Impact of the Age of Transfused Red Blood Cells in the Trauma Population

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Abstract
Following injury, transfusion of Red Blood Cells (RBCs) of greater storage duration has been associated with an increased morbidity and mortality. Prospective trials focusing on the impact of the storage age of RBCs in critically bleeding trauma patients have typically failed to accrue patients. This has been attributed to both inability to maintain a large inventory of fresh RBCs, and the difficulties in obtaining consent in severely bleeding trauma patients. To address this issue of the impact of old blood on the injury victim, we reviewed the literature on this topic.

Keywords: Transfusion practices (surgical); Red blood cells; Storage lesion; Age of blood; Trauma; Injury

Introduction
There is a well-established association between transfusion of red blood cells and increased morbidity and mortality in trauma patients [1-5] and in the critically ill population in general [6,7]. Hebert et al. in 1999 reported that a restricted red cell transfusion strategy was at least as effective and possibly superior to a liberal transfusion strategy in the critically ill population [8]. It remains unclear as to why infusion of red blood cells would be harmful and numerous investigators have reviewed the literature in order to understand the influence of duration of storage in the blood bank on outcome in the critically ill [9-11]. In the largest study to date, focusing upon the impact of duration of red cell storage and complications after cardiac surgery, Koch and colleagues suggested that individuals given exclusively older red blood cells (median 20 days old, n=2872 patients) appear to have a greater morbidity (25.9% vs. 22.4%, p=0.001), hospital and one year mortality (one year: 11.0% vs. 7.4%, p<0.001), when compared to those receiving exclusively younger red cells (median 11 days old, n=3130 patients) [6]. In the trauma patient population, data relating duration of red cell storage to complications and death is quite limited [9-11]. Following injury, transfusion of older aged red cells has been identified in retrospective trauma studies to be associated with an increased morbidity and mortality [1,2,5,11]. This detrimental effect of old red cells on tissue perfusion has not been demonstrated in normal volunteers [12] or seen in other critically ill populations [13], however. The results of existing clinical studies comparing old and young RBCs suggest that prospective clinical trials investigating the risks and benefits of prolonged red cell storage should be performed.

While randomized controlled trials are currently being performed to determine if the transfusion of RBC of increased storage duration increases the risk of morbidity and mortality in adult critically ill patients and in adults requiring complex cardiac surgery, no trials are being performed in patients with traumatic hemorrhagic shock [23]. This is despite the fact that the trauma population may be at the highest risk of RBC storage lesion effects [11]. Logistical difficulties in maintaining the availability of very large quantities of RBCs of decreased storage duration for study patients appears to be the predominant reason that age of red blood cell trials are not being conducted in patients with traumatic hemorrhagic shock. By current standards of care, when a patient is to receive a transfusion, the blood bank provides the oldest unit of blood available. Despite this practice, in areas where type O RBC donors are prevalent, an abundance of fresher RBCs is often available in stock. We performed a short survey of blood bank size, prior to conducting a trial at our trauma center at University Hospital in San Antonio. In a retrospective analysis of all type O and type A Red Blood Cells transfused between July 2005 and June 2006, we found that patients with type O blood typically received younger RBC units (17.5 ± 8.7 days) than type A blood patients (24.3 ± 9.9 days).

We previously attempted to perform a pilot trial examining the impact of age of blood on patient outcomes in severely bleeding trauma patients but were prevented from completing the study due to a lack of blood bank resources [24]. The methods in our previous trial differed in that we required a large inventory of both “young” and “old” blood available in the blood bank prior to randomizing a patient. We found that having a sufficient inventory of RBCs (particularly of “young” RBC of less common ABO types) was a major impediment to conducting our trial. In fact, we were only able to enter 17 patients during one year at a very busy trauma center. Recently we published a randomized trial of “young” type O blood (median age 6 days) compared to the usual

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Received February 12, 2014; Accepted February 27, 2014; Published March 03, 2014


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"old" type A, B and A/B blood (median age 18 days) when used in trauma patients during resuscitation after injury [25]. We were able to establish the feasibility of utilizing this scheme to develop a wide gap in the age of blood (12 days) for the trauma population. While this pilot study was not designed to identify statistically significant differences in clinical outcomes, we did note some interesting inequalities between groups (bacteremia incidence was 0 in "young" blood, versus 5 (11%) in "old" blood, p=0.31).

In conclusion, it appears feasible to conduct an age of RBC trial using ABO blood type to differentiate patients transfused either "young" or "old" blood, and it may be more efficient than alternative prospective cohort designs. Future multicenter trials could employ this methodology to assess the impact of the age of transfused blood in severely bleeding trauma patients where a classic randomized controlled trial may not be possible due to the inability to maintain an adequate inventory of all ABO types.

