A Comparison of Two Methods of Post-Bypass Hemoconcentration

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Abstract

Post-pump hemoconcentration is currently accomplished by centrifugation and saline washing, the product being packed red cells suspended in saline. This study was designed to compare centrifugation with ultrafiltration by an artificial kidney, the product of this method being whole blood.

Sixteen adult patients undergoing cardiopulmonary bypass were assigned to one of two groups. Hemoconcentration was achieved in Group I with the Cell Saver and with an artificial kidney in Group II. Coagulation data, plasma proteins, colloid osmotic pressure, hematocrit, platelet count, plasma free hemoglobin, and fibrinogen levels were collected and compared at various times during each case.

The mean total protein concentration of the ultrafiltered blood (8.01 ± 1.31 g/dl) was significantly greater than that of the Cell Saver blood (0.29 ± 0.29 g/dl, $p < .01$). Also, the mean total protein concentration in the discard was significantly greater in the Cell Saver group (1.69 ± 0.56 g/dl) than the artificial kidney group (0.09 ± 0.14, $p < .01$). There were no significant differences between the two groups in the other parameters compared.

While the artificial kidney was quite effective in conserving the plasma proteins during hemoconcentration, no additional advantages were demonstrated during this study.

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Presented at the 20th International AmSECT Conference, Hollywood, Florida, April 25–28, 1982.

Introduction

Blood remaining in the extracorporeal circuit following cardiopulmonary bypass (CPB) is currently being salvaged in many institutions by centrifugation and subsequent saline washing with the resulting packed red blood cells transfused into the patient.[1,2] A disadvantage of this technique is the discarding of the plasma fraction. An alternative to this method exists which rescues not only red blood cells but the plasma proteins as well. Ultrafiltration with an artificial kidney has proven to be effective in removing excess plasma water while conserving plasma proteins in patients with severe fluid overload as a result of acute or chronic physiological imbalances.[3–7] Recently, ultrafiltration has been used to remove the excess plasma water during CPB.[8] This study was undertaken to demonstrate the superiority of the artificial kidney in post-bypass hemoconcentration.

Methods

Sixteen adult patients undergoing routine CPB for coronary artery bypass grafting were alternately assigned to one of two groups. Hemocon-

centration was achieved in Group I with the Haemonetics Cell Saver[a] and in Group II with the Cordis Dow C-Dak Duo-Flux[b] artificial kidney. This artificial kidney has an effective surface area of 1.8 m^2 and approximately 13,000 hollow cellulose acetate fibers, 40 μ thick, which are highly permeable to water. The fibers are constructed so that particles with molecular weight exceeding 69,000 are unable to cross the membrane. This artificial kidney has an ultrafiltration rate of 15 ml. per hour per mm Hg transmembrane pressure.[9]

Perfusion was performed with the Travenol modular pump[c] and the pump circuit consisted of a Travenol Membrane Oxygenator (TMO)[c], a Travenol custom tubing pack[c], a Pall arterial line filter[d], and a Bentley Q220 cardiotomy reservoir[e]. The circuit was primed with two liters of Lactated Ringers solution, 500 ml. of 6% hydroxyethyl starch[f], and 1500 units of beef lung heparin[g]. Anticoagulation was achieved in all patients by the administration of 300 units of heparin per kilogram. Activated Clotting Times (ACT) were done to assess the state of anticoagulation and additional heparin was given as needed to keep the ACT greater than three and one-half times the baseline ACT.[10]

Prior to CPB, the following data were collected for each patient: hemoglobin/hematocrit (H/H), platelet count, fibrinogen concentration, prothrombin time (PT), partial thromboplastin time (PTT), plasma protein concentration (PPC), and colloid osmotic pressure (COP). The PPC was measured with the American Optical Refractometer[h]. The COP was then determined using the following formula:

$$COP = (PPC \times 3.32) - 2.0^{11}$$

Immediately following the termination of CPB, perfusion time was recorded and H/H, plasma free hemoglobin, platelet count, PPC, and COP values were determined. Enough protamine was then slowly administered to neutralize the heparin.[10] As the protamine was being administered, hemoconcentration by the designated method was begun. The volume of blood obtained by hemoconcentration and the volume of discard were measured as well as the PPC and COP of each. Group I's data were adjusted to eliminate the volume of saline used for washing. The time needed to deliver the first unit of blood to the patient and the total time required for hemoconcentration were recorded.

After all the hemoconcentrated blood was transfused along with two units of fresh frozen plasma, arterial blood was drawn from which the following data were collected: H/H, fibrinogen concentration, PT, PTT, plasma free hemoglobin, PPC, and COP.

