Technique Article

Modification of Sodium, Glucose, Potassium, and Osmolarity in Packed Red Blood Cells and Fresh Frozen Plasma Using a Desktop Hemoconcentrator Setup

Carrie Whittaker Striker, DHEd, CCP, FPP;*† Stacia Woldorf, MPS, CCP;† David Holt, MA, CCT†

*Children’s Mercy Hospitals and Clinics, Kansas City, Missouri; and the †University of Nebraska Medical Center, Omaha, Nebraska

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Abstract: Massive transfusion with packed blood cells (PRBCs) or fresh frozen plasma (FFP) can result in dangerous complications including stroke, kidney failure, and cardiac arrest. A simple, bench top technique using a hemoconcentrator and dialysate solution is described to correct critical values of sodium, glucose, potassium, and osmolarity in PRBCs and FFP. Sodium, glucose, and osmolarity were corrected to normal or near normal values. Elevated potassium was reduced by 65%, but not completely normalized. A simple, bench top method for correcting dangerous abnormalities with PRBCs and FFP can be used to improve the safety of massive blood transfusion. Keywords: hemoconcentrator, dialysis, dialyzed PRBCs, dialyzed FFP, osmolarity, sodium, glucose, potassium, hyperosmolarity, hypernatremia, hyperglycemia, washed blood products.

Stored packed red blood cells (PRBCs) and fresh frozen plasma (FFP) are associated with electrolytes and glucose that exceed clinically accepted physiologic values (1–3). PRBCs stored in additive solution or non-additive solutions such as citrate phosphate dextrose (CPD) become hyperkalemic with documented concentrations as high as 50–80 mEq/L (1,2,4,5). FFP stored in a non-additive anticoagulant solution such as CPD has documented potassium levels as high as 20 mEq/L after 3 weeks time (6). Hyperkalemia in both adult and pediatric patients is associated with severe cardiac arrhythmias and cardiac arrest after rapid transfusion of banked blood (1). In addition to hyperkalemia, the hyperosmolarity of PRBCs and FFP is of concern specifically in the pediatric patient undergoing cardiopulmonary bypass (CPB) (7,8). To prevent the hemoconcentration effect of the CPB circuit prime, these patients can receive banked blood products equal to native blood volume. For example, the blood volume of a 3 kg neonate is roughly 300 mL, while the entire neonatal CPB circuit can range from 185 mL with circuit miniaturization and retrograde autologous priming to 330 mL including the cardioplegia and hemoconcentrator circuits (9,10). Massive transfusion in the pediatric patient with hyperosmolar PRBCs and FFP may have a deleterious impact upon the central nervous system, the renal system, and general metabolic processes (2,11).

Osmolarity is a measurement in the number of osmoles per liter of solution (12). There are a variety of calculations for measuring osmolarity. A common formula is \( (2 \times \text{Na mEq/L}) + \left( \frac{\text{glucose mg}}{18} \right) + \left( \frac{\text{blood urea nitrogen mg}}{2.8} \right) = \text{milliosmoles/L (mOsm/L)} \) (12). In the absence of a blood urea nitrogen measurement the following formula can be substituted to estimate the osmolarity: \( (2 \times \text{Na mEq/L}) + \left( \frac{\text{glucose mg}}{18} \right) + 15 = \text{mOsm/L} \). The normal range for blood osmolarity varies depending on the authoritative source, but 270–300 mOsm/L is generally an acceptable range. A higher than normal plasma osmolarity may indicate hyperglycemia and hypernatremia and lead to
renal tubular necrosis, uremia, and stroke (4,12). A lower than normal plasma osmolarity may indicate excessive water intake and lead to hyponatremia, overhydration, and many other complications (12). In the pediatric population, hypernatremia is associated with an increased incidence of renal dysfunction and decreased intracranial pressures causing capillary dilation and subsequent vessel rupture in the brain (4,13). In adults, hypernatremia and hyperglycemia increase the risk for mortality (13). Harmful consequences of the transfusion of hyperosmolar solutions in the pediatric patient have been published (4,7,11,14). Recent studies have demonstrated an association between morbidity and mortality with relation to hyperglycemia in both the adult and pediatric patient (15,16).

Sodium ions and glucose molecules are the major contributors to the osmolarity. The published values of sodium, glucose, and calculated osmolarity in PRBCs are 156 mEq/L, 270 mg/%, and 342 mOsm/L on average (4). In FFP with CPD, the sodium, glucose, and osmolarity are 167.5 mEq/L, 308.6 mg/%, and 367.14 mOsm/L on average (3). With the need for rapid or massive transfusion of PRBCs, the literature describes the processing of PRBCs using cell salvage equipment to reduce potassium, glucose, and plasma free hemoglobin levels (PFH) (17–19). However, due to the normal saline used in the cell salvage process, the sodium remains elevated (20). In addition, cell salvage does not have the capability of processing FFP due to the complete loss of the product. To address these issues, the authors have devised a technique for dialyzing stored PRBCs and FFP for the removal of sodium and glucose, which primarily contribute to hyperosmolarity.

