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Hematologic Derangements of Cardiopulmonary Bypass: A Comparison of Two Perfusion Systems

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Abstract

A major goal of new perfusion equipment is minimal trauma to blood elements. This study compares two perfusion systems, quantifies the change in blood components and generation of microemboli, as well as compares the hospital courses of each perfusion system. Forty-four coronary patients were assigned to either Group S, a silicone rubber membrane (SciMed) and centrifugal pump (Bio-Medicus) (N=19) or Group C (our routine equipment), a microporous polypropylene membrane (COBE CML) and roller pump (COBE)(N=25). The rise in plasma hemoglobin (26±14mg* in Group S and 26±17mg* in Group C), the drop in hematocrit (-15.0±3.9* in Group S and -14.7±3.8* in Group C at the second post-op day), and the decrease in platelet count (-152,000±78,000* in Group S and -129,000±52,000* in Group C) were similar in both groups. There was no difference in rise in post-op alveolar-arterial oxygen gradients or debris generated by each system. 27.7% in Group S required red cell transfusions and only 8% required red cell transfusions in Group C. There was no significant difference in clinical endpoints such as ICU stay, hospital stay and complication rate. We found no advantage to more expensive perfusion devices and no improvement upon the extensive CPB damage to formed blood elements.

Introduction

Although cardiopulmonary bypass (CPB) is a successful technique, it represents a major derangement of homeostasis. The hematologic system in general, and red blood cells in particular, are the focus of much of this derangement. Red blood cells are damaged in the extracorporeal circuit by mechanical trauma and by the humoral chain of events set in motion by the activation of complement resulting in intravascular and extravascular hemolysis.

In an effort to reduce the amount of hemolysis, new pump systems have been developed. One such development is the centrifugal pump (a) used with a silicone rubber membrane oxygenator (b). We compared this system with our standard equipment, a double roller pump (c) with a polypropylene membrane (c).

In this study, immediate and delayed hemolysis was quantified in patients undergoing uncomplicated coronary artery bypass grafting (CABG). Also, this study evaluated other differences between the two perfusion systems in patients undergoing CABG. The parameters assessed were blood damage (the postoperative rise in plasma hemoglobin and drop in hematocrit and platelet counts, and the number of transfusions required), evidence of microemboli (measured by the amount of debris generated on oxygenator filter and by the rise in alveolar-arterial oxygen gradient following CPB), and clinical endpoints such as postoperative complications and length of intensive care and hospital stay.

Methods

Forty-three patients, ranging from age 31 to 73, 38 male and five female, undergoing routine uncomplicated CABG, were assigned to either Group S, silicone rubber membrane (SciMed) with a centrifugal pump (BioPump)(N=19) or to Group C, the polypropylene membrane (COBE CML) and roller pump (COBE Modular Roller Pump) (N=25). Patients were selected whose preoperative hematocrit was over 38% in males and 40% in females, and whose preoperative reticulocyte count and haptoglobin were normal, indicating no pre-existing hemolytic process. All patients received 1 gm. methyl-prednisolone at the onset of CPB. The Haemonetics Cell Saver (d) system was used in all patients in both groups.

Setup and priming of the two groups required the following: 1) Group S: BP-80 centrifugal pump, SciMed filtered cardiotomy reservoir, SM-35 membrane with venous reservoir bag and

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b. SciMed Life Systems, Inc., Minneapolis, MN 55441
c. Cobe Laboratories, Arvada, CO 80004
d. Haemonetics Corp., Braintree, MA 02184

* p<.001

integral heat exchanger and Pall arterial blood filter (f) (40 micron); 2) Group C: double roller head pump with 1/2" PVC pump header (g), COBE filtered cardiotomy reservoir (g) CML membrane lung with integral heat exchanger and Pall arterial blood filter. Priming fluids consisted of 150 mls Mannitol (22 gms), 1500 mls of Normosol-R and 500 mls of Hetastarch. Group S required an additional 400-500 mls of crystalloid to meet minimum priming needs. In both groups, a .5 micron pre-bypass filter was employed in the recirculation.

A sample for plasma free hemoglobin was drawn before the incision was made and then again one hour after onset of CPB (before any pump suction blood or Haemonetic™ suction blood was returned to the patient), and again approximately three hours after onset of CPB on admission to the surgical intensive care unit. Hematocrits were determined preoperatively, then three hours postoperatively and the first, second, third, and sixth postoperative days. All patients requiring blood transfusions were excluded from this measurement once the transfusion was begun. The number of red cell transfusions required was quantified per group.

Platelet counts were drawn preoperatively and again three hours following bypass. The one patient receiving platelet transfusions received them after the postoperative platelet measurement. Platelet transfusions required were quantified per group.