The Cell Saver was connected to the pump circuit by attaching the inlet line to the arterial sampling port with a male-to-male connector[i]. The blood was pumped at a speed of 150 ml./min. into the centrifuge bowl and washed with 500 ml. of 0.9% normal saline. This produces 225 ml. of packed red blood cells suspended in saline with a hematocrit of 50–80%. The blood was then pumped into the attached blood bag and transfused into the patient. This red cell suspension in saline contains no clotting factors, plasma or anticoagulant.[12]

Since the hollow fibers are stored bathed in glycerol, the artificial kidney was first flushed with saline according to the manufacturer's directions.[9] The artificial kidney was then added to the pump circuit (Figure 1) by replacing the filter purge line with a ¼" segment attached to the arterial header of the artificial kidney. Another ¼" segment connected the venous header to the cardiotomy reservoir. The dialysate inlet port was capped and negative pressure was applied to the dialysate outlet port via a graduated container. The volume of ultrafiltrate was determined and after analysis the ultrafiltrate was discarded. A total transmembrane pressure of approximately 700 mm Hg was produced by running the pump at 200 ml./min. creating an intrafiber pressure of 200 mm Hg. To this, approximately 500 mm Hg of negative pressure was added via the vacuum. The blood was allowed to recirculate through this circuit until a hematocrit of 40–45% was obtained. The blood was then collected in 375 ml. transfer packs[j]

[a] List No. 6783, Haemonetics Corp., Braintree, MA 02184
[b] Catalog No. 203-210, Cordis Dow Corp., Concord, CA 94520
[c] Travenol Laboratories, Deerfield, IL 60015
[d] EC 3840, Pall Biomedical Products Corp., Glen Cove, NY 11542
[e] Bentley Laboratories, Inc., Irvine, CA 92714
[f] American Critical Care, McGaw Park, IL 60085
[g] Upjohn Company, Kalamazoo, MI 49001
[h] American Optical Company, Buffalo, NY 14240
[i] No. 40-180, Cobe Laboratories, Inc., Lakewood, CO 80215
[j] Code 4R2014, Fenwal Laboratories, Deerfield, IL 60015

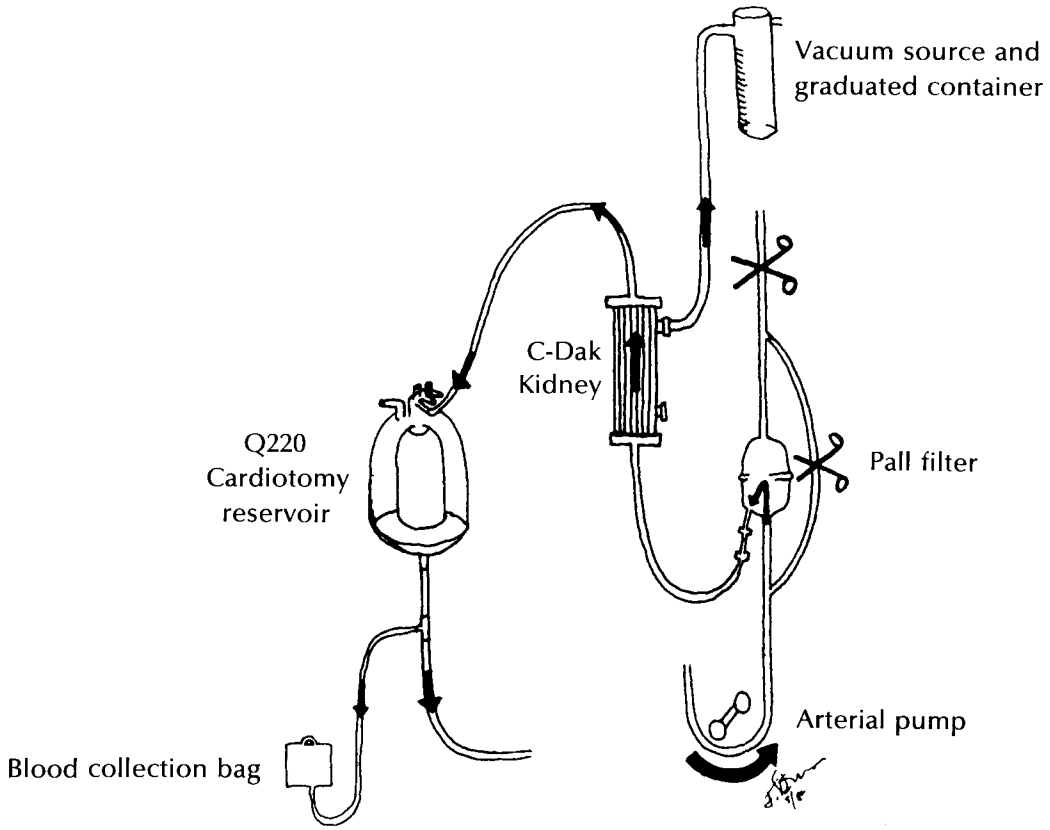

FIGURE 1. Ultrafiltration Circuit.

through a leur-lock connector located in the cardiotomy drain line. Statistical evaluations were carried out using the student's pooled t-test.[13]

Results

Table I is a summary of the pre-pump data and compares the results between the two groups. There were no statistically significant differences between the groups in any of the variables measured.

