Pathogen Inactivation and Function of Platelets and Red Cells

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Overview

• Laboratory investigations of the effect of PI on platelet and RBC function
• Clinical assessment of platelet and RBC function after PI
• Where do we go from here?
PI technologies

- Effective against most transfusion transmissible agents
- Dose must balance killing pathogens with killing the transfusion cells
- Risk mitigation must consider both infectious risks and risks to product efficacy
Laboratory Assessment of Platelet and RBC Function
Abundant laboratory data indicate that all PI treatments damage platelets


Osman A et al. *Platelets* 2015; 26:154-63
Numerous studies have demonstrated increased activation with Intercept treatment.
Mirasol treatment related damage to platelets can be modulated by inactivation approach

Platelet concentrates derived from Mirasol-treated whole blood had better quality parameters than Mirasol-treated platelet concentrates on day 7 of storage.

UV-C (Theraflex) also accelerates storage lesions

Tynngard N et al. Transfusion 2015; 55:1169
Approaches to PI for RBC vary more than platelet methods

• PI treatment protocols differ for Mirasol and Intercept and this is reflected in final product.
• Due to wash step (exchange), Intercept-treated RBC have lower hemolysis and higher ATP than control RBCs. (Wiltshire M et al. Transfus Med. 2016;26:208-14)
Intercept for RBC (S-303) causes only modest changes
## RBC quality is negatively affected by Mirasol treatment of WB

<table>
<thead>
<tr>
<th>Assay</th>
<th>Week 0</th>
<th>Week 1</th>
<th>Week 3</th>
<th>Week 6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RCC</td>
<td>RCC&lt;sub&gt;PI-WB&lt;/sub&gt;</td>
<td>RCC</td>
<td>RCC&lt;sub&gt;PI-WB&lt;/sub&gt;</td>
</tr>
<tr>
<td>Hemolysis (%)</td>
<td>0.04 ± 0.01</td>
<td>0.05 ± 0.01</td>
<td>0.06 ± 0.01</td>
<td>* 0.40 ± 0.01</td>
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<tr>
<td>Potassium (mM)</td>
<td>1.1 ± 0.2</td>
<td>* 1.7 ± 0.5</td>
<td>9.6 ± 0.2</td>
<td>* 27.1 ± 1.3</td>
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<tr>
<td>ATP (µmol/g Hb)</td>
<td>4.25 ± 0.36</td>
<td>* 4.14 ± 0.31</td>
<td>4.51 ± 0.28</td>
<td>* 4.15 ± 0.32</td>
</tr>
<tr>
<td>MP count (× µL&lt;sup&gt;-1&lt;/sup&gt; SN)</td>
<td>749 ± 220</td>
<td>765 ± 220</td>
<td>838 ± 318</td>
<td>2227 ± 929</td>
</tr>
</tbody>
</table>

Pool and split model: RCC prepared from untreated vs. Mirasol treated whole blood.

Schubert et al. Transfusion 2015; 55:815-23
Clinical Assessment of Platelet and RBC Function
Clinical Assessment of PI treatment

Upon careful assessment, effects of PI on platelet transfusions can be seen

But do these differences matter?

Experience with routine use in European centres would suggest that they do not.

Perhaps effects are masked by transfusion practice (high dosing, scheduling).
RBCs produced from Mirasol treated whole blood have a shortened shelf-life

Red blood cells derived from whole blood treated with riboflavin and ultraviolet light maintain adequate survival in vivo after 21 days of storage

Jose A. Cancelas,¹ Sherrill J. Slichter,²³ Neeta Rugg,¹ P. Gayle Pratt,¹ Shawnagay Nestheide,¹ Jill Corson,² Esther Pellham,² Marty Huntington,⁴ and Raymond P. Goodrich⁵

TRANSFUSION 2017;57:1218–1225
Clinical Assessment of PI treatment

Intercept treated RBCs are not exposed to UV and have near normal storage time
Pathogen Inactivation of Blood Products

Are concerns over use of PI-products in trauma warranted?


Beware of Pathogen Reduced blood products with reduced potency

Losses of clotting activity associated with the manipulation of blood products

**Pathogen Inactivation of Blood Products**

*In vitro simulation of in vivo PI-WB transfusion*

- **Max clot formation**
  - Normal WB
  - Diluted WB
  - Blood replacement
  - PI-treated WB

- **Fibrinogen supplementation**
  - RiaSTAP 1 µg/µL
  - Blood replacement & RiaSTAP suppl.

(♦) Normal WB (Hct40%) and hemodilution (Hct20%).
* n= 8 replicates ±SD, (p < 0.01). ROTEM monitored.

*Open symbol: WB unit
Closed symbol: PI treated WB unit

Arbaeen A. et al  ISBT Copenhagen 2017
Pathogen Inactivation of Blood Products

Perhaps not....

We need to see publications of the recent clinical studies and await the results of new studies!
Where Do We Go From Here?
Gaps to Fill Using Research Effort

- Can we develop strategies to minimize damage to platelets and RBCs?
  - Different additive solutions or storage conditions?
- Will the use of multiple types of PI-treated products in trauma really create a problem?
- How do we determine which in vitro parameters should be used for product quality assurance? DAMPS?
Thank you for your attention