Original Article

Evaluation of a Rapid Infusion System

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ABSTRACT

Operative cases where there is a potential for massive blood loss necessitates a system to rapidly warm and transfuse large volumes of blood over short periods of time. An in-house system in which both crystalloid solutions and blood products can be quickly added, warmed and available for infusion was developed to meet this need. The purpose of this study was to evaluate how blood products are affected when warmed and recirculated for an extended period of time. A recirculating rapid infusion system was assembled utilizing two filtered cardiotomy reservoirs, a centrifugal pump, a stainless steel blood heat exchanger, and 1/4 inch tubing, and applied in six adult orthotopic liver transplantations. The system was primed with 2 to 4 units each of fresh frozen plasma and packed red blood cells. The prime was recirculated and warmed to 37°C. Samples for blood gases, oxygen saturation, hematocrit, plasma free hemoglobin, sodium and potassium levels were drawn after initial priming and then every 30 minutes until additional blood products were added. Results show no significant change in pH (6.57 ± 0.21), pO_2 (56 mmHg ± 23 mmHg), pCO_2 (173 mmHg ± 138 mmHg), hematocrit (27% ± 8.7%) and plasma free hemoglobin values (125 mg/dl ± 9.4 mg/dl), following 3 hours of recirculation. However, potassium levels significantly decreased from 11.6 meq/L ± 2.6 meq/L to 10.0 meq/L ± 2.3 meq/L ($p<0.05$), sodium levels significantly increased from 144 meq/L ± 5.9 meq/L to 147 meq/L ± 5.3 meq/L ($p<0.05$) and oxygen saturations significantly increased from 59% ± 9.1% to 70% ± 16% ($p<0.05$). The results demonstrate that this system can maintain banked blood warm and available for immediate infusion without significant deterioration for up to 3 hours.

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INTRODUCTION

Massive blood loss during liver transplantation is a common complication. Pre-existing coagulopathy due to liver disease, in addition to collateral blood flow to the affected area, and thrombocytopenia resulting from portal hypertension or splenomegaly may all be contributing factors (1-3). These inherent risk factors necessitate a system to rapidly replace lost volume. The system must be able to infuse volume at a sufficient flow rate while maintaining the patient's temperature at or near 37°C (4,5). At The University of Iowa Hospitals and Clinics, rapid infusion is accomplished by the system shown in Figure 1. Once primed, packed red blood cells and fresh frozen plasma are added to the system and recirculated through a centrifugal pump while being warmed to 37°C with a heat exchanger integral to the system.

The recirculating of unoxygenated erythrocytes through the system at 37°C for an extended period of time has a questionable effect upon the structural integrity of the cells. The purpose of this study was to evaluate the effects of the infusion system upon red blood cell lysis by taking periodic samples of the recirculating blood and analyzing it for signs of hemolysis. Blood gases, saturations and electrolytes were also measured periodically to determine any concurrent changes.

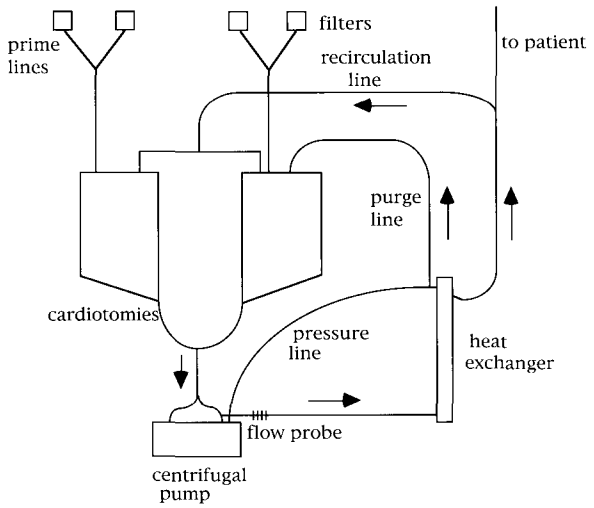
MATERIALS AND METHODS

The infusion system used consisted of two 20 micron filtered cardiotomy reservoirs[a], a centrifugal pump[b] and a stainless steel heat exchanger[c] used to maintain the blood at normothermia (Figure 1). Connected to each cardiotomy was a 1/4" "Y" connector and a rapid prime line with attached 40 micron screen filter. The outlet line on the heat exchanger was connected in a fashion to allow volume to be administered to the patient or to recirculate to a filtered port on the cardiotomy reservoir. A luer outlet at the top of the heat exchanger allowed for pressure monitoring and a purge line attachment. The purge line outlet was attached to a filtered cardiotomy port. The entire circuit utilized 1/4" tubing except for a six inch piece of 3/8" tubing on the outlet of each cardiotomy.

