Unique Challenges in Neonatal Transfusion

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Question #1

• How to safely transfuse very tiny neonates with limited access?

• Current practice at TCH: No transfusion with <2.0-Fr Neo-PICC, PIV (>24 gauge needle) for all transfusions

• Why can’t nurses use Neo-PICC for transfusion of blood products?
Standard Guidelines

• AABB Technical Manual 15th edition: RBC transfusion through 24-25 gauge needles (ID of 0.31 / 0.26 mm) is considered safe.

• Canadian Blood Service: “Transfusion for newborn may be administered through a very small 23 gauge needle”

• No clear guidelines on transfusion through central venous catheters (Neo-PICC).
Pubmed – Transfusion + Neo-PICC

• “Feasibility of red blood cell transfusion through small bore central venous catheter used in neonates” – Pediatr Crit Care Med 2004

1.9-Fr Neo-PICC central venous catheter (ID: 0.028 inches / 0.77mm) : 2 or 20 cc/hr up to 4 hours
Results

“No clinically significant hemolysis was evidenced with red blood cell transfusion through small-bore central venous catheters when using fresher or older CPDA-1 RBC at 2 or 20 mL/hr.”

Wong, ECC. Pediatr Crit Care Med 2004
Google Search

• Allnurses.com: “Do NICUs and PICUs routinely transfuse blood products via 24g IVs or must the patient have some type of central line? They say you must have a 20g IV or larger to transfuse blood products at my hospital. I work with adults in an MICU. I am just curious what gauge IVs are used for all the little patients out there receiving blood products.” - 2011

• 24-26 gauge needles, Neo-PICC lines policy vary (>3.0-Fr), transfuse slowly
Questions

• Can smaller (<3.0-Fr) Neo-PICC be used for transfusion?

• Does it cause significant hemolysis in pRBC?
  - LDH / Plasma Hgb

• For non-pRBC products, does it decrease quality of transfused products?
  - PT / PTT / Fibrinogen / vWF / Platelets activation

• Does it harm the Neo-PICC?
## Neo-PICC Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Argyle 1.9-Fr</th>
<th>Argyle 1.9-Fr (DL)</th>
<th>Vygon 1.0-Fr</th>
<th>24-Gauge Needle</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outer Diameter (mm)</strong></td>
<td>0.6</td>
<td>0.6</td>
<td>0.35</td>
<td>0.556</td>
</tr>
<tr>
<td><strong>Inner Diameter (mm)</strong></td>
<td>0.4</td>
<td>~ 0.2</td>
<td>0.17</td>
<td>0.311</td>
</tr>
<tr>
<td><strong>Lumen Cross Sectional Areas (mm²)</strong></td>
<td>0.111</td>
<td>0.057</td>
<td>0.027</td>
<td>-</td>
</tr>
</tbody>
</table>
The Setup

3 Different Neo-PICC lines

2 Different Rates
1. 5cc/hr or 20cc/hr
2. 10cc/hr or 40cc/hr

37°C Water Bath

Syringe Pump

Pediatrics
## RBC Hemolytic Index

### LDH

<table>
<thead>
<tr>
<th></th>
<th>Pre-Transfusion</th>
<th>5cc/hr</th>
<th>10cc/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argyle 1.9-Fr</td>
<td>324</td>
<td>353</td>
<td>324</td>
</tr>
<tr>
<td>Argyle 1.9-Fr (DL)</td>
<td>324</td>
<td>346</td>
<td>330</td>
</tr>
<tr>
<td>Vygon 1.0-Fr</td>
<td>324</td>
<td>322*</td>
<td>345*</td>
</tr>
</tbody>
</table>

### Plasma Free Hemoglobin

<table>
<thead>
<tr>
<th></th>
<th>Pre-Transfusion</th>
<th>5cc/hr</th>
<th>10cc/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argyle 1.9-Fr</td>
<td>104</td>
<td>107</td>
<td>110</td>
</tr>
<tr>
<td>Argyle 1.9-Fr (DL)</td>
<td>104</td>
<td>97</td>
<td>119</td>
</tr>
<tr>
<td>Vygon 1.0-Fr</td>
<td>104</td>
<td>118*</td>
<td>108*</td>
</tr>
</tbody>
</table>

