Adding to platelet safety & life: Experience with Platelet Additive Solution (PAS)

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Single Donor Platelet Transfusion

• Single Donor Platelet (SDP) is widely used component for various Thrombocytopenic patients
• SDP generally prepared and stored with 200-300ml of donor plasma and shelf life if 5 days
• Due to large volume of plasma ABO incompatible SDP transfusion is not practiced routinely
Platelet additive solutions

• Platelet Additive Solutions (PAS) are crystalloid nutrient media used in place of plasma for platelet storage.
• They replace 60-70% of plasma in platelet components, so the amount of storage plasma can be decreased.
Platelet additive solutions: Benefits

• Lower risk for allergic transfusion reactions
• Lower incidence of other plasma-associated transfusion reactions, such as ABO hemolytic reactions and TRALI
• Extended Storage
• Facilitates ABO incompatible SDP Tx
• Compatible with pathogen reduction technology (PRT)
• Equivalent clinical efficacy to control bleeding, compared to platelets stored in 100% plasma
Extended storage of platelets in SSP⁺ platelet additive solution

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Table 1 Additive composition

<table>
<thead>
<tr>
<th></th>
<th>PAS-II</th>
<th>PAS-III</th>
<th>SSP⁺/PAS-III M</th>
<th>Composol</th>
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<tbody>
<tr>
<td>NaCl</td>
<td>115.5 mm</td>
<td>77.3 mm</td>
<td>69.3 mm</td>
<td>90.0 mm</td>
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<tr>
<td>NaH₂PO₄/Na₂HPO₄</td>
<td>–</td>
<td>28.2 mm</td>
<td>28.2 mm</td>
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<tr>
<td>Trisodium citrate</td>
<td>10.0 mm</td>
<td>10.8 mm</td>
<td>10.8 mm</td>
<td>10.9 mm</td>
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<tr>
<td>Sodium acetate</td>
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<td>32.5 mm</td>
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<tr>
<td>KCl</td>
<td>–</td>
<td>–</td>
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<tr>
<td>MgCl₂/MgSO₄</td>
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<tr>
<td>Gluconate</td>
<td>–</td>
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<td>23.0 mm</td>
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### PAS III: Chemical Composition

**Focus on SSP+**

Formulation and principle of action

<table>
<thead>
<tr>
<th>Components</th>
<th>Action</th>
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</thead>
<tbody>
<tr>
<td><strong>EFFECTS ON PLATELETS METABOLISM</strong></td>
<td></td>
</tr>
</tbody>
</table>
| Acetate | - Substrate for platelet metabolism (with glucose)  
- Maintains pH stable (storage) |
| Phosphate | - pH buffer  
- Maintaining good in vitro characteristics during interruption of agitation |
| **EFFECTS ON THE FUNCTION OF PLATELETS MEMBRANE** | |
| Citrate | - Prevention of coagulation |
| Magnesium | - Prevention of aggregation  
- Reduction of platelets activation |
| Potassium | - Prevention of aggregation  
- Reduction of platelets activation  
- Reduction of glycolysis  
- Maintaining pH levels |
PAS: Bangalore Experience

- Rotary Bangalore TTK Blood Bank, a non-profit organization
- Engaged in issuing safe blood and blood components to patients in and around Bangalore over the past 32 years
- Collects an average of 40,000 blood units per year from VNRBD only
- Performs nearly 2500 Single Donor Platelets (SDP) donations every year
- All the whole blood units are collected from Voluntary blood donors & tested by NAT along with the serology testing
PAS: Bangalore Experience

- Intended to collect all SDPs also from voluntary blood donors & get the NAT testing done

**CHALLENGE**
- ABO match SDP transfusion is practiced
- Due to short shelf life & high cost,
  - Maintaining inventory of SDPs units

- Started using SDP with PAS (SSP+, MacoPharma, Moveaux, France)

- For better inventory management & to facilitates ABO incompatible SDP transfusion
PAS: Bangalore Experience

• Started using SDP with PAS (SSP+, MacoPharma, Moveaux, France)
• For better inventory management & to facilitates ABO incompatible SDP transfusion
PAS: Bangalore Experience