Cannulation of the patient was accomplished with a 12 gauge angiocatheter needle. Access was obtained via either the right internal jugular vein or a large vein in the right arm. This was connected directly to the rapid infusion system.

Three of the systems were flushed with CO_2 prior to priming and three were directly primed with 1000 ml of Plasmalyte A[d] via the rapid prime line. The system was circulated, debubbled and the prime warmed to 37°C. Two to four units each of packed red blood cells and fresh frozen plasma were added through the filtered rapid prime lines, allowed to recirculate at 0.60 to 0.80 L/min and warmed to 37°C. After allowing recirculation for 1 to 2 minutes, a sample was drawn from a stopcock on the purge line at the point of entry into the cardiotomy. Analysis of plasma free hemoglobin was accomplished on an Hitachi 747-100 System[e].

Figure 1
The rapid infusion device.



Blood was further analyzed for pH, pCO_2, pO_2, base excess, bicarbonate, sodium and potassium on a Nova Stat Profile 1[f]. Hematocrits were spun in a microhematocrit centrifuge[g] and hemoglobin and oxygen saturation levels were measured on an OSM3 hemoximeter[h].

Samples were collected in this manner every 30 minutes until additional blood products were added to the system. At that point sample collection was halted. Data was analyzed utilizing a paired t-test to determine any significant changes in measured values over time. Statistical significance was accepted at $p<0.05$.

RESULTS

Samples were taken from the rapid infusion system on six adult patients undergoing liver transplantation. Recirculation times of the six circuits ranged from 60 to 180 minutes. The average temperature of the recirculating blood was 37.0°C with an average pump speed of 0.61 L/min when recirculating.

The mean plasma free hemoglobin concentrations over a three hour recirculation period showed no significant change. However, the potassium level significantly decreased from a

a Model H-3700, Bard Cardiopulmonary Division, Tewksbury, MA 01876
b Model BP-80, Medtronic Biomedicus Inc., Eden Prairie, MN 55344
c Model HE-4, Gish Biomedical Inc., Santa Ana, CA 92705
d Travenol Laboratories Inc., Deerfield, Il 60015
e Boehringer Mannheim Corporation, Diagnostic Laboratory Systems Division, Indianapolis, IN 46250-0446
f Nova Biomedical, Waltham, MA 02254
g Damon/IEC Division, Needham Hts., MA 02194
h Radiometer America Inc., Carrollton, TX 75006

Figure 2
There was a significant decrease in potassium from 11.6 meq/L ± 2.6 meq/L to 10.0 meq/L ± 2.3 meq/L ($p<0.05$) during the first hour of recirculation. Data is mean ± SD. * = statistically significant decrease from baseline; ( ) = number of samples at each point.

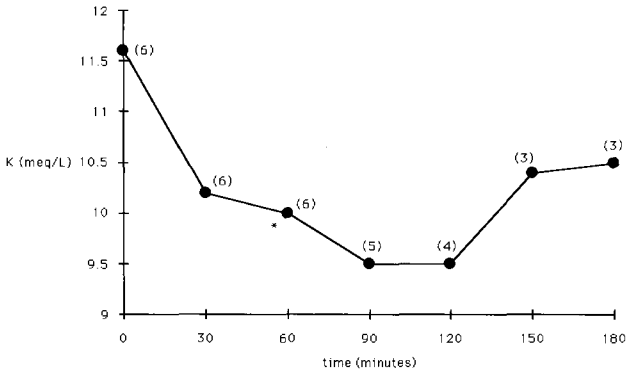


Figure 3
Sodium values significantly increased from 144 meq/L ± 5.9 meq/L to 147 meq/L ± 5.3 meq/L ($p<0.05$) over the first hour of recirculation. Data is mean ± SD. * = statistically significant decrease from baseline; ( ) = number of samples at each point.