To evaluate microemboli generated by each perfusion system, the arterial blood filter was taken following bypass, flushed in reverse direction with two liters of normal saline through a 25 micron filter that was dried and weighed. In this way, the particulate matter trapped by the final oxygenator filter just prior to return to the patient was quantified. To quantify any microemboli to the lungs, Aa gradients on 100% oxygen were measured preoperatively and three hours postoperatively and the rise in gradients following CPB was compared between the two groups.

Results

Although the two groups were very similar preoperatively, this was not a randomized or blind study, due to the logistics of pump and membrane availability. There was no difference in the two groups in regard to age, sex, weight, body surface area, or preoperative Aa O_2 gradient. Patients in Group S had a mean age of 60.11±7.68 (N=18) and in Group C 58.16±11.76 (N=25). There were four females assigned to Group S and one to Group C. The average weight in Group S was 85.52±12.69 kg and 91.88±18.62 kg in Group C. The average body surface area in Group S was 2.02±0.18 m^2 in Group S and 2.13±0.25 in Group C. The preoperative Aa gradient was 215±64.41 in Group S and 228±79.39 in Group C.

Also, there were no significant differences in the procedures and operative course between the two groups, as measured by number of grafts, number of patients receiving IMA grafts, pump time, maximum flow rate, amount of pump or haemonetic suction or chest tube output measured during the first 24 hours postoperatively. The mean number of bypasses was 3.17±0.99 per patient for Group S and 3.23±1.07 for Group C. Seventeen of 18 patients (94%) in Group S received an internal coronary artery graft and 22 of 26 patients (85%) in Group C. The average pump time was 63±16 minutes for Groups S and 69±18 minutes for Group C. The mean maximum flow rate was 5.9±0.64 for Group S and 5.8±0.54 for Group C. The mean cardiotomy pump suction blood measured during bypass was 661±447.1 cc for Group S and 773±716.8 cc for Group C. The mean volume of "cell saver" suctioned blood to each patient was 4.5±1.7 units for Group S and 4.3±1.4 units for Group C. Chest tube output over the first 24 hours postoperatively was 1052.89±465.27 in Group 5 and 1095.95±436.99 in Group C.

Warming times for the two groups ranged from 25°C to 37°C naso-pharyngeal (N-P) and 36°C urine (U) temperatures as follows: Group S, n=19, 33 minutes (N-P) and 37 minutes (U); Group C, n=17, 29 minutes (N-P) and 35 minutes (U).

Venous return (venous inlet resistance) was not directly quantitated; however, in both groups the surgical table was raised approximately 25% of the time to facilitate venous return.

The setup and priming times of the two systems were not equal. Group S required about 15 minutes longer than Group C.

The rise in plasma hemoglobin from preoperative level to one hour after the onset of CPB (before any pump or haemonetic suction return) was 25±14 mg% in Group S (N=18) and 25±17 mg% in Group C (N=25), showing a significant rise but no substantial difference between the groups.

The hematocrit drop from preoperative levels to three hours after onset of CPB was 14±4% in Group S (N=18) and 15±4% in Group C (N=25). The drop from preoperative levels to the first postoperative day was 14±3% in Group S (N=17) and 13±4% in Group C (N=25). The drop from preoperative levels to the second postoperative day was 15±3 in Group S (N=16) and 14±3 in Group C (N=23). The drop to the third postoperative day was 14±4 in Group S (N=15) and 14±3 in Group C (N=20). The final measurement on the sixth postoperative day showed a drop of 11±4 in Group S (N=12) and 11±4 in Group C (N=20) (see diagram). At each measurement, patients who had received blood transfusions were excluded.

In Group S there were 10 units of packed red cells given (five patients received two units each) (N=18) and in Group C, there were four units of packed cells (two patients received two units each) (N=24). 27.8% of patients received red cell transfusions in Group S while 8.0% of Group C's patients received transfusions.

There was a large drop in platelet count in both groups, but no significant difference between the two groups (-152,000±-78,000 in Group S and -129,000±52,000 in Group C). Platelet measurements were taken prior to any platelet transfusions. Eight units of platelet transfusions were required (one patient of 18 required eight units of platelets or 5.6% of patients) in Group S (N=18) and no platelet transfusions in Group C (N=25).

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The rise in Aa gradients was 127±87 in Group S (N=15) and 143±105 in Group C (N=21), which indicated no significant difference between the groups. The gain in filter weight, which measured the amount of debris generated by each perfusion system, was 0.1016±0.0057 grams in Group S (N=13) and 0.1030±.0080 grams in Group C (N=15), again showing no significant difference.

