Erythrocyte Depletion of Bone Marrow in Stem Cell transplantation in a Pediatric Center Comparison of two Systems

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bone marrow
bone marrow aspiration
Criteria for HPC donors

- Healthy
- HLA typing
- CMV status
- Number of pregnancies
- Age
- ...
- Not ABO match
# How do I approach ABO-incompatible hematopoietic progenitor cell transplantation?

Jennifer Daniel-Johnson and Joseph Schwartz

**TRANSFUSION** 2011;51:1143-1149.

## Table 1. Types of ABO incompatibility, potential adverse consequences, and recommended interventions

<table>
<thead>
<tr>
<th>Definition</th>
<th>Major</th>
<th>Minor</th>
<th>Bidirectional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor-recipient ABO pairs</td>
<td>Recipient isoagglutinins (anti-A, anti-B, anti-A,B) incompatible with donor RBCs</td>
<td>Recipient RBCs incompatible with donor isoagglutinins.</td>
<td>Combination of both incompatibilities</td>
</tr>
<tr>
<td></td>
<td>Group A, B, and AB donor and Group O recipient</td>
<td>Group O donor and group A, B, or AB recipient</td>
<td>Group A donor and B recipient</td>
</tr>
<tr>
<td></td>
<td>Group AB donor and group A or B recipient</td>
<td></td>
<td>Group B donor and A recipient</td>
</tr>
<tr>
<td></td>
<td>Immediate hemolysis</td>
<td>Immediate hemolysis</td>
<td>Combination of potential adverse consequences seen with major and minor incompatibility</td>
</tr>
<tr>
<td></td>
<td>Delayed RBC engraftment</td>
<td>Passenger lymphocyte syndrome causing delayed hemolysis</td>
<td>Combination of interventions used for major and minor incompatibility</td>
</tr>
<tr>
<td></td>
<td>PRCA</td>
<td>Plasma reduction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RBC reduction if &gt;30 mL RBC and/or if recipient isoagglutinin titers &gt;32</td>
<td>Close clinical and laboratory observation, between Days +5 and 15 after HPC transplantation for hemolysis (e.g., Hb/Hct, LDH, bilirubin, hemoglobinemia)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transfuse ABO appropriate blood products</td>
<td>Transfuse ABO appropriate blood products</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Replacement of recipient RBCs with donor type via RBC exchange (rarely), rituximab</td>
<td></td>
</tr>
<tr>
<td>Additional or alternate interventions that may be performed</td>
<td>Recipient's isoagglutinins removal before transplantation via TPE or immunoadsorption</td>
<td></td>
<td>Combination of interventions used for major and minor incompatibility</td>
</tr>
</tbody>
</table>
Donor

Recipient

matched
Donor

Recipient

minor

A

©
Donor  

Recipient  

minor

0

AB
Donor  

Recipient  

bidirectional
# Immunohematological consequences of ABO-incompatible transplantation

<table>
<thead>
<tr>
<th>Incompatibility</th>
<th>Consequence</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABO major</td>
<td>Acute hemolysis</td>
<td>Infusion of incompatible red cells. Loss of HPC from processing to remove red cells. Expression of ABO antigens in granulocytes and platelets.</td>
</tr>
<tr>
<td></td>
<td>Delayed granulocyte and platelet engraftment</td>
<td>Loss of HPC from processing to remove red cells. Expression of ABO antigens in granulocytes and platelets.</td>
</tr>
<tr>
<td></td>
<td>Delayed red cell engraftment</td>
<td>Host anti-donor isoagglutinins.</td>
</tr>
<tr>
<td></td>
<td>Pure red cell aplasia</td>
<td>Persistence of anti-donor isoagglutinins.</td>
</tr>
<tr>
<td>ABO minor</td>
<td>Acute hemolysis</td>
<td>Donor plasma with high isoagglutinin titers.</td>
</tr>
<tr>
<td></td>
<td>Delayed hemolytic reaction</td>
<td>Passenger lymphocytes producing anti-host isoagglutinins.</td>
</tr>
</tbody>
</table>

Rowley et.al. BMT 2011
ABO Mismatch Is Associated with Increased Nonrelapse Mortality after Allogeneic Hematopoietic Cell Transplantation

Aaron C. Logan¹, Zhiyu Wang², Kamran Alimoghaddam³, Ruby M. Wong², Tze Lai², Robert S. Negrin⁴, Carl Grumet⁵, Brent R. Logan⁶, Mei-Jie Zhang⁶, Stephen R. Spellman⁷, Stephanie J. Lee⁸, David B. Miklos⁴,* on behalf of the Center for International Blood and Marrow Transplantation

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⁸ Fred Hutchinson Cancer Center, Seattle, Washington
Red cell salvage and reinfusion in pediatric bone marrow donors

M Kletzel1,2, M Olszewski2, K Danner-Koptik1, K Coyne1 and PR Haut1

1Division of Pediatric Hematology/Oncology, Stem Cell Transplant Program and 2Stem Cell Processing Laboratory, Children’s Memorial Hospital/Northwestern University Medical School, Chicago, IL, USA

- Use of a semi-automated processing technique to salvage red blood cells from pediatric bone marrow donors to minimize the risk of severe anemia following bone marrow harvest and ABO incompatibility in the recipient.

