Cost-Effective Consideration of CMV Status When Ordering Blood Products: A Clinical Efficacy and Safety Project
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Pediatric Hematology-Oncology

Disclosure

• Drs. Frei-Jones and Sugalski do not have any relationship with commercial companies to disclose.

Clinical Safety and Effectiveness Course

• Center for Patient Safety and Health Policy
  – The Center’s Mission is:
    • to increase quality and safety of clinical care,
    • enhance clinical effectiveness, and
    • integrate quality improvement efforts into health services research and health policy,
  • train the next generation of health professionals to incorporate quality improvement practices in their work.
• Many Department of Pediatric Faculty have participated.

Learning Objectives

• At the end of this presentation the participant will be able to:
  – Identify patients at risk of transfusion associated cytomegalovirus (CMV) infections.
  – Request appropriate special processing of blood products for high risk populations.
  – Use decision tools in routine clinical practice.

What Were We Trying to Accomplish?

OUR AIM STATEMENT

We proposed to decrease by 50% the number of unnecessary CMV negative red blood cell transfusions in pediatric hematology-oncology (PDHO) patients at the Children’s Hospital of San Antonio over 90 days.

Step 1 - Blood Donation

• US blood supply based on voluntary donation
  – 30 million units of blood products transfused annually
• Screening and deferral
  – Any time during screening, collection or processing
  – Temporary or permanent
  – http://www.aabb.org/resources/donation/questionnaires/Pages/dhqaabb.aspx
• Donation takes 20 min

Give Blood
8 Billion Mosquitos
Can’t Be Wrong
Step 2 - Making Packed Red Blood Cells (PRBC)

- Additive Solution
- Spin down whole blood
- Wash and add PRBC

Step 3 & 4 - Testing and Storage

- PRBC Storage
  - Stored at 3-6°C for 42 days in Adsol (additive solution)
- PRBC Testing
  - Routine Screening on all units collected.
  - Antibody testing
    - Hepatitis B, Hepatitis C, HIV, HTLV, Syphilis
  - Nucleic Acid Testing (NAT)
    - HIV, HCV, West Nile
  - Random unit screening.
  - Antibody testing - CMV

Step 5 – Blood Safety

- Infectious Transmission

<table>
<thead>
<tr>
<th>Disease</th>
<th>Window Period</th>
<th>Risk (Per units transfused)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV, plus NAT</td>
<td>10 days</td>
<td>1.500,000</td>
</tr>
<tr>
<td>HBV</td>
<td>59 days</td>
<td>1,200,000-488,000</td>
</tr>
<tr>
<td>HIV, plus NAT</td>
<td>11 days</td>
<td>1.2135,000</td>
</tr>
<tr>
<td>West Nile, plus NAT</td>
<td></td>
<td>0.4:10,000</td>
</tr>
<tr>
<td>CMV</td>
<td>N/A</td>
<td>1.5-4*</td>
</tr>
<tr>
<td>Bacterial Contaminants</td>
<td>N/A</td>
<td>2.6:100,000</td>
</tr>
</tbody>
</table>

* In post-Hematopoietic Stem Cell Transplant (HSCT) patients

CMV Virus

- Member of human herpesvirus family
- First described in 1904 but not isolated until 1957
- Most common perinatal infection in developed countries; 40,000 infections/yr in US
  - Most common congenital cause of sensorineural hearing

CMV Infection

- Overall seroprevalence is ~ 50% in the US
  - Post-natal exposure can occur from almost all body fluids including blood products
  - Post-natal infection is usually asymptomatic in immunocompetent individuals
  - Immunocompromised individuals at risk for serious disease manifestations
    - Sepsis like illness, pneumonia, hepatomegaly, colitis, neuropathy, cytopenias
    - Also at risk for disease reactivation

Transfusion Associated CMV Infection

- Blood product options:
  - Un-tested blood is standard for general population.
  - CMV-negative
  - CMV “Safe”
  - CMV-negative blood is rare.
    - 30-80% of blood donors are CMV sero-positive.
      - CMV survives in circulating white blood cells in CMV positive blood donors.

Leukoreduction = CMV safe

- Each unit of PRBC = 2-5 X10⁹ White Blood Cells (WBC)
  - Leukoreduction reduces risk of Transfusion associated CMV.
  - Third generation leukocyte filters decrease below 1-5 X10⁹ WBC
- PRBC and Platelets that have been leukoreduced are considered CMV-Safe.
  - Fresh Frozen Plasma (FFP) and Cryoprecipitate do not need leukoreduction.