The hypothesis is that a simple dialysis method can be used to normalize the osmolar composition of PRBCs and FFP by reducing the sodium, glucose, and potassium levels prior to transfusion. The purpose of this study was to evaluate an in-vitro method to bring hyperosmolar PRBCs and FFP into normal sodium, glucose, and potassium ranges, thereby hypothetically reducing the risk of massive transfusion, which can cause detrimental changes to normal homeostasis.

**MATERIALS AND METHODS**

This experiment was designed to examine the alteration of sodium, glucose, and potassium composition of PRBCs, FFP, and a mixed combination of the two (PRBCs + FFP) through a simple dialysis system. Expired PRBCs and FFP anticoagulated with CPD were obtained from a hospital blood bank. The parameters tested before and after passage through the dialysis set-up included sodium, glucose, and potassium. PFH can be used as a quality control parameter for cell salvage evaluation and product quality. However, the hemoconcentrator used in this experiment did not remove it, so, PFH was not measured in this experiment.

A dialysate solution of 1 L Plasmalyte, 1 L .45% normal saline, and 75 mEq of 8.4% sodium bicarbonate was combined in a 2 L transfer pack with a coupler (Baxter, Deerfield, IL). The calculated osmolarity of this solution was 316 mOsm/L, which was slightly hyperosmolar. However, this dialysate solution was chosen due the Children’s Mercy Hospitals and Clinics Perfusion Services’ success using it for the normalization of extracorporeal membrane oxygenation circuit blood primes via a similar method.

The bag of blood product with a pressure bag around it was hung below the dialysate solution bag on an intravenous pole. The pressure bag was inflated to 150 mmHg to overcome the viscous nature of the PRBCs and promote flow. The effluent and final blood product was collected in a 2 L transfer bag. Both bags were connected to the inflow and outflow hemoconcentrator blood ports, respectively, using a single spike adaptor (BRAT, Arvada, CO).

The HF400 Hemoconcentrator (HC) (Minntech, Minneapolis, MN) was clear primed with a volume of 75 mL of .9% normal saline, which was infused before testing using a spike adaptor. Once the HC was primed, it was replaced...
with the blood product/pressure bag at the point of the spike adaptor.

A 2 L transfer pack with coupler (dialysate bag #1), which contained the dialysate solution, was hung above a similar but empty dialysate bag #2; the height differential allowed for gravity flow from bag #1 to #2, which collected the dialysate solution effluent. The dialysate bags were connected to the HC dialysate ports using 36" non-vented, quick prime lines (GISH Biomedical Inc., Rancho Santa Margarita, CA). The blood product and dialysate solution were run through the HC twice by reversing the position of the bags, with test samples taken from the blood after each pass. No provisions were made to control the flow rates of the blood flow or dialysate solution through the HC other

Table 1. Data for PRBCs, FFP, and PRBCs+FFP before dialysis, after one pass, and after two passes through the hemofiltrator.

<table>
<thead>
<tr>
<th>Trial 1: 1 L .45 Normal Saline, 1 L Plasmalyte and 75 mEq Bicarbonate</th>
<th>Normal Range</th>
<th>Glucose (80–120)</th>
<th>Sodium (135–153)</th>
<th>Potassium (3.5–5.0)</th>
<th>Osmolarity (270–300)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-dialysis</td>
<td>510</td>
<td>200</td>
<td>12.6</td>
<td>443</td>
<td></td>
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<tr>
<td>Post-dialysis pass 1</td>
<td>113</td>
<td>123</td>
<td>8.0</td>
<td>267</td>
<td></td>
</tr>
<tr>
<td>Post-dialysis pass 2</td>
<td>79</td>
<td>125</td>
<td>8.2</td>
<td>270</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Trial 2: 1 L .45 Normal Saline, 1 L Plasmalyte and 75 mEq Bicarbonate</th>
<th>Normal Range</th>
<th>Glucose (80–120)</th>
<th>Sodium (135–153)</th>
<th>Potassium (3.5–5.0)</th>
<th>Osmolarity (270–300)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-dialysis</td>
<td>600</td>
<td>200</td>
<td>12.0</td>
<td>448</td>
<td></td>
</tr>
<tr>
<td>Post-dialysis pass 1</td>
<td>146</td>
<td>126</td>
<td>7.8</td>
<td>274</td>
<td></td>
</tr>
<tr>
<td>Post-dialysis pass 2</td>
<td>77</td>
<td>128</td>
<td>6.9</td>
<td>275</td>
<td></td>
</tr>
</tbody>
</table>

Glucose, sodium, and potassium were measured and osmolarity was calculated.
than the resistance of the tubes within which they passed (Figure 1). A new set-up was used for each set of data and .9% normal saline was run through the system before the second trial of each set. This HC/dialysis setup was less expensive than the traditional cell salvage setup by 33% with the added advantage of being able to modify FFP, but the disadvantage of being unable to remove plasma free hemoglobin from the PRBCs.