References

Table 1: Literature Review of Age of Blood and Trauma.

<table>
<thead>
<tr>
<th>Author (ref)</th>
<th>Design</th>
<th>No.</th>
<th>Study Population</th>
<th>ISS</th>
<th>Blood age</th>
<th>Major Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zallen et al. [18]</td>
<td>Retro single</td>
<td>63</td>
<td>Trauma patients with 6 to 20 units PRBC</td>
<td>~30</td>
<td>24 vs. 31 days</td>
<td>Older PRBC associated with organ failure (&gt;14 or &gt;21 days)</td>
</tr>
<tr>
<td>Schultz et al. [24]</td>
<td>Pros single</td>
<td>17</td>
<td>RCT Type A trauma patients ≥ 2 units PRBC</td>
<td>NA</td>
<td>&lt;11 vs. &gt;20 days</td>
<td>Lack of accrual due to PRBC bank inventory</td>
</tr>
<tr>
<td>Offner et al. [17]</td>
<td>Retro single</td>
<td>61</td>
<td>Trauma patients with 6 to 20 units of PRBC</td>
<td>~30</td>
<td>27 ± 1 day</td>
<td>&gt;14 or 21 days old PRBC associated with infections</td>
</tr>
<tr>
<td>Keller et al. [20]</td>
<td>Retro single</td>
<td>86</td>
<td>Trauma patients with 1 to 4 units of PRBC</td>
<td>13</td>
<td>23 ± 1 days</td>
<td>&gt;14 days old PRBC associated with increasing hospital stay</td>
</tr>
<tr>
<td>Murrell et al. [19]</td>
<td>Retro single</td>
<td>275</td>
<td>Trauma patients receiving ≥ 1 unit PRBC</td>
<td>18</td>
<td>NA</td>
<td>Older PRBC associated with longer ICU stay</td>
</tr>
<tr>
<td>Weinberg et al. [15]</td>
<td>Retro single</td>
<td>1,813</td>
<td>Trauma patients receiving ≥ 1 unit PRBC</td>
<td>26</td>
<td>≥ 14 vs. &lt;14 days</td>
<td>Older PRBC associated with mortality in subgroup with ≥ 6 units received.</td>
</tr>
<tr>
<td>Leal-Naval et al. [22]</td>
<td>Retro single</td>
<td>1,624</td>
<td>ISS &lt;25, no PRBC in first 48 hours</td>
<td>14</td>
<td>&gt;14 days</td>
<td>Older PRBC associated with higher mortality, renal failure and pneumonia.</td>
</tr>
<tr>
<td>Leal-Naval et al. [22]</td>
<td>Pros single</td>
<td>66</td>
<td>Brain injured</td>
<td>~30</td>
<td>&lt;10, 10-14, 15-19, &gt;19 days</td>
<td>Increased cerebral oxygenation, except in &gt;19 days old PRBC.</td>
</tr>
<tr>
<td>Vandromme et al. [16]</td>
<td>Retro single</td>
<td>1,615</td>
<td>Trauma patients receiving ≥ 1 unit PRBC</td>
<td>27</td>
<td>≥ 14 vs. &lt;14 days</td>
<td>Older PRBC associated with increase pneumonia.</td>
</tr>
<tr>
<td>Spinella et al. [5]</td>
<td>Retro single</td>
<td>202</td>
<td>Trauma patients receiving ≥ 5 units PRBC</td>
<td>24</td>
<td>≥ 28 vs. &lt;28 days</td>
<td>Older PRBC associated with increased venous thrombosis and mortality.</td>
</tr>
<tr>
<td>Kiraly et al. [21]</td>
<td>Pros single</td>
<td>32</td>
<td>Trauma patients with anemia</td>
<td>~25</td>
<td>≥ 21 vs. &lt;21 days</td>
<td>Thrombosis decreased with receipt of older PRBC.</td>
</tr>
<tr>
<td>Cohn et al. [25]</td>
<td>Pros single</td>
<td>63</td>
<td>Trauma patients</td>
<td>22</td>
<td>&lt;10 vs. &gt;20 days</td>
<td>It is feasible to conduct a study using ABO blood type to differentiate between young and old blood</td>
</tr>
</tbody>
</table>

Retro=Retrospective Study; Pros=Prospective Study; RCT=Randomized Control Trial; PRBC=Packed Red Blood Cells; Single=Single Institution Study; ISS=Injury Severity Score.
transfused blood is an independent risk factor for postinjury multiple organ failure. Am J Surg 178: 570-572.