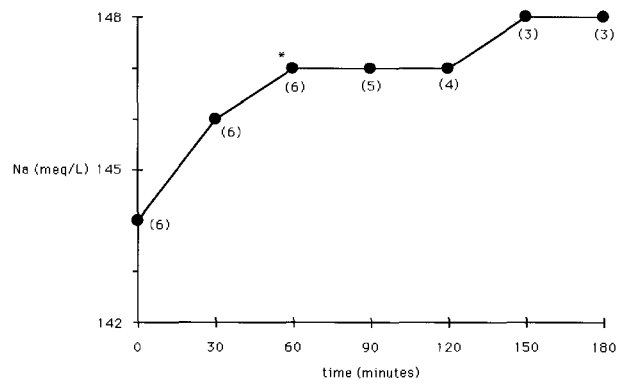


Figure 4
Oxygen saturation values increased significantly ($p<0.05$) from 59% ± 9.1% to 70% ± 16% over the first hour of recirculation. Data is mean ± SD. * = statistically significant decrease from baseline; ( ) = number of samples at each point.

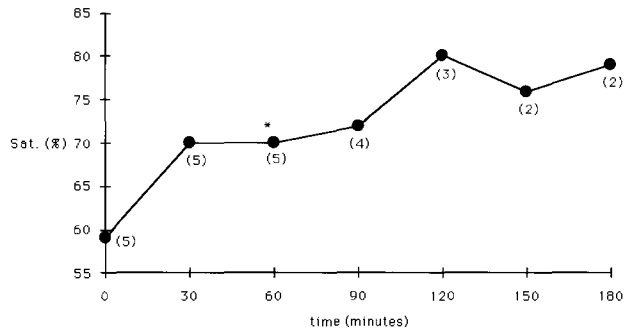
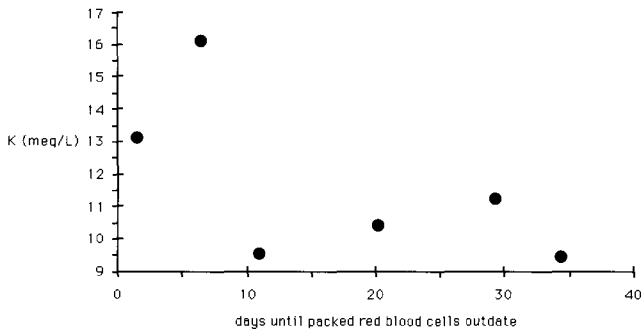


Figure 5
The correlation between the initial potassium level in the perfusate and the number of days until the packed red blood cell units expired ($r=-0.61$) was not significant.



mean of 11.6 meq/L to 10.0 meq/L ($p<0.05$) over the first hour of recirculation (Figure 2). This was accompanied by a significant rise in the extracellular sodium concentration from 144 meq/L to 147 meq/L ($p<0.05$) (Figure 3).

There were three systems which were CO_2 flushed prior to priming and three which were not CO_2 flushed. When the system was not flushed, the initial mean pCO_2 was 64 mmHg ± 13 mmHg. When flushed with CO_2, the initial mean pCO_2 was 332 mmHg ± 63 mmHg. No significant trends exist over time.

Mean pO_2 values increased from 48 mmHg to 84 mmHg over a two hour period, but this rise did not prove to be statistically significant due to a decreasing sample size. A concurrent increase in oxygen saturation (sO_2) was significant (Figure 4). Over the first hour of recirculation, sO_2 mean values increased from 59% to 70% ($p<0.05$). This trend continued at two and three hours, but did not continue to be significant.

The average pH of the perfusate was 6.57 ± 0.21 with a mean base excess of -21. The pH value did vary according to whether the circuit was CO_2 flushed or not. When CO_2 flushed, the mean pH value was 6.46. When the circuit was not flushed, the mean pH was 6.80. This proved to be a significant difference ($p<0.05$). The initial hematocrit of the blood in the rapid infusion system varied according to the volume and number of blood products added and averaged 27% ± 8.7%. There was no significant change in the hematocrit over time.

The relationship between the number of days until the units of packed red cells outdated and the initial potassium level is shown in Figure 5. The correlation ($r=-0.61$) between the two did not prove to be statistically significant. The number of days until outdate was determined by averaging the outdates of all the red

cell units used to prime the system for each patient. The unit outdates ranged from 1 to 39 days, but the range of outdates between red cell units within each circuit was not greater than six days.