Table II summarizes and compares the results of the post-pump data. Prior to centrifugation or ultrafiltration there were no significant differences between the groups. In both groups the hematocrit decreased by an average of 45% and the PPC decreased an average of 42%.

Table III compares hemoconcentration and lab-

TABLE I
Pre-pump Data

	Group I	Group II	Significance*
Age (years)	54 ± 3	56 ± 6	NS
BSA (m^2)	2.06 ± 0.17	2.03 ± 0.16	NS
Hemoglobin (g/dl)	14.1 ± 1.8	15 ± 1.6	NS
Hematocrit (%)	41.4 ± 5.0	43.4 ± 4.3	NS
Platelet Count (thousand/mm^3)	245 ± 80	259 ± 109	NS
Fibrinogen (mg/dl)	345 ± 98	301 ± 67	NS
Prothrombin Time (sec)	12.2 ± 0.4	12.4 ± 0.5	NS
Partial Thromboplastin Time (sec)	29.6 ± 5.8	28.0 ± 1.9	NS
Plasma Protein (g/dl)	7.0 ± 0.54	7.1 ± 0.45	NS
COP (mmHg)	21.2 ± 1.8	21.6 ± 1.5	NS

* Comparing Groups I and II

TABLE II
Post-Pump Data

	Group I	Group II	Significance*
Perfusion Time (min)	146 ± 38	148 ± 35	NS
Hemoglobin (g/dl)	7.7 ± 0.8	8.0 ± 1.6	NS
Hematocrit (%)	22.6 ± 2.5	23.7 ± 4.6	NS
Platelet Count (thousand/mm^3)	108 ± 46	104 ± 60	NS
Plasma Free Hemoglobin (mg/dl)	33.0 ± 6.0	26.5 ± 20.3	NS
Plasma Protein (g/dl)	4.10 ± 0.54	4.14 ± 0.51	NS
COP (mmHg)	11.6 ± 1.8	11.7 ± 1.7	NS

* Comparing Groups I and II

oratory data between groups. There were no statistically significant differences between the groups in the volume of blood obtained from hemoconcentration, the time required to deliver the first unit of hemoconcentrated blood to the patient, or the total time required for hemoconcentration. However, statistically significant differences did exist between groups in the volume of discard, the PPC and COP of the hemoconcentrated blood and of the discard ($p < .01$ for all). Group I's average discard volume, 1950 ± 526 ml., was significantly greater than Group II's (1002 ± 341 ml.). In the hemoconcentrated blood of Group II, there was an average PPC of 8.01 ± 1.31 g/dl and an average COP of 24.4 ± 4.2 mm Hg which were significantly greater than those in Group I (0.29 ± 0.29 g/dl, 0 mm Hg). Group I's PPC in the discard averaged 1.69 ± 0.56 g/dl. This was an average of 32.96 ± 2.95 grams of protein in the discard, whereas in Group II the amount discarded was insignificant.

Table IV is a summary of the post-protamine data and compares results between the two groups. There were no statistically significant differences between the groups. Group I's hematocrit increased an average of 21% following the transfusion of the hemoconcentrated blood while Group II's hematocrit increased an average of 4% following the transfusion. The PPC increased an average of 16% in both groups.

Discussion

During this study hemodilutional CPB resulted in a decrease in all blood constituents of approximately 42%. The Cell Saver rescued only the red blood cells during hemoconcentration. The artificial kidney recovered not only the red blood cells, but the plasma proteins as well.

The plasma proteins serve several physiological purposes. They create the COP which helps to control fluid distribution between fluid compartments of the body. A decrease in these plasma proteins may lead to third spacing.[14] While safe

TABLE III
Hemoconcentration Data

	Group I	Group II	Significance*
Hemoconcentrated Blood (cc)	553 ± 136	707 ± 218	NS
Discard (cc)	1950 ± 526	1002 ± 341	$p < .01$
Plasma Protein—Blood (g/dl)	0.29 ± 0.29	8.01 ± 1.31	$p < .01$
COP—Blood (mmHg)	0	24.4 ± 4.2	$p < .01$
Plasma Protein—Discard (g/dl)	1.69 ± 0.56	0.09 ± 0.14	$p < .01$
Proteins Discarded (g)**	32.96 ± 2.95	0.90 ± 0.48	$p < .01$
COP—Discard (mmHg)	3.48 ± 2.08	0	$p < .01$
Time for 1st Unit (min)	14 ± 7	17 ± 10	NS
Total Time for Hemoconcentration (min)	36 ± 11	32 ± 13	NS