*High pressure alarm
# FFP Coagulation Index

<table>
<thead>
<tr>
<th></th>
<th>Pre-Transfusion</th>
<th>20cc/hr</th>
<th>40cc/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PT (INR) / PTT / Fibrinogen</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Argyle 1.9-Fr</td>
<td>15.9 (1.29) / 39.7 / 329</td>
<td>15.9 (1.29) / 39 / 319</td>
<td>15.6 (1.26) / 40 / 325</td>
</tr>
<tr>
<td>Argyle 1.9-Fr (DL)</td>
<td>15.9 (1.29) / 39.7 / 329</td>
<td>15.6 (1.26) / 39.2 / 344</td>
<td>16.1 (1.32) / 39.2 / 313</td>
</tr>
<tr>
<td>Vygon 1.0-Fr</td>
<td>15.9 (1.29) / 39.7 / 329</td>
<td>15.9 (1.29) / 38.7 / 327</td>
<td><strong>15.9 (1.29) / 39.6 / 338</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>vWF:Ag / vWF:Rco / Multimer Analysis (H/L)</strong></th>
<th>Pre-Transfusion</th>
<th>20cc/hr</th>
<th>40cc/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argyle 1.9-Fr</td>
<td>54 / 26 / 0.8</td>
<td>76 / 46</td>
<td>49 / 29</td>
</tr>
<tr>
<td>Argyle 1.9-Fr (DL)</td>
<td>54 / 26 / 0.8</td>
<td>59 / 27</td>
<td>54 / 27</td>
</tr>
<tr>
<td>Vygon 1.0-Fr</td>
<td>54 / 26 / 0.8</td>
<td>76 / 37</td>
<td><strong>51 / 19 / 0.8</strong></td>
</tr>
</tbody>
</table>
Cryoprecipitate Coagulation Index

Fibrinogen / vWF:Ag / vWF:Rco / Multimer Analysis (H/L)

<table>
<thead>
<tr>
<th></th>
<th>Pre-Transfusion</th>
<th>20cc/hr</th>
<th>40cc/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argyle 1.9-Fr</td>
<td>1575 / 569 / 638 / 1.4</td>
<td>1626 / 594 / 636</td>
<td>1551 / 567 / 748</td>
</tr>
<tr>
<td>Argyle 1.9-Fr (DL)</td>
<td>1575 / 569 / 638 / 1.4</td>
<td>1600 / 582 / 599</td>
<td>1528 / 571 / 690</td>
</tr>
<tr>
<td>Vygon 1.0-Fr</td>
<td>1575 / 569 / 638 / 1.4</td>
<td>1600 / 559 / 518</td>
<td><strong>1652 / 544 / 628 / 1.4</strong></td>
</tr>
</tbody>
</table>

Pre-Transfusion

Vygon 1.0-Fr @ 40cc/hr
# Platelet Activation Index

<table>
<thead>
<tr>
<th>% of Platelet Doublets</th>
<th>Pre-Transfusion</th>
<th>20cc/hr</th>
<th>40cc/hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argyle 1.9-Fr</td>
<td>6% $</td>
<td>NP $</td>
<td>NP</td>
</tr>
<tr>
<td>Argyle 1.9-Fr (DL)</td>
<td>6% $</td>
<td>NP</td>
<td>NP</td>
</tr>
<tr>
<td>Vygon 1.0-Fr</td>
<td>6% $</td>
<td>NP*</td>
<td>9% **</td>
</tr>
</tbody>
</table>

*High pressure alarm, $EM performed*

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*Baseline*

Argyle 1.9-Fr @ 20cc/hr

Vygon 1.0-Fr @ 40cc/hr
Neo-PICC SEM

After 30 mins of 20 cc/hr and 40cc/hr infusion
Neo-PICC SEM

After 30 mins of 20 cc/hr and 40 cc/hr infusion
Conclusion #1

• No evidence that transfusion of RBC, FFP, Cryoprecipitate through the three Neo-PICC caused deterioration of the products at both high and low transfusion rate.

• However, the concern about clotting is a possibility especially with platelet transfusion using DL Neo-PICC.

• Transfusion of RBC and plasma products through small (1.9-Fr) Neo-PICC may be considered if there is no alternative access for neonates.
Question #2

• Why are we not giving only young RBC to neonates? TRAGI and age of blood

• Current practice at TCH: We reserve specific units for neonates to minimize blood exposure (unique to neonatal setting)

• What kind of impact will a change in policy on our neonates?
Ongoing Discussion

• Growing concerns about storage lesions for RBC and research in adults have led researchers to assess the benefit of transfusing fresh blood to neonates

• According to current guidelines, donated RBC can be safely stored for up to 42 days
Storage Lesion

• Decreased 2,3-DPG
• Increased rigidity of the RBC cytoskeleton
• High PA I (plasminogen activator inhibitor) level
• High CD40 ligand if not leukoreduced
• Nitric oxide depletion
• Increase in interleukin-10
• Decrease in tumor necrosis factor-α.
Fresh RBC in Adults