• Strategy: Calling Voluntary donors from near by colleges & offices
• SDP donation after routine med check like WB as well as CBC
• SDPs are collected in PAS
• Samples tested by Serology(Vitros, OCD) & ID NAT
• SDPs available on shelf to issue any pt
• Doctors asking for SDPs were informed about PAS & any ABO group transfusion
• Storage centers: Keep SDP with them for emergencies
• Individual patient request: bring request & collect SDP, NO donation required
PAS: Bangalore Experience

• Objective: validation of SDP using PAS and also to analyze their clinical outcome

• Total 1674 SDP collected in Platelet additive Solution (PAS) from June-Oct 2016 by different apheresis systems Amicus device (n=1024), Trima Accel (n=446) & MCS+ (n=204).

• Amicus & MCS+ has automated programming for PAS but in Trima, SDP was collected as concentrate & then PAS was added with sterile connecting device.

• PAS to Plasma ratio was 70:30
Parameters analyzed

• Platelet count: Day 1 & day 5
• Antibody titers of anti-A & anti-B
• pH
• Swirling
• Transfusion reaction reported
PAS: Bangalore Experience

<table>
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<th>2016</th>
<th>SDP collected</th>
<th>QC Analysis</th>
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<tr>
<td>June</td>
<td>347</td>
<td>152</td>
</tr>
<tr>
<td>July</td>
<td>450</td>
<td>92</td>
</tr>
<tr>
<td>Aug</td>
<td>344</td>
<td>44</td>
</tr>
<tr>
<td>Sept</td>
<td>267</td>
<td>33</td>
</tr>
<tr>
<td>Oct</td>
<td>266</td>
<td>35</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1674</td>
<td>356</td>
</tr>
</tbody>
</table>

QC Analysis
SDP collected

June July Aug Sept Oct TOTAL
### Platelet Count: Day 1-2

<table>
<thead>
<tr>
<th>Machine</th>
<th>&lt;3.0×10^{11}</th>
<th>3.0-4.0×10^{11}</th>
<th>&gt;4.0×10^{11}</th>
<th>Total</th>
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<tbody>
<tr>
<td>Amicus</td>
<td>8</td>
<td>156</td>
<td>68</td>
<td>232</td>
</tr>
<tr>
<td>Trima Accel</td>
<td>6</td>
<td>56</td>
<td>22</td>
<td>84</td>
</tr>
<tr>
<td>MCS+</td>
<td>0</td>
<td>32</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>14 (3.9%)</strong></td>
<td><strong>244 (68%)</strong></td>
<td><strong>98 (27%)</strong></td>
<td><strong>356</strong></td>
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# Platelet Count: Day 4-5

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<thead>
<tr>
<th>Machine</th>
<th>&lt;3.0×10ⁱ¹</th>
<th>3.0-4.0×10ⁱ¹</th>
<th>&gt;4.0×10ⁱ¹</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amicus</td>
<td>7</td>
<td>23</td>
<td>6</td>
<td>36</td>
</tr>
<tr>
<td>Trima Accel</td>
<td>0</td>
<td>20</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>MCS+</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>7(11.2%)</td>
<td>49(79.1%)</td>
<td>9(9.6%)</td>
<td>62</td>
</tr>
</tbody>
</table>
Antibody titres: Day 1-2

<table>
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<tr>
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<th>Anti-A Titre Results</th>
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<th>Anti-B Titre Results</th>
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<tr>
<td>NEG</td>
<td>1:1</td>
<td>NEG</td>
<td>1:1</td>
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<tr>
<td>32</td>
<td>68</td>
<td>21</td>
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<td>68</td>
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<td>86</td>
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<tr>
<td>74</td>
<td>96</td>
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<tr>
<td>96</td>
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</tr>
<tr>
<td>69</td>
<td>15</td>
<td>29</td>
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</tr>
<tr>
<td>15</td>
<td>2</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>
pH & Swirling

• All the units checked for pH & found >6.4, checked at Day one
• Swirling checked & found satisfactory on Day one & on the day of issue
Adverse Transfusion reaction reporting

- No adverse transfusion reaction reported from June-Oct due to SDP transfusion
- Year 2015, we have 14 allergic & 2 Febrile transfusion reported out of 2364 SDP transfusion
Feedback from Hospitals/Users

