Clinical Evaluation of Platelet Concentrates Stored for One to Five Days

By Charles A. Schiffer, Edward J. Lee, Paul M. Ness, and James Reilly

There are no large-scale data available describing the increments obtained with platelet concentrates stored for varying durations. Platelet concentrates prepared by standard techniques were stored at 22 °C with horizontal agitation in PL-732 bags and administered to clinically stable, nonalloimmunized recipients known to respond well to random donor platelet transfusions. The platelet concentrates were stored in a mean volume of 65.0 mL (range 54–80 mL) with an average yield of .72 × 10¹¹ platelets per unit of platelet concentrates (N = 100 consecutive units).

Until a few years ago, platelet concentrates could be stored at 22 °C to 24 °C for a maximum of three days. The development of new plastics and thinner plastic bags which allowed increased oxygen transport with preservation of aerobic metabolism has permitted further extension of storage initially to five days, and more recently to seven days. The licensing of these containers was based on a relatively small number of studies which, in general, compared platelet storage for extended periods with results derived from platelets prepared in the same fashion and stored at room temperature for 72 hours in the “standard” polyvinyl chloride plastic bags. Implicit in this decision was the assumption that 72-hour storage was “state of the art” and platelets thus stored were equivalent to platelets which were either fresh or stored for <24 hours. In addition, only a relatively small number of observations were provided, some of which consisted of transfusions of autologous labeled platelets to normal volunteers.

Notably lacking in the medical literature are the results in the clinical setting of platelets which have been transfused after any duration of storage. Thus, although a number of research laboratories have published results in small numbers of patients using platelets stored for 72 hours, there are no larger descriptions of clinical results in a more routine, less research-oriented setting. Data are also lacking for more extended storage durations. Although it is difficult to document, one frequently has the impression that clinicians have been distrustful about the effectiveness of stored platelets and frequently either demanded fresh platelets, single-donor platelets, or increased the number of units ordered when stored platelets were administered.

The present study was undertaken shortly after “five-day” platelet bags were licensed in an attempt to provide further information about posttransfusion results after varying durations of storage.

MATERIALS AND METHODS

Platelet concentrates were collected and stored in CPDA-1 plasma at the Chesapeake Regional Red Cross using standard techniques. All platelets were collected in storage bags which were manufactured by Fenwal Laboratories, Morton Grove, Ill (Fenwal PL-732 bags), which at that time were licensed for five-day storage. Whole blood was centrifuged at 2,170 g × three minutes with centrifugation of the platelet-rich plasma (PRP) at 3,450 g × six minutes. Platelets were delivered to the University of Maryland Cancer Center 12 to 24 hours after preparation. At both the Red Cross and the UMCC, the platelets were stored in a Forma Platelet Incubator at 22 °C with gentle horizontal agitation (70 rpm/min).

Prior to transfusion, multiple ABO identical units were pooled (between 4 to 10 U depending on the recipient’s size) and administered through standard blood filters within one hour of pooling. In this study, only platelets that had been stored for the same duration of time were pooled in a single bag. Specimens for platelet count were obtained on the pooled bag prior to transfusion.

The UMCC has a policy of prophylactic platelet transfusion with patients transfused at platelet counts of 10,000 to 20,000/mL. When further decrements in platelet count due to chemotherapy or underlying disease were expected to occur,3 plateau transfusions were administered to recipients who were clinically stable without evidence of severe infection, hepatosplenomegaly, disseminated intravascular coagulation or severe bleeding, and who had a temperature <101 °C as described previously.4 Posttransfusion specimens were obtained one hour after transfusion and usually on the next day, 18 to 24 hours after transfusion. Patients were known to be nonalloimmunized as documented serologically by negative lymphocytotoxic antibody titers5 and had known adequate responses to random-donor platelet transfusions administered within 1 week of the study transfusions (one hour posttransfusion corrected count increments (CCI) ≥7,500). Increments were expressed as CCI where: CCI = Absolute increment × body surface area (m²)/Number of platelets transfused × 10¹¹. Thus, if a 2 m²-individual received 4 × 10¹¹ platelets and had an absolute count increment of 40,000, the CCI = 40,000 × 2 = 80,000.