* Comparing Groups I and II
** Proteins Discarded = Discard (dl) × Plasma Protein—Discard

TABLE IV
Post-Protamine Data

	Group I	Group II	Significance*
Hemoglobin (g/dl)	9.4 ± 1.2	8.4 ± 0.6	NS
Hematocrit (%)	27.4 ± 3.5	24.7 ± 1.8	NS
Fibrinogen (mg/dl)	175 ± 28	177 ± 40	NS
Prothrombin Time (sec)	15.7 ± 1.8	15.3 ± 1.9	NS
Partial Thromboplastin Time (sec)	32.9 ± 3.9	30.8 ± 2.1	NS
Plasma Protein (g/dl)	4.74 ± 0.31	4.83 ± 0.24	NS
COP (mm Hg)	13.7 ± 1.0	14.0 ± 0.8	NS
Plasma Free Hemoglobin (mg%)	34 ± 21	32 ± 13	NS
ACT (sec)	115 ± 19	116 ± 27	NS

* Comparing Groups I and II

levels of COP during CPB have not been determined, the COP is substantially decreased by hemodilutional CPB and should be considered when choosing methods of hemoconcentration.[11] The dilution of the plasma proteins which serve as the clotting factors should be a major concern when choosing methods of hemoconcentration. The hemostatic mechanism of patients undergoing open heart surgery is completely immobilized during surgery and restoring the function of this mechanism is imperative. Finally, the plasma proteins also contribute to the immune response system. Their dilution may contribute to a disproportionately higher incidence of post-operative infection seen in open heart patients.[15]

Hemoconcentration with the artificial kidney appears to produce a larger volume of processed blood, but in actuality the artificial kidney produces whole blood (hematocrit approximately 40%) while the Cell Saver produces packed red blood cells (hematocrit approximately 60%). Multiplying the hematocrit and the volume of hemoconcentrated blood for each group would reveal that the larger volume of red blood cells is being recovered with the Cell Saver. It was easier with the set ups used to recover nearly all the residual volume from the TMO with the Cell Saver technique. This accounts for the larger total volume (cells + discard) collected via the Cell Saver.

The artificial kidney's effectiveness in conserving plasma proteins was clearly demonstrated in this study. However, despite the loss of a significant amount of protein in the Cell Saver discard (32.96 ± 2.95 grams), there was no significant difference between groups in PPC or COP following transfusion of the processed blood. Also, there was no significant difference between groups in coagulation data. The fact that all patients received fresh frozen plasma probably masked any differences that may have existed in these parameters. The next step in this investigation is to compare these two methods of hemoconcentration by administering fresh frozen plasma to the centrifugation group and not to the ultrafiltration group. Finally, the fact that there was no significant difference between post-pump and post-protamine plasma free hemoglobin levels for both groups indicates that neither method of hemoconcentration increases the fragility of the red blood cells.

Extra tubing, connectors, adaptors, and blood bags were required in the assembly of the artificial kidney circuit, and thus the possibility of contamination was greater with this method. Industry could resolve this assembly problem with the production of a hemoconcentration pack similar to the Open Heart Pack[k] marketed by Haemonetics. Despite our subjective opinion that our ultrafiltration set-up was cumbersome, the time required for delivery of the first unit of processed blood to the patient and the total time required for hemoconcentration were equivalent in both groups.

A potential problem that was not encountered during this study, but one that should be considered is the concentration of free hemoglobin via ultrafiltration. If a patient has an abnormally high plasma free hemoglobin following CPB, the potential for renal damage does exist if concentrated hemoglobin is transfused. Since heparin does not

[k] Catalog No. 8618, Haemonetics Corp., Braintree, MA 02184

cross the artificial kidney membrane, another potential problem that was not encountered, but should be considered, is the concentration of heparin via ultrafiltration. The patient's clotting studies should be closely monitored in the event more protamine is required.[9]

The cost of equipment required for these two methods of hemoconcentration should be mentioned. The C-Dak Duo-Flux artificial kidney used in this study costs approximately $35. Cordis Dow now manufactures the Hemo-Concentrator[1] specifically for hemoconcentration and this costs $80. The Haemonetics Cell Saver sells for approximately $13,500 and individual Open Heart Packs sell for approximately $56.

This study has demonstrated the validity of using the artificial kidney for post bypass hemoconcentration. This investigation shall be continued using a variety of artificial kidneys to determine the system which produces the best results.

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[1] Catalog No. 300-100, Cordis Dow Corp., Concord, CA 94520