- Written feedback was taken from the hospitals (specially storage center) at 1 week of using PAS and after 45 days
  - No Tx reaction (Allergic/Hemolytic)
  - No difference (clinically significant) in platelet increment noticed as compare to Plasma SDP
  - Access of SDP is easy & quick
  - Availability: smaller hosp/ NH are comfortable in admitting low count Dengue/ at risk dengue cases
The Impact of Platelet Additive Solution Apheresis Platelets on Allergic Transfusion Reactions and Corrected Count Increment

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2Department of Epidemiology and Biostatistics, Case Western Reserve University, Cleveland, OH
3American Red Cross, Rockville, MD

Abstract

Background—Allergic transfusion reaction (ATR) incidence ranges from 1 to 3 percent of all transfusions. We evaluated the impact of InterSol platelet additive solution (PAS) platelets (APs) on the incidence of ATRs and the post-transfusion platelet increment.

Study Design and Methods—This retrospective study evaluated all ATRs among patients at a university hospital that maintained a mixed inventory of PAS APs and non-PAS APs (standard plasma suspended platelets). Corrected count increments (CCI) were calculated for AP transfusions of individuals who received both a PAS and non-PAS AP transfusion within a 7 day period. Hypothesis testing was performed with chi-square test for dichotomous variables and Student's t-tests for continuous variables.

Results—The incidence of ATRs among the non-PAS APs was 1.85% (72 ATRs/3884 transfusions) and 1.01% (12 ATRs/1194 transfusions) for PAS APs (RR=0.54, 95%CI=0.30–0.99, p=0.04). However, there was no difference in the incidence of febrile non-hemolytic transfusion reactions between non-PAS APs (incidence 0.70%, 27/3884) compared to PAS APs (incidence 0.59%, 7/1194, p=0.69). Among 223 individuals with paired non-PAS and PAS AP transfusions, the CCI at 1–4 hours after transfusion was 4932 (95%CI 4452–5412) for non-PAS APs and was lower for PAS APs, CCI=3766 (95%CI 3375–4158, p<0.001). However, there was no significant difference in CCI at 12–24 hours between non-PAS (CCI=2135, 95%CI 1696–2572) and PAS APs (CCI=1745, 95%CI 1272–2217, p=0.14).

Conclusions—PAS APs substantially reduce the number of ATRs. CCIs for PAS APs were lower immediately after transfusion, but not significantly different at 12–24 hours.

Keywords

allergic transfusion reaction; apheresis platelet; wash; concentrate; urticaria; hives; anaphylaxis; premedication; diphenhydramine; hypersensitivity; platelet additive solution
**In vitro and in vivo effects of potassium and magnesium on storage up to 7 days of apheresis platelet concentrates in platelet additive solution**

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**Background and Objective** Prolonged storage of platelets up to 7 days provides improved availability, logistical management and decreased wastage. Beside methods of bacterial detection, addition of magnesium and potassium to the platelet storage solution (SSP+) may further improve the quality of platelets with extended storage.

**Materials and Methods** Apheresis platelets from 10 donors were divided and stored in two different platelet additive solutions (PAS) (Intersol and SSP+) for a paired comparison. A variety of *in vitro* platelet function and metabolic assays were performed both on day 1 and after 7 days of storage. For *in vitro* study, platelets were labelled with either ⁴¹Indium or ⁵¹Chromium after 7 days of storage and were injected into the corresponding donor. Serial blood samples were drawn for recovery and survival measurements.

**Results** *In vitro* parameters for SSP+ showed significantly reduced glycolysis (lower glucose consumption and decreased production of lactate), a higher hypotonic shock response (HSR) and the extent of shape change reactivity and a lower degree of platelet activation by means of RANTES (regulated on activation, normal, T cell-expressed, and secreted), CD62p and CD63 expression. Platelet recovery on day 7 was higher for Intersol as compared to SSP+, 65 ± 11 vs. 53 ± 13% (*P* = 0.023), and survival showed no difference 4.2 ± 1.9 vs. 3.6 ± 1.4 days.

**Conclusion** *In vitro* characteristics of platelets stored in PAS with addition of potassium and magnesium indicated higher quality, but this could not be verified by the *in vitro* parameters by means of recovery and survival.

