Chapter 3

MASSIVE TRANSFUSION OF RECONSTITUTED WHOLE BLOOD IS WELL TOLERATED IN PEDIATRIC BURN SURGERY

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ABSTRACT

**Background:** Massive transfusions can produce cardiovascular instability, metabolic abnormalities, dilutional coagulopathy and pulmonary dysfunction. They also have been related to a higher incidence of infections. The purpose of this study was to assess the safety of massive transfusion of reconstituted whole blood.

**Methods:** Twenty consecutive severely burned pediatric patients underwent near-total burn excision on admission and blood transfusion with reconstituted whole blood. Patients were studied for coagulopathies and postoperative complications related to massive transfusion.

**Results:** Only one patient presented with postoperative bleeding related to acute renal failure. No other complications occurred. There were no septic episodes or pulmonary dysfunction. The amount of massive blood transfusion did not correlate with any laboratory or clinical disturbance.

**Conclusions:** Massive transfusion of reconstituted whole blood in severely burned pediatric patients is safe; it does not compromise hemostasis nor is it associated with an increased rate of septic episodes or pulmonary complications. A prospective randomized clinical trial comparing its effectiveness vs. packed red cells is necessary.
INTRODUCTION

Extensive bleeding during burn surgery is common in severe burns. Massive transfusions have been related to cardiovascular instability, postoperative coagulopathy, pulmonary dysfunction, metabolic abnormalities and increased incidence of infection. The replacement of blood loss during burn surgery with packed red cells, crystalloids and colloids is ordinary practice but may vary in different institutions. Blood replacement with reconstituted whole blood has been the preferred practice in our center for the last decade. Double- and even triple-exchange transfusions may occur during near-total burn excision, making complications in this particular population more deleterious, because these patients affected by severe burns have a profound metabolic response and their hemodynamics can be profoundly altered. The effect of reconstituted whole blood in this setting is still to be defined.

MATERIAL AND METHODS

To study the effect and safety of massive transfusion of reconstituted whole blood during pediatric burn surgery, we reviewed a cohort of severely burned pediatric patients admitted between January 1996 and June 1997. Only patients with burns over 60% total body surface area (TBSA) and admitted within 24 hours after the injury were included in the present study. Burned patients admitted later in hospital course were not included, because previous local and general treatments in other institutions may vary and it would have produced a bias in the study.

All patients received near-total burn excision, including all full thickness burns on admission. Blood was transfused during the operation as reconstituted whole blood (1 unit of packed red cells + 1 unit of fresh frozen plasma) to maintain intraoperative hematocrits in a range between 30% to 35%. The former followed the previously published method of the senior authors for the management of severe burns with near-total burn wound excision1. Because of the high demand for blood in our burn center, all blood products were used, regardless of the length of the storage time. Minimal crystalloids were infused during the operation (governed by the urine output, which was maintained at 1 ml / Kg / hour). Ketamine and inhalant agents were used for anesthesia. The patients were not paralyzed and maintained their spontaneous ventilation. Only the first operation was studied, when all full-thickness burns were excised and autografts or homografts were applied. The areas that were excised were not injected with epinephrine solution. Burns were tangentially excised to viable tissues, and active bleeding was controlled with electrocautery and topical thrombin (1000 units/ml). We compiled all the demographic data, characteristics of the injury, preoperative and postoperative laboratory values, operative data, follow up and complications.

Laboratory data included complete blood cell count, coagulation parameters, blood chemistry and arterial blood gases. Hemoglobin, hematocrit and arterial blood
gases were monitored every thirty minutes during the operation. Postoperative laboratory values were collected at the time of admission to the burn intensive care unit, as well as 8 hours, 24 hours, and 48 hours post-admission to the burn intensive care unit. Hospital course was followed for 7 days to detect potential complications of massive transfusion and the ultimate outcome noted. Estimated circulating volume and blood loss was calculated with the previously published method and formula developed by the senior authors\textsuperscript{1}. Hematocrit and hemoglobin were monitored intraoperatively in order to maintain their levels above 30\% and 10.0 g/dl. Resuscitation was started according to the Galveston formula (5000 ml/m\textsuperscript{2} of burned area + 2000 ml/m\textsuperscript{2} body surface area in the first 24 hours) and blood loss during the operation was replaced with reconstituted whole blood. Crystalloids were infused during the operation according to the amount mandated by the resuscitation formula. Only extra boluses of crystalloids were considered if the patients did not maintain an urine output of 1 ml/kg/hr. Monitoring included an arterial line, core temperature with a bladder probe, capnometer, central line, and large bore peripheral access.

