferred from another institution

• Those that do are under-resuscitated
  – Median transfusion volume 10cc/kg; 40% received less

• Even fewer receive plasma
  – Only 7 received plasma prior to arrival

Behr, Pediatric Trauma Society, 2020
Emergency Department

- Hypotension and delay of transfusion until trauma center ED associated with high mortality
- 50% of children who are transfused in the ED of a trauma center die!!!

Leeper, JTACS, 2018
Trauma-induced coagulopathy

Even a mildly elevated INR at admission is associated with an increased risk of death

* Cotton, et al, demonstrated 100% mortality in a pediatric cohort with an admission INR>3  (J Am Coll Surg, 2017)
Coagulopathy happens early after injury

- Physiologic phenotype was predominant within 1 hour of injury (51%)
- Beyond 1 hour, fibrinolysis shutdown was the predominant phenotype
  - 1-3 hours = 46%
  - >3 hours = 59%

Leeper, Annals of Surgery, 2019
Summary of the problem

• Shock is under-recognized
• Children with shock are inadequately resuscitated
• By the time shock is recognized, it may be irreversible
• The pathophysiology leading to coagulopathy begins early after injury
What we should be doing...

• Early identification of shock
• Minimize crystalloid in acutely bleeding patients
• Transfuse blood products
• Transfusion should be as close to a 1:1:1 ratio of PRBC/FFP/platelets (Noland, J Pediatr Surg, 2019)
• Challenge:
  – Products not all available at the same time (particularly in children’s hospitals)
  – Exposes children to multiple donors
  – Potential for clerical error
The potential solution...Whole Blood

- Group O negative whole blood from male donors (decrease incidence of TRALI)
- Cold stored
- Low titer anti A and anti B antibodies (<50)
- Leukocyte-reduced (platelet sparing filter)
Balance

• Benefits
  – More “physiologic resuscitation”
  – Fewer donor exposures
  – Decreased risk for medical error
  – Easier administration

• Risks
  – HEMOLYSIS (only in non group O recipients)
  – rH sensitization
  – Specially prepared units
  – Potential for waste
  – Does it work as well as component therapy?
Who receives it...

- One unit cold stored in ED refrigerator; second unit in the blood bank
- Whole blood is the product of choice in eligible children
  - Traumatic mechanism
  - Greater than one year of age
  - Signs of **SHOCK** due to hemorrhage (persistent tachycardia, evidence of poor perfusion, elevated SIPA, hypotension, evidence of large volume hemorrhage, trauma surgeon discretion)
More details

• Maximum transfusion volume: 40cc/kg (estimated total blood volume ~80cc/kg)
• Initiation of MTP
• After initial transfusion, goal-directed administration of product (TEG and standard labs)
• Children are monitored closely for evidence of hemolysis
  – Clinical signs of transfusion reaction
  – Haptoglobin, LDH, reticulocyte count, Tbili, LDH obtained in the ED and daily for 2 days
• If whole blood unit is NOT used in 14 days, the unit is removed from the ED, reprocessed to pRBC, and a fresh unit is placed in the ED refrigerator
TEG and resuscitation

- TEG routine for all highest level alerts
- Blood product transfusion (and TXA) dependent upon abnormalities in TEG
Initial WB experience

- Severely injured cohort
- Significantly shortened time to administration of all three blood components

Table. Demographic and Injury Characteristics of Children Receiving Whole-Blood Transfusion

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Patients (N = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient and injury</td>
<td></td>
</tr>
<tr>
<td>Age, y, median (IQR)</td>
<td>11 (5-14)</td>
</tr>
<tr>
<td>Sex, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>7 (39)</td>
</tr>
<tr>
<td>Male</td>
<td>11 (61)</td>
</tr>
<tr>
<td>Race, No. (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>15 (83)</td>
</tr>
<tr>
<td>Black</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Mechanism of injury, %</td>
<td></td>
</tr>
<tr>
<td>Blunt</td>
<td>14 (78)</td>
</tr>
<tr>
<td>Penetrating</td>
<td>2 (11)</td>
</tr>
<tr>
<td>Abusive</td>
<td>2 (11)</td>
</tr>
<tr>
<td>Admission GCS^7</td>
<td>3 (3-15)</td>
</tr>
<tr>
<td>Injury severity score^8</td>
<td>34 (26-38)</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
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<tr>
<td>Mortality, No. (%)</td>
<td>8 (44)</td>
</tr>
<tr>
<td>Hospital length of stay, d, median (IQR)</td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>7.5 (3-13)</td>
</tr>
<tr>
<td>Survivors</td>
<td>13 (9-14)</td>
</tr>
<tr>
<td>ICU Length of stay, d, median (IQR)</td>
<td>3.5 (2-6)</td>
</tr>
<tr>
<td>Time receiving mechanical ventilation, d, median (IQR)</td>
<td>2 (1-5)</td>
</tr>
</tbody>
</table>

Abbreviations: GCS, Glasgow coma scale; ICU, intensive care unit; IQR, interquartile range.

^8 Use of whole blood is restricted to patients aged ≥3 years and weighing ≥15 kg.

Leeper, JAMAPeds, 2018
Safety Outcomes

- No adverse transfusion reactions reported.
- There was no evidence of hemolysis; labs did not differ between type O and type non-O at any time point.
Program Evolution

• Based on safety data, broadened indications
  – Initially ≥3 years and 20 cc/kg
  – Life-threatening intra-operative hemorrhage

• To date, 35 patients have received whole blood
  – No transfusion reactions
  – No evidence of hemolysis
  – Whole blood recipients critically injured (median ISS>30)
Cold Platelet Function

• Previous barriers to transfusion of whole blood in civilian trauma populations included the concern that cold storage causes loss of platelet function.

• Recent literature suggests that cold-stored whole blood platelets not only retain function, but may be superior to room temperature platelets.

• In vivo platelet function of cold-stored whole blood had not been evaluated in a civilian pediatric trauma cohort.
Comparison of historical cohort receiving component transfusion and those receiving whole blood

- No difference in platelet count (129x10⁹/L vs 135x10⁹/L)
- No difference in rTEG MA (59.5mm vs 60.2mm)

Leeper, JTACS, 2019
Is whole blood worth it???

• Makes sense
• Military experience suggests “yes”
• Houston experience (Williams, JTACS, 2019)
  – 198 whole blood recipients compared to 152 PRBC ± plasma
  – No difference in overall survival, transfusion reactions,
  – Whole blood recipients required fewer total number of product
  – Adjusted for severity, whole blood associated with a doubling of survival (OR 2.19)
Research opportunities

• Safety
  – Maximum dose/minimum age
• Does whole blood improve clinical outcome?
  – MORTALITY
  – Attenuation of trauma induced coagulopathy
  – VTE
  – Total transfusion volume
  – Number of donor exposures
  – Disability
Summary

• Shock is under-recognized and under-treated in injured children
• Balanced resuscitation is best practice for bleeding children and adults
• Transfusion of cold-stored whole blood provides rapid administration of functional blood components
• Transfusion of whole blood is safe in injured children (at least for those over the age of 1 years)
• Considerable opportunity for collaborative research