Suggestions for Optimizing Use of Plasma in the Era of TRALI Risk Reduction

March 27, 2014  Steve Kleinman, MD
TRALI: A brief history

• Identified as a non-infectious serious hazard of transfusion in the mid 1980s with concern increasing over the next two decades

• The Canadian Consensus Conference on TRALI provided a standard definition in 2004

• AABB issued TRALI risk reduction recommendations in 2006

• AABB conducted a workshop on the topic of a proposed TRALI standard in July 2013
Standard 5.4.1.2 / 29th Ed of Standards

• “Plasma and whole blood for allogeneic transfusion shall be from males, females who have not been pregnant, or females who have been tested since their most recent pregnancy and results interpreted as negative for HLA antibodies.”

• This standard takes effect on April 1, 2014, though many blood collection organizations have already partially or completely implemented the standard

• Association Bulletin #14-02, provides recommendations on methods to meet the Standard

www.aabb.org
Components covered

- Fresh Frozen Plasma (FFP) obtained from whole blood.
- FFP obtained from apheresis [plasmapheresis, or collected concurrently with a cellular component (red cells or platelets)] (combined) red cell plasmapheresis, concurrent (combined) platelet-plasmapheresis.
- Plasma, Cryoprecipitate Reduced (ie, cryo-poor plasma) obtained from whole blood.
- Plasma Frozen Within 24 Hours After Phlebotomy (PF24) obtained from whole blood or apheresis.
- Plasma Frozen Within 24 Hours After Phlebotomy Held At Room Temperature Up To 24 Hours After Phlebotomy (PF24RT24) obtained from apheresis.
- Thawed Plasma from any of the above products.
- Liquid Plasma.
- Whole Blood (if designated for transfusion as whole blood rather than for component preparation).
Evidence for efficacy of interventions in Standard 5.4.1.2

• Supported by published data:
  – ARC hemovigilance program data (reported in Transfusion and summarized in Association Bulletin #12-02)
    • Risk reduction was achieved for Groups A, B, and O plasma where interventions were fully implemented
    • Risk reduction was not achieved for Group AB plasma where such interventions were not fully implemented
  – Other US and international publications also document the efficacy of the intervention (see Association Bulletin #14-02)
TRALI Mitigation, American Red Cross

Before Intervention (2006)  
After Intervention (2008-11)

Eder et al. *Transfusion* 2013;53:1442-1449
Supply of Plasma

• AABB has learned that there is the potential for temporary shortages of plasma, particularly group AB plasma

• With April 1 approaching, this webinar provides recommendations for hospitals to optimize use of plasma to alleviate possible shortages

• Speakers to follow: Kevin Land, MD (Blood Systems), Mark Yazer, MD (U. Pittsburgh) and Jean Otter (AABB)
Suggestions for Optimizing Use of Plasma in the Era of TRALI Risk Reduction

Dr. Kevin Land & Dr. Mark Yazer
Dr. Yazer’s disclosures

- Grifols/Novartis: Speaker’s bureau, advisory board
- Octapharma: Advisory
Solutions to a plasma shortage

KISS Principles

Q1: What is the most commonly used indication for plasma therapy in your hospital?

Q2: When was the last time you got every department together to update policies and protocols based on 21st century EBM?

Right Outcome = Right Patient + Right Product + Right Reason + Right Dose + Right Time

Patient Blood Management Goals

A. Promote better patient outcomes
   • Reduce complications and infection rates
   • Shorten length of stay

B. Optimize blood usage (by reason and dose)
   • Peri-operative blood
   • Blood product utilization

Finding common ground: Or even a reference librarian can tell a doctor something!

“Patients should get every therapeutic they need and none that they don’t.”

PROBLEM: We give too many patients FFP they do not need, yet have a tendency to under dose those really needing it.

SOLUTION: We must support patient need and respect physician want while still giving the lab a voice in promoting sound component therapy.

KJL

Med Techs and Pathologists have every right to talk about appropriate clinical usage of blood components
AB Plasma is just one part of the entire Plasma story: Demand on US Plasma

3% of donor pool group AB

Yazer M, Eder A, Land KJ. How we manage AB plasma inventory in the blood center and transfusion service. Transfusion
What is the right dose of plasma?