Additional Benefits of Leukoreduction

- Decreases risk of virus transmission
- Decreases risk of febrile reactions
- Decreases risk of Transfusion associated Graft Versus Host Disease (TA-GVHD)
- Decreases risk of HLA alloimmunization

Leukoreduction vs CMV Negative PRBC in High Risk Patients

  - 502 CMV-seronegative recipients of allogeneic/autologous
  H SCT
  - Randomized to leukoreduced vs. CMV-negative products

<table>
<thead>
<tr>
<th></th>
<th>Seronegative Blood</th>
<th>Seronegative PRBC</th>
<th>Platelets</th>
<th>FFP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time After HSCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 hours</td>
<td>2.1%</td>
<td>2.3%</td>
<td>1.9%</td>
<td>2.1%</td>
</tr>
<tr>
<td>48 hours</td>
<td>1.5%</td>
<td>1.9%</td>
<td>1.7%</td>
<td>1.9%</td>
</tr>
<tr>
<td>72 hours</td>
<td>2.1%</td>
<td>2.4%</td>
<td>1.7%</td>
<td>2.4%</td>
</tr>
<tr>
<td>96 hours</td>
<td>1.6%</td>
<td>2.1%</td>
<td>1.6%</td>
<td>2.1%</td>
</tr>
<tr>
<td>120 hours</td>
<td>0.9%</td>
<td>1.7%</td>
<td>1.5%</td>
<td>1.7%</td>
</tr>
<tr>
<td>144 hours</td>
<td>0.9%</td>
<td>1.8%</td>
<td>1.3%</td>
<td>1.8%</td>
</tr>
<tr>
<td>168 hours</td>
<td>1.3%</td>
<td>1.9%</td>
<td>1.6%</td>
<td>2.0%</td>
</tr>
<tr>
<td>192 hours</td>
<td>1.0%</td>
<td>2.1%</td>
<td>1.5%</td>
<td>2.2%</td>
</tr>
<tr>
<td>216 hours</td>
<td>1.0%</td>
<td>2.2%</td>
<td>1.7%</td>
<td>2.2%</td>
</tr>
<tr>
<td>240 hours</td>
<td>1.6%</td>
<td>2.6%</td>
<td>1.9%</td>
<td>2.6%</td>
</tr>
<tr>
<td>250 hours</td>
<td>1.4%</td>
<td>2.5%</td>
<td>1.8%</td>
<td>2.5%</td>
</tr>
<tr>
<td>264 hours</td>
<td>1.4%</td>
<td>2.7%</td>
<td>1.8%</td>
<td>2.7%</td>
</tr>
<tr>
<td>288 hours</td>
<td>1.2%</td>
<td>2.6%</td>
<td>1.7%</td>
<td>2.6%</td>
</tr>
</tbody>
</table>

For any given day the actual number of patients with the % seronegative recipients.

Clinical Significance

  - 2-5 additional deaths attributable to CMV pneumonia for every 250 HSCT recipients if only leukoreduced blood products were used.

Consensus Statements

- Canadian Consensus Conference in 2000
  - Provide products that are both Leukoreduced and CMV-negative for pregnant women, fetal intrauterine transfusions, and allogeneic HSCT recipients
  - "Probably indicated" for solid organ transplants, HIV, and patients likely to receive allogeneic HSCT in the future
  - Did not recommend use of both for low birth weight neonates
- American Association of Blood Banks in 2002
  - Prestorage leukoreduced products can be used instead of CMV-seronegative donors for high-risk populations
  - Prior to data from Nichols study

Transfusion Associated CMV in HSCT

- Prospective randomized cohort with incidence during 2 time periods
  - 867 CMV-negative allogeneic/autologous HSCT recipients
- Results
  - Period 1 – CMV seronegative or leukoreduced
    - 0.7-1.2% of donors were CMV+ or unscreened
    - 1.7% risk of transfusion transmitted
  - Period 2 – Apheresis (as leukoreduced) platelets also used
    - 1.5% of RBC donors were CMV+ or unscreened
    - 15.8% of platelet donors were CMV+ or unscreened
    - 4% risk of transfusion transmitted CMV
  - Patients who received leukoreduced products had higher risk of CMV infection compared to those who had only seronegative products

What about Pediatric Hematology-Oncology?