• Use of red cells stored for more than two weeks was associated with a significantly increased risk of postoperative complications and a reduction in short- and long-term survival\textsuperscript{1}

• Adult study reporting the association between transfusion of older blood and outcomes after trauma concluded that patients receiving \( \geq 7 \) units of older blood had a higher risk of complicated sepsis than patients receiving one or fewer units (adjusted OR =1.9, \( p=0.03 \))\textsuperscript{2}

• Meta-analysis older stored blood significantly increased risk of death (OR=1.16, 95% CI 1.07-1.24)\textsuperscript{3}

1. Koch CG. NEJM 2008
2. Hassan M. Shock 2011
3. Wang, D Transfusion 2012
Studies in Pediatrics

• Transfusion of less than 48 hours old whole blood is associated with significantly less post-op blood loss than the transfusion of packed red blood cells, FFP, and platelets in children under 2 years old who underwent complex cardiac surgery¹

• Reconstituted fresh whole blood used for the prime, throughout cardiopulmonary bypass, and for all transfusion requirements within the first 24 hours postoperatively results in reduced chest tube volume loss and improved clinical outcomes in neonatal patients²

• Ongoing ARIPI Study - necrotizing enterocolitis, intraventricular hemorrhage, bronchopulmonary dysplasia, retinopathy of prematurity, nosocomial infection, length of stay in NICU and length of mechanical ventilation³

1. Manno CS. Blood 1991
3. AABB 2012 Plenary Session
Exposure vs. Inventory Management

• In adult population (First-in first-out)\(^1\)
  - If guidelines recommend the use of RBCs less than 14 days old, then it is expected that 5-10% of the inventory may be lost
  - Larger inventories may be required to keep up the demand for younger RBCs ensuing temporary shortages\(^2\)

• In neonatal population
  - Inventory likely not as big an issue as in adults
  - Exposure is an unique issue with neonates

2. Fontaine MJ. Transfusion 2010
The Setup

- RBC transfusion data for all neonates (<4 months old) at TCH in a six month period (June to November 2011)

- Each neonatal RBC transfusion during the specified time period was recorded with the calculated age of the transfused blood

- Using this retrospective data we predicted the number of neonates who would require additional units / exposures, if < 7 and < 14 days old RBC is needed

- Comparisons of these patient groups against the proportion of patients receiving RBC <42 days old (current practice)
## Retrospective Review of Current Practice

<table>
<thead>
<tr>
<th>Current Observation</th>
<th>7 - 42 days RBC</th>
<th>14 - 42 days RBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total # of transfusions</td>
<td>938</td>
<td>393 (42%)</td>
</tr>
<tr>
<td>Total # of neonates</td>
<td>216</td>
<td>99 (46%)</td>
</tr>
</tbody>
</table>

- A total of 216 neonates received 938 RBC transfusions of which 163 (17%) transfusions were >14 days old and 393 (42%) transfusions were >7 days old.
- Out of 216 neonates: 51 (24%) and 99 (46%) received RBC >14 and >7 days old respectively.
## Predictive Models

<table>
<thead>
<tr>
<th>Policy change to use RBCs of age</th>
<th>Total # of neonates (# with additional exposure)</th>
<th>Projected # of neonates that would be exposed to</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No additional exposure</td>
</tr>
<tr>
<td>&lt; 7 day old</td>
<td>99 (71)</td>
<td>28</td>
</tr>
<tr>
<td>&lt; 14 day old</td>
<td>51 (41)</td>
<td>10</td>
</tr>
</tbody>
</table>
Impact on Inventory

• Our first prediction model (transfusion of only <14 days old RBC) demonstrates that
  - An addition of 67 units of RBC was required.

• Our second model (transfusion of only <7 days old RBC) illustrates that
  - The inventory has to be increased by 120 units.
Conclusion #2

• Significant increase in the number of neonates exposed to additional RBC units while comparing the two models to the current practice

• The majority of neonatal patients (76%) at TCH are being transfused with <14 days old RBC, even without a guideline to transfuse fresh RBC’s

• The more conservative transfusion model <7 days old RBC would significantly increase blood exposure

• A policy of <14 days old RBC’s for neonatal transfusion would provide the most potential benefits with small impact on patient’s exposure (20%) and minimum impact on RBC inventory
Final Thoughts

• Little babies are not tiny adults

• Unique challenges in neonatal transfusion

• Evolving and incomplete

• Innovative ideas to solve clinical problems