DISCUSSION

With the potential for massive blood loss a possibility during orthotopic liver transplantation, there is a need for a system to rapidly replace lost volume while maintaining the blood at normothermia. Most systems available for this purpose are single pass devices, warming the blood as it flows through an integral heat exchanger (6-9), although recirculation utilizing a roller pump and physiological adjustment of the blood prime has been reported (10). These systems have the disadvantage of a decreasing perfusate temperature with increasing flow rates. The system used at this institution recirculates the blood through an extracorporeal circuit utilizing a centrifugal pump while warming and maintaining the blood at 37°C. It is able to infuse at flow rates from 100 ml/min. to 1.5 L/min. Recirculation for an extended period of time can be very traumatic to the formed elements of the blood, and warming the blood tends to accelerate the deterioration of stored red blood cells (11). Two of the simplest tests to evaluate erythrocyte integrity are plasma free hemoglobin (PFH) and serum potassium. An increase in either of these indicates lysis is occurring. The measured PFH of this system did not demonstrate a significant change over time. This would indicate that red blood cell integrity was maintained, although at a damaged state from routine storage conditions.

An increasing level of potassium is also associated with red blood cell lysis. The results show that the potassium level did not increase but in fact showed a statistically significant decline over the first hour of recirculation, even though no additional volume was added to the system during the sampling period (Figure 2). This level continues to fall over the second hour and levels off in the third hour of recirculation. Associated with the decrease in potassium is a statistically significant increase in extracellular sodium (Figure 3). These two events may be attributed to the sodium- potassium adenosine triphosphate (ATPase) pump on the erythrocyte membrane. As red blood cells are stored at 1-6°C, ATPase has been shown to be only 1/1000th as active as at 37°C (12). Potassium is no longer actively transported into the cells, nor sodium out. There remains a passive diffusion of potassium ions out of the cells and a net shift of sodium ions in the opposite direction. An equilibrium is reached at 25 to 30 days of storage (12). As the blood is warmed to 37°C and returned to a more physiological state, the ATPase pump activity increases and the electrolytes are once again moved against their concentration gradient. This movement of ions is well documented and has been shown to result in hypokalemia following massive transfusions (13-15).

Flushing the system with CO_2 prior to priming makes the system easier to debubble, but also makes for a very unphysiological blood gas with pCO_2 values greater than 300 mmHg. This system has no oxygenator to blow this gas off as in a heart bypass pump circuit. It is infused directly into the patient. Since the system is primed with blood and appears to be adequately debubbled without the CO_2 flush, the system is no longer flushed at this institution. The pCO_2 values for the samples which were not CO_2 flushed were 64 mmHg ± 13 mmHg, which are much closer to physiological values. If CO_2 flushing is desired, there is the possibility of flushing the cardiotomies with an oxygen/air mixture following the CO_2 flush, entering through one of the filtered/non-filtered ports, with the exhaust port unobstructed. This could be a means of normalizing blood gas values of the system prior to infusion.

Red blood cells tend to become very acidic in storage due to the lactic acid produced by red blood cell metabolism. Even after mixing with fresh frozen plasma and crystalloid the initial mean pH and base excess was 6.63 and -20 meq/L, respectively. Flushing with CO_2 also affected the pH value of the blood. It was significantly more acidic when the system was flushed with CO_2 than when it was not flushed. The less acidic the blood is, the fewer adjustments will need to be made in the patient's blood gases. Any acid-base abnormalities were adjusted in the patient following administration of the blood. Patient lab values were not recorded in this study.

The action of the blood recirculating through the cardiotomies also serves to oxygenate the blood (Figure 4). The banked blood begins with an initial oxygen saturation and pO_2 of 59% and 56 mmHg, respectively. After one hour of recirculation the oxygen saturation had increased to 70% ($p<0.05$). This trend continued up to three hours, but the small sample size precluded a significant change in the values. The action of the blood recirculating through the cardiotomies is similar to a screen oxygenator in oxygenating the blood. One of the six patient samples was eliminated from the oxygen saturation and pO_2 data due to a change in the setup of the purge line, from which samples were drawn, on the cardiotomy. Instead of placing the purge line on a filtered, cardiotomy port, it was placed on an unfiltered port. Blood was allowed to splash into the bottom of the cardiotomy, thereby oxygenating the blood. The initial oxygen saturation of this sample was 95% with a pO_2 of 99 mmHg. Although only one system was purged in this way, theoretically it may be beneficial to infuse oxygenated blood as opposed to deoxygenated blood.

Potassium slowly leaks out of the red cells as they age in storage (13,14), so the relationship between the age of the packed red blood cell units and the initial potassium concentration of the perfusate was examined (Figure 5). The correlation found between the two did not prove to be statistically significant.

It can be concluded from these results that blood may be recirculated through a centrifugal pump at normothermia for up to three hours without any significant signs of hemolysis. Plasma levels of potassium decrease and sodium increase. The blood becomes oxygenated as it passes through the cardiotomies. This method appears to be a capable way of replacing massive blood losses in a safe and effective manner.

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