- Survey of 264 institutions
- Question: leukoreduction with or without CMV-negative blood products to prevent CMV transmission
- 67% used universal leukoreduction
  - 7.2% used CMV-negative for all patients
  - 4.9% reserved CMV-negative for CMV negative patients
- 33% did not use universal leukoreduction
  - 56% used CMV-negative for CMV negative patients
  - 44% did not use CMV negative products (leukoreduced only)


Current Recommendations

- CMV sero-negative oncology patients who are candidates for HSCT should receive CMV negative blood products.
- CMV negative blood products should be reserved for CMV sero-negative patients.

Review of Our Practice

- High rate of CMV negative blood product ordering
  - 66% (27/41) did not require CMV negative products but received them anyways.
  - Expected CMV negative product order rate based on our population and guidelines = 30%.

Why is this important?

- CMV negative blood products are rare
  - Poor use of limited resources
- Additional cost of testing to product
- Delay in identification of blood product

The Team

- Melissa Frei-Jones, MD MSCI
  - PDHO Faculty
- Aaron Sugalski, DO
  - PDHO Fellow/Faculty
- Bradley Scoggins, MD
  - PGY-2, Pediatrics
- Leopoldo Cobos
  - Transfusion Services Supervisor

Project Milestones

- Team Created: February 2012
- AIM statement created: March 2012
- Bi-Monthly Team Meetings: March 2012
- Background Data, Brainstorm Sessions, Workflow and Fishbone Analyses: June 2012
- Interventions Implemented: June 2012
- Data Analysis: January 2012 - Ongoing
- CS&E Presentation: Sept. 14, 2012
**Process Flow Chart**

1. Pt identified needing blood transfusion
2. MD/PNP Order for Transfusion
3. Order Entry (MA or RN)
4. Blood Bank Receives Order (Electronic)
5. Nurse Collect Type and Cross
6. Two Nurses Verify Blood Unit
7. Pt identified needing blood transfusion
8. Nurse Collect Type and Cross
9. Blood Bank Identifies Unit
10. Medical Assistant
11. Nurse
12. Patient
13. Blood Bank
14. Fishbone Analysis

**Intervention - Education**

- Medical Providers
  - Meeting of Heme-Onc Faculty and PNPs
  - Creates and disseminates decision tree
- Housestaff
  - Resident Inpatient School
    - Brad Scoggins, MD
  - Discussed CMV Decision Tree and standardized transfusion orders.
- Inpatient and Outpatient Nursing staff
  - Reviewed decision tree
  - Transfusion labels on patient charts

**Intervention – Blood Bank**

- Review and correct CMV status for existing patients
- Revise Order Process for Existing Patients
  - Question any CMV order if it varies from known status
- Create Order Process for New Patients
  - CMV status reviewed by MD and included in medical record

**Implementing the Change**

- April 26, 2012 - Faculty Create CMV Decision Tree
- May, 2012 – Transfusion Labels
- May 8, 2012 – Updated CMV status with Blood Bank
- June, 2012 – Nursing Meeting
- August 9, 2012 – Housestaff Inpatient School
Initial PRBC Results

• Pre-intervention = 81% CMV-negative
  – 4-month average (165/204)
• After Faculty Meeting = 61% (33/54)
• After Blood Bank Intervention = 40% (17/43)
• After Resident Education = 35% (32/91)
  – Sustained over 2 months

Return on Investment

• South Texas Blood and Tissue charge to hospital for CMV negative PRBC = $36/unit
• Annual cost prior to intervention = $17,280
  – Assume 80% of units ordered CMV negative and we average 50 PRBC units/month over 12 months
• Annual cost after intervention = $7,560
  – 35% of units ordered CMV negative
• Annual Savings for PRBC = $9,720

Future Goals and Directions

• Type of blood product
  – Platelets
• Other medical and surgical services
• CPOE
  – Standardized order sets created to be implemented with CPOE hospital wide

Conclusion

• Through simple, inexpensive measures, we successfully reduced unnecessary CMV negative PRBC ordering in Pediatric Hematology-Oncology patients.
• Creation of a CMV Decision Tree aided faculty, nursing, housestaff and laboratory personnel to change ordering practices.

Thank you!