In vitro studies. Specimens were obtained aseptically from units stored 1, 2, 3, 4, or 5 days, and platelet count and pH were determined. No air was allowed in the collection syringes, and the syringes were sealed immediately, thereby minimizing any pH effect that might be incurred by loss of CO₂ from the plasma to surrounding air.6 One hundred units of platelet concentrate (PC) were analyzed for each of the storage intervals.

RESULTS

The platelet concentrates were stored in a mean volume of 65.0 mL (range 54 to 80 mL) with an average yield of .72 × 10¹¹ platelets per unit of platelet concentrate (data

From the Cell Component Therapy Section, Division of Hematologic Malignancies, University of Maryland Cancer Center; and Chesapeake Regional Red Cross, Baltimore.

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Address reprint requests to Dr Charles A. Schiffer, University of Maryland Cancer Center, 22 S Greene St, Baltimore, MD 21201.
from 100 consecutive units). As can be seen in Table 1, there was no significant deterioration of pH during storage. Of note is that between 17% to 25% of the units tested at different storage intervals had relatively high platelet concentrations of >1.5 x 10^6/μL. The lowest pH noted in the entire study was 6.9, suggesting that the improved oxygen transport prevented the development of significant anaerobic metabolism even at higher platelet concentrations. In contrast, between 14% to 30% of units had elevated pH (>7.4) following storage (Table 1). As would be expected, this was most common in units with lower platelet concentrations (<1 x 10^6/μL).

The corrected count increments are shown in Table 2. Results are presented both for the total number of evaluable transfusions as well as for the transfusions administered to nonsplenectomized patients in each group. These latter data are provided because of a fortuitous disproportion of splenectomized recipients in the one- to three-day storage groups. There was a statistically significant effect of storage on CCI in both groups which began after three days of storage (P < 0.003, analysis of variance). The overall deterioration was quite modest, however. The frequency of transfusions with CCI <7,500 are presented for the nonsplenectomized patients. Although there was an increased frequency of such transfusion “failures” after three to five days of storage, only 10% of transfusions stored for these durations had CCI of <6,500.

The 18- to 24-hour posttransfusion data are shown in Table 3. Not all patients had counts performed the next day. Most often, these were patients who had been transfused as outpatients and in whom, because one-hour increments had been acceptable, it had not been clinically necessary or appropriate to obtain counts the next day. Therefore, the 18- to 24-hour data might have a slight bias against patients with the highest one-hour posttransfusion increments. In addition, there was a greater variability in the interval posttransfusion than in the one-hour posttransfusion data. Nonetheless, the results were similar with a statistically significant effect (P < 0.02, analysis of variance) for the total group. The difference was not statistically significant (P = 0.19, analysis of variance) in the group of nonsplenectomized patients.

The ratios of the 18- to 24-hour increments to the corresponding one-hour increments are shown in Table 4. There was no significant difference when either all cases or nonsplenectomized patients were considered (P = 0.39 and 0.19, respectively). On average, the one-day increments were approximately two-thirds of the immediate posttransfusion increments.

**DISCUSSION**

These data demonstrate that acceptable posttransfusion increments can be obtained after five days of storage in Fenwal PL-732 bags with evidence of minimal deterioration over time. It is to be emphasized that the present study was performed using standard collection and storage techniques, and therefore should be similar to other transfusion settings. In a previous study performed 2 to 3 years earlier in a similar patient population at our institution,4 PC stored for three days in the then-standard plastic bags (CL-3861, Cutter Labs, Berkeley, Calif) had a mean one-hour posttransfusion
PLATELET STORAGE

Table 3. Corrected Count Increments (18- to 24-Hour)

<table>
<thead>
<tr>
<th>Duration of Storage (Days)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
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<tr>
<td>Total patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCI (range)</td>
<td>12.4 ± 6.7*</td>
<td>11.7 ± 6.7</td>
<td>11.3 ± 5.7</td>
<td>8.8 ± 4.6</td>
<td>8.9 ± 4.8</td>
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<tr>
<td>No. of transfusions</td>
<td>84</td>
<td>57</td>
<td>26</td>
<td>37</td>
<td>20</td>
</tr>
<tr>
<td>Nonsplenectomized patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCI (range)</td>
<td>10.9 ± 5.3</td>
<td>10.5 ± 5.5</td>
<td>10 ± 5.2</td>
<td>8.5 ± 4.4</td>
<td>8.9 ± 5</td>
</tr>
<tr>
<td>No. of transfusions</td>
<td>74</td>
<td>50</td>
<td>22</td>
<td>34</td>
<td>19</td>
</tr>
</tbody>
</table>

*Mean ± SD × 10⁻³.