<table>
<thead>
<tr>
<th>Max Pt wt (lbs) for 10cc/kg</th>
<th># units</th>
<th>Max Pt wt (lbs) for 15cc/kg</th>
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<tbody>
<tr>
<td>60</td>
<td>1</td>
<td>40</td>
</tr>
<tr>
<td>120</td>
<td>2</td>
<td>80</td>
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<td>300</td>
<td>5</td>
<td>200</td>
</tr>
<tr>
<td>360</td>
<td>6</td>
<td>240</td>
</tr>
</tbody>
</table>

Recommended adult therapeutic dose of FFP is **10-15mL/kg** to provide a 15-20% in coagulation factors.

Total units = Kg * 15 ml/ ~250cc (round up to nearest whole number)
References Supporting using Trigger of INR ~1.8-2.0

• Patients on Warfarin don’t show risk of bleeding until the INR is above 4-4.5. With Plasma treatment, INR decreased to ~2.0.

• Moderately ↑INR do NOT predict/correlate with blood loss.
  - Usefulness of international normalized ratio to predict bleeding complications in patients with end-stage liver disease who undergo cardiac catheterization. Am J Cardiol. 2012 Oct 1;110(7):1062-5.

• No rationale amount of Plasma will "correct" INRs of ≤1.85.

• Plasma INRs extend up to 1.3
  - L L. Holland, Transfusion 2005; 45 :1234

[Diagram of coagulation factors and INR coagulation reserve]
# ABO compatibility for plasma: Compatibility Charts in your Hospital

<table>
<thead>
<tr>
<th>Patient’s ABO group</th>
<th>ABO compatible plasma</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>A, AB</td>
</tr>
<tr>
<td>B</td>
<td>B, AB</td>
</tr>
<tr>
<td>AB</td>
<td>AB</td>
</tr>
<tr>
<td>O</td>
<td>Any ABO group</td>
</tr>
</tbody>
</table>

- Does your hospital have an ABO switching policy?
- When is it used?
- WHO has to be involved to approve switching?
Emergency medicine and trauma surgery use a lot of plasma.

Fixed ratio resuscitation protocols are controversial.
- Providing specific components as necessary is now in vogue.

Without a known ABO group, AB plasma is a bridge to providing compatible plasma.
- AB plasma is a temporary measure!
Solutions to a plasma shortage

- AB plasma is a limited resource
- A severely bleeding patient can deplete a city’s inventory
- Really impress on ED and trauma service the need to send a specimen to the blood bank early in the resuscitation
  - Hard to determine ABO group after 10+ O RBCs administered
- Allows for a prompt transition to ABO compatible plasma for the duration of the resuscitation
Solutions to a plasma shortage

- Pittsburgh solution:
  - ED draws a specimen
  - OR always draws a second specimen
- This increases the odds of receiving at least 1 sample
- The second sample acts as a check type sample for quick transition to ABO compatible plasma

- Delay in providing the check type sample to blood bank delays transition to ABO compatible plasma
- A friendly reminder to send it promptly reduces reliance on AB plasma bridge
Solutions to a plasma shortage: More preparedness

- Not all surgical patients need a transfusion
- Maximum surgical blood ordering guide (MSBOS) should specify those who do
  - A list of all surgical procedures performed at an institution along with a recommendation for the extent of pre-transfusion testing to be obtained before the case begins
- Having one in place, and adhering to its recommendations, reduces reliance on emergency issue plasma
  - For an example of how to create an MSBOS see Frank SM et al. Optimizing preoperative blood ordering with data acquired from an anesthesia information management system. Anesthesiology. 2013;118:1286-1297
Solutions to a plasma shortage:
More preparedness

- Patients who have not been transfused or pregnant in past 90 days can have pre-transfusion testing drawn weeks before surgery date
- Allows blood bank time to perform ABO group, identify antibodies and find units
- Reduces reliance on emergency AB plasma
Solutions to a plasma shortage: Novel uses of A plasma

- 80-85% of recipients will be groups A or O
  - Can safely receive A plasma
- Some trauma centers now use A plasma as part of the initial trauma resuscitation
  - Some screen for units with “low titer” anti-B, others do not
  - “Low titers” generally range from 50-100
- No AABB/FDA standard guiding this practice
- Safety (i.e., lack of hemolysis or worse outcomes) has not been demonstrated in large, systematic trials but anecdotally many centers are happy with the results
Solutions to a plasma shortage: Education