There were no postoperative complications in nine patients (50.0%) in Group S (N=18) and no postoperative complications in 14 patients (56.0%) in Group C (N=25) (Table 1). In Group S, 5/18 patients (27.8%) had pericarditis requiring treatment, 1/18 (5.6%) had atrial fibrillation requiring discharge medications, 2/18 (11.1%) had clinically significant pleural effusions and 1/18 (5.6%) had ventricular ectopy requiring discharge medication. All patients in Group S were extubated on the first postoperative day and all patients stayed in the intensive care unit for two days (N=18) excluding one patient kept electively sedated and intubated four days due to an intraoperative tear in the aorta.

In Group C, 2/25 (8.0%) patients had pericarditis requiring medication, 5/25 (20%) had atrial fibrillation requiring discharge medication, 2/25 (8.0%) had clinically significant pleural effusions, 1/25 (4.0%) had a cerebral vascular accident (CVA), 2/25 (8.0%) had ventricular ectopy requiring discharge medication, 1/25 (4.0%) had a superficial wound infection, and 1/25 (4.0%) had pneumonia. All patients were extubated on the first postoperative day except one patient extubated on the second postoperative day. All patients in this group stayed in the intensive care unit two days (N=24) except for the above patient with pneumonia who developed ventricular ectopy and required four days in the intensive care unit (Table l).

Postoperative day of discharge was 7.4±1.1 in Group S (N=18) and 7.2±2.3 in Group C (N=24). This excluded one patient in Group S mentioned above who required prolonged elective intubation following an intraoperative aortic tear, and one patient in Group C who had an extended hospitalization after a CVA occurring on the third postoperative day.

Discussion

It has been known for some time that hemolysis occurs both during and immediately after bypass and then continues for several days (1, 2). The major immediate hemolysis appears to be from intracardiac venous return returned to pump via the sucker tips (3). The negative pressures of suction and turbulence explain the major sources of mechanical hemolysis via increased cation permeability of red cells and red cell membrane fragmentation (4).

A source of delayed (or ongoing) hemolysis may be deposition of C5b-9 activated by the CPB system and deposited on red cells causing intravascular hemolysis, reflected by the presence of elevated plasma C5b-9 complexes and presence of C5b-9 complexes on red cells following CPB (5, 6).

Damage to red cells during CPB is associated with changes in morphology, metabolism, and functional properties of the cell. Damage to cell membrane structures leads to an increase in permeability, loss of membrane pliability, loss of cell fluidity and loss of the biconcave shape, all of which decrease the red cell deformability, leading to disposal by the reticular endothelial system (7, 8).

Many efforts to reduce blood trauma have been made in the development of both the pump and the oxygenator components of the extracorporeal circuit. One is the development of a silicone rubber membrane oxygenator (TRUE Membrane) which offers molecular (gaseous) diffusion across the silicone membrane so that there is no actual blood-gas interface. This solid, nonporous barrier reportedly prevents gaseous microemboli and reduces platelet destruction and hemolysis (9, 10, ll).

The centrifugal, nonpulsatile pump (BioPump) uses centrifugal force to generate energy and move blood in the circuit, as opposed to the forward pulsatile displacement used in the traditional roller pumps. It is pressure sensitive and generates relatively low flow in response to high line resistance. A lower rate of microemboli generation, blood trauma, and hemolysis have been noted with the centrifugal pump (12, 13, 14, 15).

The cost of the two perfusion systems is $752 for the new system and $485 for the existing system in our hospital. Because of this cost difference, this study was undertaken to evaluate the possible advantages of the new system.

Red cell destruction during CPB has been quantified several ways. Although immediate red cell destruction occurring intravascularly can be measured with plasma hemoglobin, this alone as a measure of hemolysis can be misleading, since the ability to clear a given level of plasma hemoglobin varies from person to person (16). Red cell destruction occurring after 24 hours must be quantified differently since destruction of damaged cells takes place in the reticulo-endothelial system and is not reflected by increased plasma hemoglobin.

By taking the first one hour plasma hemoglobin sample prior to the return of blood to the patient from pump and Haemonetic™ suction (both a major source of hemolysis), the elevation in plasma hemoglobin during this period most accurately reflects intravascular hemolysis from the perfusion system alone. Again, the lack of difference in rise in plasma hemoglobin between the two pump systems does not show any progress in eliminating hemolysis.

The measurement of hematocrit drop from preoperative level to 2, 3, and 6 days postoperatively allows for equilibration of fluid status and may show the effect of delayed hemolysis. These changes again failed to show any significant difference between the two pump systems (Figure l).

We also found no significant difference in the generation of microemboli. Also, there was no significant difference in the number or extent of postoperative complications or hospital stay (Table l).

Conclusion

This study evaluated hemolysis in patients undergoing routine CPB and the possible clinical differences between these two CPB systems.