Table 4. Ratio of 18- to 24-Hour Posttransfusion CCI/One-Hour Posttransfusion CCI

<table>
<thead>
<tr>
<th>Duration of Storage (Days)</th>
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</tr>
</thead>
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<tr>
<td>Total patients</td>
<td></td>
<td></td>
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<tr>
<td>Mean ± SD</td>
<td>0.7 ± 0.3*</td>
<td>0.6 ± 0.2</td>
<td>0.6 ± 0.2</td>
<td>0.6 ± 0.2</td>
<td>0.6 ± 0.2</td>
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<tr>
<td>(range)</td>
<td>(0.1-1.8)</td>
<td>(0.1-1.0)</td>
<td>(0.2-1.1)</td>
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<td>(0.3-1.0)</td>
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*Mean ± SD.

CCI of 12,200 (N = 16). All units in this earlier study had pH determinations done pretransfusion. Units with pH values of >6.0 (21% of the PC tested) were not transfused, and the figure of 12,200 is therefore an overestimate of what is likely to be achieved in more routine practice. Thus, the increments noted with the newer bags in the present study represent an important improvement over these earlier results. Bleeding times were not done in the current study, and we cannot comment on the relative hemostatic effectiveness of PC stored for differing durations. Small studies with platelets stored for five days have shown shortening of bleeding times after transfusion however, and refractory bleeding was not a problem in any of the recipients in the current study.

These data also indicate that the pH of platelet concentrates can be uniformly and adequately maintained for the 5 days of storage. It has been shown that platelet viability deteriorates at a final pH of 6.0 to 6.2. The lowest pH noted in this study was 6.9 despite an appreciable number of units with relatively high platelet bag counts and final platelet concentrations (Table 1). This is consistent with previous observations by Murphy et al who noted a pH of <6.7 in only 1 of 101 units of PC stored for five days in PL-732 bags in volumes of 30 to 60 mL. In fact, the only concern may be that in some bags the pH might actually be higher than desirable because of increased diffusion of CO₂ (Table 1). Morphological changes and platelet clumping can be noted at these higher pHs. It should be noted, however, that the mean PC volume of 65 mL in the present study is higher than the 50- to 55-mL volumes used in many blood centers. It may be that a higher pH will occur less frequently in these smaller preparations. Indeed, in the study by Murphy and colleagues pH values of >7.4 were noted in only 7 of 101 units stored for five days. Nonetheless, there is legitimate concern about the potential for higher pH in PC with lower platelet counts, particularly after shorter periods of storage, and further studies describing the in vivo correlates of these observations are necessary.

A potential concern about extension of platelet storage is the theoretical risk of increased bacterial growth in any unit contaminated inadvertently during collection. Cultures were not obtained during the present study, and there were no posttransfusion episodes suggestive of infusion of bacterially contaminated platelets. Although more recent studies have tended to minimize the concern raised by an earlier investigation describing episodes of transfusion of bacterially contaminated platelets, clinicians should nonetheless be aware of the potential for this serious but fortunately rare complication.

The improvement in plastic bags for platelet storage has had a number of major impacts. First, the ability to extend storage to five days allows blood banks to stockpile platelets over holidays, long weekends, and other periods of donor shortage. This has become of even greater importance recently because of the further delays in distribution imposed by HTLV-III antibody testing. In addition, ~10% to 20% of units of platelet concentrate had unacceptably low pH after 72 hours of storage in the older bags, and recipients of such units were exposed to the risks of transfusion with no chance of clinical benefit. The improvement in gas transport...
has eliminated these falls in pH even at higher bag platelet counts. Last, these technical advances have improved the quality of stored platelets at all points after collection and preparation. Most platelets are transfused after two to four days of storage, and the newer bags have further "guaran-

teed" the quality of such platelets. The data presented demonstrate that platelets stored for as long as five days in newer containers are clinically acceptable and will provide adequate transfusion support any time during their five-day storage period.

REFERENCES

6. Schiffer CA: What are the parameters to be controlled in platelet concentrates in order that they be offered to the medical profession as a standardized product with specific properties? Vox Sang 40:122, 1981
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