Four bags of PRBCs and four bags of FFP were used. For each trial, an initial sample was taken from the blood product before being washed, as well as a post-wash sample. The sample was tested on the Bayer Rapid Point 400 blood gas analyzer (East Walpole, MA) to measure the desired components. The first test set consisted of PRBCs, the second set of FFP, and the third set of PRBCs + FFP. Each of these sets consisted of two trials per blood product and each trial was processed twice to ensure maximum equalization of the dialysis solution and the blood products.

**Data Analysis**

All data were recorded on a Microsoft Excel spreadsheet (Microsoft Corporation, Redmond, WA) for creating tables and figures (Table 1). Data was then transferred for analysis to the University of Nebraska Medical Center statistics department. Continuous variables are expressed as tables and figures using 90% confidence intervals (Table 2). These were computed for the interval of the means at the two dialysis points. The specific values evaluated include osmolarity and potassium. Results falling within the normal intervals (Figure 2: 270–310 mOsm/L for osmolarity, Figure 3: 3.5–5 mmol/L for potassium) support the hypothesis that this method is effective.
RESULTS

Raw test values are listed in Table 1. Before dialysis was performed, the PRBCs, FFP, and the PRBCs + FFP were hyperglycemic and hyperosmolar. Hyperkalemia was noted only in the PRBCs and the PRBCs + FFP. Only one bag of FFP was hypernatremic, but both were hypokalemic before the dialysis was performed.

Following the first pass of the dialysate through the HC, the PRBCs, FFP, and the PRBCs + FFP were hyperglycemic and hyperkalemic. Sodium concentrations were hyponatremic in the PRBCs, and normal in the FFP and PRBCs + FFP. Osmolarity was normal in the PRBCs and PRBCs + FFP. Only the FFP was slightly hyperosmolar.

Following the second pass of dialysate through the HC, slight hypoglycemia was measured in the PRBCs and FFP (average 78.5 mEq/L). Normal glucose was observed in the PRBCs + FFP. Hyponatremia was noted in the PRBCs (average 127 mEq/L), but the FFP and the PRBCs + FFP were normal. Hyperkalemia was noted in the PRBCs (average 7.5 mEq/L), hypokalemia was noted in the FFP, and slight hyperkalemia was noted in the PRBCs + FFP combination (average 5.3 mEq/L). In all cases, on average, the osmolarity was normal following the second pass.

DISCUSSION

The purpose of this study was to evaluate an in-vitro method to bring hyperosmolar PRBCs and FFP into normal osmolarity and potassium ranges. The 90% confidence intervals for osmolarity in Table 2 illustrate the interval (Figure 2) to be within the boundaries, therefore demonstrating that the products were brought into the normal or near normal range. The 90% confidence intervals for potassium in Table 2 illustrate the interval (Figure 3) to be outside the boundaries, therefore demonstrating that the products were not brought into the normal range. Even though the potassium was not completely normalized, it was decreased from its abnormally high values in the PRBCs and PRBCs + FFP trials by approximately 65% and increased from the abnormally low values by approximately 35% in the FFP trials. Fresher PRBCs would perhaps have less of a potassium load, which could more easily be corrected to the normal range. The best results were observed in the PRBCs + FFP trials, where the glucose, sodium, potassium, and osmolarity were observed as normal on average (Table 1). Perhaps the PRBCs + FFP trials were most physiologic because the dialysate solution was devised for use with the combination of banked PRBCs and FFP, but not PRBCs or FFP alone. Dialyzing PRBCs and FFP alone may require the revision of the dialysate solution to accomplish more physiologic results in terms of glucose, sodium, and potassium levels even though the osmolarity was normal. This study supports the hypothesis that modifying blood products with the use of a desktop dialysis setup can normalize the osmolarity. Secondarily, this technique allows FFP to be normalized for glucose, which cannot be accomplished within the operating room with cell salvage techniques.

A practical application of this technique would be the assembly of this apparatus on a bedside intravenous pole. Blood being given to patients requiring massive transfusion could be passed through the HC while the dialysate normalizes the sodium, glucose, potassium, and osmolarity. Heating the dialysate would offer the additional advantage of warming the blood products before infusion into the patient. Rapid infusion devices are designed to heat blood products to prevent patient cooling during transfusion, but have no means of physiologic normalization of the blood product.

REFERENCES