Data are depicted as mean ± SEM. Results were analyzed with one way repeated measures analysis of variance with Turkey’s test for all pairwise multiple comparison, Pearson’s moment test, and multiple linear regression.

RESULTS

Between January 1996 and June 1997, 20 consecutive pediatric patients were admitted to our institution with burns over 60\% TBSA within 24 hours after their injury. All patients received near-total burn excision including all full thickness burns on admission. The patient sample passed the normality test. Mean age was 6.4 ± 1.2 years. Percent of TBSA burned was 80 ± 2.2 \%, and percent of TBSA full thickness burns was 72 ± 4.8 \%. Extensive bleeding occurred during the operations. The patients estimated circulating volume was 1694 ± 308 ml, and blood transfused during the near-total burn excision was 4133 ± 1692 ml, which consisted of more than a double exchange transfusion per patient. Operative data is summarized in Table 1. A significant decrease in white blood cells and platelet count (p<0.001) occurred in all

| TABLE 1 |
| Operative data |
| Blood transfused | 4133 ± 1692 ml |
| Area excised | 6742 ± 1112 cm\textsuperscript{2} |
| Area autografted | 2137 ± 472 cm\textsuperscript{2} |
| Blood loss | 0.51 ± 0.1 ml/cm\textsuperscript{2} |
| Crystalloids administered | 45 ± 28 ml/kg |
Massive transfusion of reconstituted whole blood is well tolerated in all patients. The depressed values returned to normal within 48 hours without treatment in all patients. At 48 hours, values were similar to those found on admission and significantly higher than values found immediately after and 24 hours after surgery (see Table 2). Coagulation parameters did not change significantly after surgery, and remained the same for 48 hours (see table 3). None of the patients required coagulation factors or platelets to maintain good hemostasis. All patients tolerated enteral nutrition postoperatively.

Only one patient had bleeding complications, which was related to acute renal failure. This particular patient presented with delayed resuscitation and elevated BUN and creatinine preoperatively. In the postoperative period, this patient required peritoneal dialysis for acute renal failure, which resolved within 2 weeks. None of the remaining patients had a bleeding complication. There were no sings of disseminated intravascular coagulopathy or disseminated intravascular coagulopathy-like syndrome in any of the patients.

Fourteen out of 20 patients were intubated and ventilated before admission. Only 5 of the 14 previously ventilated patients required ventilation after operation. There were no re-intubations during the first 7 days after the operation nor clinical evidence of cardiogenic or non-cardiogenic pulmonary edema. None of the patients died.

Multiple linear regression showed a relationship between high amounts of crystalloids administered during resuscitation and hyponatremia, postoperative acidosis, and low levels of pO₂ (R square=0.801, p<0.05); whereas the amount of whole blood transfused did not affect respiratory parameters.

### TABLE 2
Hematologic laboratory parameters

<table>
<thead>
<tr>
<th></th>
<th>Pre-op</th>
<th>Post-op</th>
<th>24 hours</th>
<th>48 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hematocrit (%)</strong></td>
<td>40.0 ± 2.0</td>
<td>36.5 ± 1.7</td>
<td>31.2 ± 2.5</td>
<td>30.2 ± 3.4</td>
</tr>
<tr>
<td><strong>Hemoglobin (g/dl)</strong></td>
<td>13.6 ± 0.7</td>
<td>12.2 ± 0.5</td>
<td>10.9 ± 0.6</td>
<td>10.1 ± 0.8</td>
</tr>
<tr>
<td><strong>White blood cells  (x1000)</strong></td>
<td>32.2 ± 4.3</td>
<td>6.7 ± 0.9 (*)(†)</td>
<td>7.1 ± 1.8 (*)(†)</td>
<td>8.4 ± 2.6</td>
</tr>
<tr>
<td><strong>Platelets (x1000)</strong></td>
<td>237 ± 26</td>
<td>53.8 ± 8.4 (*)(†)</td>
<td>69.0 ± 5.6 (*)(†)</td>
<td>105 ± 21.3</td>
</tr>
</tbody>
</table>