- Education on evidence based plasma transfusion!
- A long term objective
- Not always easy to change a practice culture
- Now is a good time to start

- Education can take many forms
- Traditional rounds style
  - Labour intensive
  - Selection bias?
  - Hard to know what
Solutions to a plasma shortage

- Time of plasma ordering decision support
- AKA...”alerts”
- Free (once implemented)
- Reaches everyone trying to order plasma

<table>
<thead>
<tr>
<th>Feature*</th>
<th>Adjusted odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary analysis (all CDSS, n=71)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Automatic provision of decision support as part of clinician workflow</td>
<td>112.1 (12.9 to ∞)</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Provision of decision support at time and location of decision making</td>
<td>15.4 (1.3 to 300.6)</td>
<td>0.0263</td>
</tr>
<tr>
<td>Provision of recommendation rather than just an assessment</td>
<td>7.1 (1.3 to 45.6)</td>
<td>0.0187</td>
</tr>
<tr>
<td>Computer based generation of decision support</td>
<td>6.3 (1.2 to 45.0)</td>
<td>0.0294</td>
</tr>
</tbody>
</table>

Kawamoto et al BMJ 2005;330:765-768
Computerized Physician Order Entry Alert

PLASMA TRANSFUSION ALERT

Your patient's most recent INR is 1.3.
The institutional guideline for plasma transfusion is INR => 1.6.
The published literature indicates that for an INR < 1.6 the risk of a plasma transfusion exceeds its minimal if any hemostatic benefits. Please choose the appropriate action below to resolve this alert.

Alert Action

- Cancel Plasma Transfusion Order
- Proceed with Plasma Transfusion Order
Plasma alerts and ordering trends

*Statistics compare 4 month pre-adaptive alert period vs. 10 month post-adaptive alert period

Yazer MH et al. Transfusion 2013;53:3120-3127
Solutions to a plasma shortage: Pharmacological hemostatic agents

- 4-factor prothombin complex concentrate (PCC) is FDA approved for use in warfarin treated patients with either bleeding or who require urgent pre-procedure INR reversal
- Non activated clotting factors, includes PC and PS
- How we use PCC in Pittsburgh:
  - INR <4: 25 U/kg
  - INR 4.1-6: 35 U/kg
  - INR >6: 50 U/kg
- So if the patient requires urgent surgical intervention and/or is at risk of TACO, 4-factor PCC should be first choice ahead of plasma
Solutions to a plasma shortage: Use less

Develop plasma utilization guidelines

Passive enforcement by technical staff

Active enforcement by medical director

Tavares M et al. *Transfusion* 2011;51:754
Solutions for Plasma Shortage

Suggestion Summary

- Adopt evidence-based plasma guidelines
  - Dose appropriately
  - CPOE/MSBOS best practices
  - INR 1.8-2.0

- Determine % of AB plasma transfused to non-AB patients and determine why?
  - Too much thawed AB plasma (wastage concerns, other types)
  - ED, MTP, and OB hemorrhage (sample TAT, delays in ABO compatibility switching, confidence issues with lab TAT)

- Review Laboratory and Hospital (including nursing) policies that mandate the exclusive use of AB plasma
Solutions to a plasma shortage: Summary

- Prompt provision of specimen in trauma resuscitation
  - Also check type sample
- Obtain specimen weeks in advance of surgery
- No need for AB plasma for all neonates
- A plasma in emergency situations
- Ongoing educational efforts
- Implement automated alerts in CPOE
- Pharmacological hemostatic
Notification Considerations for Previously Collected Non-TRALI-Mitigated Inventory

Jean Otter, MT(ASCP)SBB
Division Director, Programs
AABB - March 27, 2014
Potential Impact on Plasma Inventory

• Standard: Effective date April 1, 2014
• Association Bulletin #14-02: use of plasma collected before April 1 and held in inventory
• Potential for AB Plasma shortages
• Pre-April 1 inventory, specifically AB Plasma, may not meet the standard
Notification Considerations

• Blood Centers: consider notification and discussion of mixed inventory with hospital customers

• Transfusion Services: consider notification and discussion of mixed inventory with clinicians ordering plasma components

• Facilities: consider a discussion with risk manager or legal counsel regarding approach for notification
• Mixed inventory will be temporary, given expiration of frozen plasma components

• Facilities, considering options and interventions, should adopt an approach that addresses the needs of their patients and patient populations