Figure 1

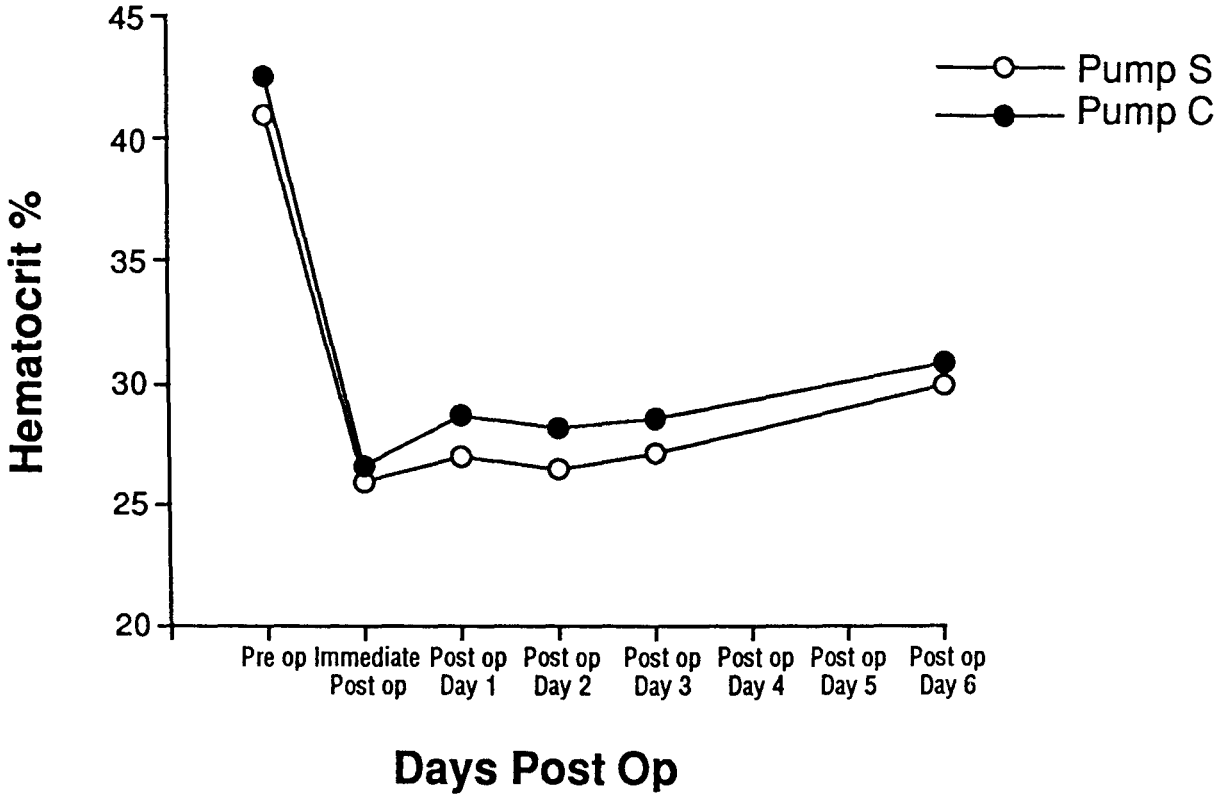

Table 1

COMPLICATIONS

	PUMP S	%	PUMP C	%
NONE	9/18	50.0	14/25	56
PERICARDITIS (requiring treatment)	5/18	27.8	2/25	8
ATRIAL FIBRILLATION (requiring discharge medication)	1/18	5.6	4/25	16
PLEURAL EFFUSION	2/18	11.1	2/25	8
CVA	0/18	0	1/25	4
VENTRICULAR ECTOPY (requiring discharge medication)	1/18	5.6	2/25	8
WOUND INFECTION	0/18	0	1/25	4
PNEUMONIA	0/18	0	1/25	4
VENTILATION OVER ONE DAY	0/18	0	1/25	4
PATIENTS REQUIRING RED CELL TRANSFUSIONS	5/18	27.8	2/25	8
PATIENTS REQUIRING PLATELET TRANSFUSIONS	1/18	5.6	0/25	0

Parameters assessed were blood damage (measured by changes in plasma free hemoglobin, hematocrit, and platelet counts and red cell and platelet transfusions required), particulate matter generated (Aa gradient and debris flushed from oxygenator filter), postoperative course, and length of hospital stay. There is very significant damage to blood elements that occurs with cardiopulmonary bypass, and this damage does not seem to have been reduced in our institution by the development and use of the silicone membrane oxygenator and centrifugal pump. This failure to show an improvement thus does not warrant the increase in cost of the newer perfusion system in our institution.

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