(*) p<0.001 compared to pre-op values, One way repeated measures ANOVA

(†) p<0.05 compared to 48 hours values, One way repeated measures ANOVA
Bleeding is a major concern during early excision of burned skin. Massive blood transfusion is most commonly defined as complete replacement of a patient’s blood volume within a 24-hour period. Replacing more than one circulating volume during major excisions is not uncommon. Commonly, packed red cells, colloids, and crystalloids are used for blood replacement. Under these circumstances, patients undergoing massive burn excisions can present with severe coagulopathies. Impaired fibrin-platelet interaction, elongated prothrombin time, and altered fibrinogen and factor VIII activities have been reported during massive blood replacement with crystalloids and packed red cells. Maintaining above-normal core temperatures in burn patients is also extremely important to prevent coagulopathies. In the present study, core temperatures were monitored continuously with temperature probe Foley catheters. Temperature was maintained pre-operatively, intra-operatively, and post-operatively above 37 Celsius degrees. In this series of patients, massive transfusions were ordinarily performed during near-total burn excision. Only one out of twenty patients presented bleeding complications and coagulopathy. In this case, the complication was related to an acute renal failure present preoperatively, which has been shown to alter platelet function, prolonging bleeding time. No prolongations of coagulation studies were encountered, and fibrinogen remained within normal limits, in contrast to the experience of other authors transfusing crystalloids, colloids and packed red cells. We did not find any clinical or laboratory findings of disseminated intravascular coagulopathy, and fibrinogen and degraded products of fibrin were within normal limits. Platelets were profoundly decreased, but their level returned to normal in 48 hours without intervention. Patients received limited crystalloids according to their resuscitation needs. Three of them, however, presented with mild hyponatremia reflecting some degree of crystalloid overload, which was related to increased levels of acidosis, decreased levels of oxygenation and slight elongation of coagulation parameters. The same effect could not be found related to the amount of reconstituted whole blood transfused, which supports the concept that crystalloids rather than blood transfused have a greater impact on postoperative coagulopathy.

**TABLE III**

Coagulation laboratory parameters

<table>
<thead>
<tr>
<th></th>
<th>Pre-op</th>
<th>Post-op</th>
<th>24 hours</th>
<th>48 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT (seconds)</td>
<td>16.9 ± 1.5</td>
<td>15.4 ± 0.5</td>
<td>16.7 ± 1.8</td>
<td>15.9 ± 1.5</td>
</tr>
<tr>
<td>PTT (seconds)</td>
<td>47.6 ± 5.9</td>
<td>51.7 ± 3.3</td>
<td>52.7 ± 4.1</td>
<td>49.8 ± 3.9</td>
</tr>
<tr>
<td>Fibrinogen (mg/dl)</td>
<td>205 ± 28.3</td>
<td>208 ± 14.1</td>
<td>223 ± 20.1</td>
<td>239 ± 22.0</td>
</tr>
</tbody>
</table>
Massive transfusion of reconstituted whole blood is well tolerated following major burn excision. Pulmonary dysfunction following massive transfusion was not noted. Only five patients required ventilation postoperatively, and none required re-intubation.

All patients included in this prospective cohort survived, despite the severity of their burns and the associated inhalation injury. Patients did not present with septic complications either. Recent studies in trauma patients have shown a good survival rate following massive blood transfusions\textsuperscript{7,8}. Moreover, it has been shown that there is no actual limit to massive blood transfusion after severe trauma, because it is not the number of blood units but the use of vasopressors, time in hypotension, and need for aortic clamping that is related to mortality. Up to 68 units of blood can be transfused without a significant impact in mortality\textsuperscript{9}.

Other authors, however, have postulated a relationship between blood transfusions in burn patients and an increased risk and incidence of infections\textsuperscript{10,11}. None of the patients had any kind of septic episode during the period of the study. All patients received perioperative antibiotics in order to prevent bacterial seeding during massive excision and grafting. The effect of plasma exchange and surgical excision and grafting procedures have been shown to have a beneficial effect in restoring lymphocyte function in burn patients, which may account for the absence of complications and septic episodes observed in our study population\textsuperscript{12}.

Our study, however, was merely descriptive, given the fact that it does not present a comparison group. Reconstituted whole blood proved to be very well tolerated and safe in pediatric burn surgery. A prospective randomized study, however, is necessary to analyze whether the use of plasma-reconstituted blood replacement is superior to packed red cells alone. Furthermore, the safety of this transfusion technique needs to be explored in patients operated on later during hospital course.
REFERENCES