- Red cell salvage performed in a semi-automated closed system is safe and reduces the risk of post-bone marrow harvest anemia in pediatric donors, decreases the volume infused into the donor and enriches the mononuclear and CD34+ cell population, without affecting hematopoietic reconstitution.
the rational for erythrocyte depletion of the bone marrow

• Major and minor ABO incompatibility between donor and recipient, to avoid acute hemolytic reactions.
• Discrepancy between bone marrow volume harvested and bodyweight of the recipient (> 20 ml/kg bw) especially in cardiorespiratory instable patients
• Before further manipulation like positive or negative selection of the bone marrow harvest
bone marrow procedure

- Priming pRBC
- Bone marrow bag
- Inlet line
- Return line
Why priming?
bone marrow procedure

- from 2008 to 2015
- 21 procedures with the COBE spectra in 21 patients
- 15 with the COBE OPTIA in 15 patients
- ABO mismatched allogeneic bone marrow transplantations
- Diagnosis mainly ALL, AML, HLH, SCIDS

- COBE spectra
  - KMV program
  - 3 times priming with ABO compatible pRBC
- COBE OPTIA
  - Bone marrow program
  - 3 times priming with ABO compatible pRBC
<table>
<thead>
<tr>
<th></th>
<th>COBE spectra</th>
<th>COBE OPTIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of procedures</td>
<td>21</td>
<td>15</td>
</tr>
<tr>
<td>Major ABO</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Minor ABO</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Bidirectional</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Volume</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Age [y]</td>
<td>8.64 +/- 2.58</td>
<td>8.76 +/- 4.74</td>
</tr>
<tr>
<td>Bw [kg]</td>
<td>32 +/- 9.46</td>
<td>27 +/- 14.24</td>
</tr>
<tr>
<td>BM volume [ml]</td>
<td>1019 (787 – 1252)</td>
<td>960 (759 – 1161)</td>
</tr>
<tr>
<td>Product volume [ml]</td>
<td>98 +/- 15</td>
<td>91 +/- 17</td>
</tr>
</tbody>
</table>
$p = 0.960$
p = 0.589
p = 0.650
<table>
<thead>
<tr>
<th>Recovery [%]</th>
<th>COBE spectra</th>
<th>COBE OPTIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte</td>
<td>40</td>
<td>50*</td>
</tr>
<tr>
<td>Erythrocytes</td>
<td>5.5</td>
<td>1.4*</td>
</tr>
<tr>
<td>Platelets</td>
<td>48</td>
<td>79*</td>
</tr>
<tr>
<td>CD3</td>
<td>104</td>
<td>99&lt;sub&gt;ns&lt;/sub&gt;</td>
</tr>
<tr>
<td>CD19</td>
<td>98</td>
<td>96&lt;sub&gt;ns&lt;/sub&gt;</td>
</tr>
<tr>
<td>Granulo</td>
<td>21</td>
<td>35*</td>
</tr>
<tr>
<td>Mono</td>
<td>96</td>
<td>82&lt;sub&gt;ns&lt;/sub&gt;</td>
</tr>
<tr>
<td>CD34+ HPC</td>
<td>98</td>
<td>103&lt;sub&gt;ns&lt;/sub&gt;</td>
</tr>
<tr>
<td>CD34+/CD19-</td>
<td>99</td>
<td>96&lt;sub&gt;ns&lt;/sub&gt;</td>
</tr>
</tbody>
</table>
p = 0.096
p = 0.851
p < 0.0001
$p = 0.017$
p = 0.471
p = 0.785
$p = 0.159$
p = 0.035
CD34+ HPC/kg before and after
p = 0.580
p = 0.795
cox regression p = 0.965

U-Test p = 0.8329
cox regression p = 0.788

U-Test p = 0.9556
For long-term overall survival, the data are too preliminary.
bone marrow procedure

CD34+ collection efficiency

U-Test p = 0.12278

residual erythrocyte volume

U-Test p = 0.1783

days to reach > 1 G/l leukocytes

The erythrocyte depletion of bone marrow with OPTIA system is regarding the leukocytes and leukocyte subpopulations as efficient as the procedure with the COBE spectra, even in pediatric patients.

The engraftment for Leukocytes and platelets were not statistically significant different in the 2 groups.

The platelet and granulocyte contamination of the product was higher in the OPTIA system.

The OPTIA system showed lower erythrocyte contamination, which is superior to the older system and also superior to Fenwal CS 3000 plus and AMICUS (V.Witt, JCA, 2011) if we compare our former published data with this data.

In this evaluation 4 more patients were included, than in the abstract published, all 4 were in the OPTIA group.