**Keywords:** apheresis platelets, chromium, indium, platelet additive solution, platelet storage.
Evaluation of the automated collection and extended storage of apheresis platelets in additive solution

Lacey Johnson, Kelly M. Winter, Tanja Hartkopf-Theis, Samantha Reid, Matthew Kwok, and Denese C. Marks

BACKGROUND: Collecting apheresis platelets (PLTs) into additive solution has many potential benefits. The new Trima software (Version 6.0, Cardian-BCT) allows automated addition of PLT additive solution (PAS) after collection, compared to Trima Version 5.1, which only collects PLTs into plasma. The aim of this study was to compare PLT quality during extended storage, after collection with the different Trima systems.

STUDY DESIGN AND METHODS: Apheresis PLTs were collected using both Trima Accel apheresis systems. The test PLT units (n = 12) were collected using the new Trima Version 6.0 into PLT A8 (PAS-IIIM), while the control units (n = 8) were collected into autologous plasma using Trima Version 5.1. All units were stored for 9 days, and in vitro cell quality variables were evaluated during this time.

RESULTS: PLTs collected in PAS-IIIM maintained a stable pH between 7.2 and 7.4, whereas plasma-stored apheresis units exhibited significantly increased acidity during storage, due to lactate accumulation and bicarbonate exhaustion. Plasma-stored PLTs also demonstrated a more rapid consumption of glucose. However, there was little difference in PLT activation or cytokine secretion between PAS-IIIM and control PLTs.

CONCLUSION: These data indicate that apheresis PLT concentrates collected in PAS-IIIM, using Trima Version 6.0 software, maintained acceptable PLT metabolic and cellular characteristics until Day 9 of storage.

In Australia, buffy coat-derived pooled platelets (PLTs) are currently prepared in approximately 70% additive solution (PAS-IIIM, SSP+), whereas apheresis PLTs are collected and stored in 100% plasma. Collection of apheresis PLTs into PLT additive solution (PAS) would allow standardization of PLT production in Australia, as well as additional benefits. First, the use of PAS allows more plasma to be recovered for fractionation and clinical use. Reducing the amount of plasma in a PLT component also has the potential to reduce the number of transfusion reactions, particularly allergic transfusion reactions and TRALI, where plasma proteins have been implicated. Further, PLTs in PAS are compatible with pathogen reduction technology (PRT). PAS-IIIM has been shown to be an effective substitute for plasma in both apheresis and buffy coat PLT concentrates stored for up to 12 days. PAS-IIIM is a third-generation PAS containing acetate, a substrate for oxidative phosphorylation, phosphate to provide improved buffering capacity as well as potassium, citrate, and magnesium. The composition of PAS-IIIM used in this study is shown in Table 1. Storage of PLTs in this additive has been shown to reduce the rate of glycolysis, leading to better retention of pH and hypotonic shock response (HSR) reactivity.

ABBREVIATIONS: HSR = hypotonic shock response; PAS(s) = platelet additive solution(s); PLTs = platelet; PRT = pathogen reduction technology.
Conclusion

- At the edge of 100% voluntary SDP donation
- Achieved 100% NAT- SDP
- ABO antibody titers were significantly reduced PAS-SDP
- Facilitates the ABO incompatible SDP transfusion
- Better inventory management
- Quality of SDP-PAS is comparable to SDP-Plasma
- No effect on clinical outcome observed by SDP-PAS
- Risk of allergic transfusion reaction decreases
Thank you

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Platelet additive solutions: Types

• PAS-II is the simplest of these additives, containing only sodium chloride, sodium citrate and sodium acetate.

• When phosphate was added to PAS-II to act as a buffer, the resulting additive was renamed PAS-III.

• This addition of phosphate increased the metabolism of glucose, thus resulting in increased lactate production.

• PAS-III M contains potassium and magnesium to counteract this
PAS-III M: Currently available

• PAS-III M has been shown to be an effective substitute for plasma in both apheresis and buffy coat PLT concentrates stored for up to 12 days

• PAS-III M is a third-generation PAS containing acetate, a substrate for oxidative phosphorylation, phosphate to provide improved buffering capacity as well as potassium, citrate, and magnesium

• Storage of PLTs in this additive has been shown to reduce the rate of glycolysis, leading to better retention of pH and hypotonic shock response (HSR) reactivity