Original Article

Hematological Assessment of Patients Undergoing Plasmapheresis During Cardiac Surgery

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Keywords: autologous blood, blood conservation, plasmapheresis

ABSTRACT

Methods of reducing patient exposure to homologous blood transfusions include the technique of intraoperative plasmapheresis for the production of platelet rich plasma (PRP). The present study was designed to determine the patient benefits of PRP by examining hemostatic changes in coagulation screens and viscoelastic whole blood monitoring (Thrombelastography, [TEG]). One hundred fifteen patients undergoing elective cardiac surgery were prospectively randomized into a blinded study. Sixty-three patients had 20 percent of the circulating plasma volume sequestered prior to heparinization and pheresed into PRP, which was reinfused 10 minutes following heparin reversal with protamine. The control (CTR) group of 52 patients were exposed to no sequestration procedure. Patients were followed to discharge and 112 parameters, including anthropometric, operative, and postoperative factors, were measured.

There were no significant differences between patient groups in preoperative, cardiopulmonary bypass (CPB), or surgical parameters. Average PRP volume was 660±100 ml with a total platelet yield of 1.1 billion platelets per patient. TEG indices were determined at four distinct times during the surgical procedure. The CTR group had significantly higher pre-CPB TEG indices of 2.3±1.2 and 2.1±1.2 (mean±SD), vs. 1.8±1.5 and 1.4±1.7 in the PRP group ($p<.04$). Following heparin reversal, pre-PRP reinfusion TEG values were similar between groups, although both groups had significantly decreased indices when compared to pre-CPB values. Thirty minutes post-PRP infusion the treatment group had significantly improved TEG recovery when compared to the CTR group, 1.0±1.2 vs. 0.3±1.7 ($p<.05$). Fibrinolysis increased significantly in both groups post-CPB, but following PRP reinfusion, the treatment group returned to baseline values, while the CTR patients remained significantly elevated. There were no differences between groups in postoperative routine coagulation screens, nor significant changes in postoperative chest tube drainage. Packed red blood cell, fresh frozen plasma, and platelet transfusions in the CTR group were approximately twice as great as the PRP group (p=ns). CTR total homologous blood exposure rate was 3.06±6.6 units compared to 1.41±3.2 units in the PRP group ($p<.0007$). Discharge hematocrit was 31.5±5.2 percent in the PRP group, and 29.8±4.8 in the CTR group ($p<.07$). Total length of stay in the hospital was 10.8±4.2 days in the PRP patients, compared to 13.4±4.8 days in non-treated patients ($p<.03$).

This study has shown demonstrable hematological benefits of preoperative plasmapheresis during cardiac surgery, with the major reduction of bleeding occurring immediately following the administration of PRP.

INTRODUCTION

During cardiac surgery, blood conservation techniques are utilized in an effort to limit patient exposure to homologous blood products. (1-3) Plasmapheresis is an aggressive autologous blood sequestering process that can produce platelet rich plasma (PRP) for perioperative administration. PRP has been shown to produce a high quality blood product rich in procoagulants. (4,5) The benefits of PRP during cardiac surgery have included reducing patient risk of homologous blood exposure by preserving both platelet function and circulating blood proteins involved in hemostasis. (6,7) Removing the PRP fraction prior to CPB limits leukocyte and platelet activation by sequestering the blood from exposure to mechanical and physical processes associated with air-to-blood interfaces, and synthetic surfaces of the extracorporeal circuit. (8,9) Reduction in platelet counts occurs rapidly with the onset of CPB as a result of hemodilution and endogenous sequestration. (10) Removing PRP prior to CPB and infusing the product immediately after heparin neutralization increases platelet availability in the immediate post-CPB period.

The administration of autologous PRP has been shown to reduce postoperative chest tube drainage and lower transfusion of blood products. (7,8,11,12) However, methods of procuring the PRP require additional software representing increased hospital and patient costs. A recent study challenged the benefits of PRP compared to whole blood sequestration because of centrifugal packing of platelets, with the optimal, more potent platelets trapped in the red cell layer. (13) A frequent complaint also stems from the time requirements necessary to generate PRP, combined with additional personnel requirements. Furthermore, the process of plasmapheresis is not risk free. Complications associated with PRP may be classified into technical, vascular, and hemodynamic groupings (14,15), in addition to concomitant problems associated with fluid replacement and product storage.

The present study was designed to address two interrelated questions: 1) The efficacy of plasmapheresis as a means of reducing patient dependence on blood banking products, and 2) To assess hematological changes associated with PRP removal and post-CPB infusion.

MATERIALS AND METHODS

All cardiac patients were evaluated for inclusion into the study and were excluded according to the following criteria: ejection fractions less than 35%, critical aortic stenosis with valve areas less then 0.7 cm^2, left ventricular end diastolic pressure greater than 20 mmHg, preoperative platelet counts less than 150,000, preoperative hematocrit levels less than 35%, weight less than 50 kg, or left main artery lesions greater than 50% occlusion. Patients were prospectively randomized into either the plasmapheresis group (PRP) or a control group (CTR). The study was blinded in so far as postoperative management and care.

All patients received standard anesthetic management and were premedicated with narcotics and amnestic agents as appropriate. Intraoperative monitoring consisted of a three-lead electrocardiogram, pulse oximeter, capnograph and arterial and pulmonary artery pressure monitoring. Anesthesia was induced with sufentanyl citrate and pancuronium bromide and supplemented when needed with inhalation anesthetics and narcotics. Patients randomized to the PRP group were fitted with additional 8.5 French indwelling catheters in either the internal or external jugular veins. The patients' circulating plasma volume was calculated from the hematocrit just prior to plasmapheresis, and 20% of that amount was removed by a dedicated plasma collection system.[a]

The technique for plasmapheresis has previously been described in detail. (16) Volume replacement was carried out both prior and during plasmapheresis with colloids (hetastarch and 5% albumin), and crystalloid (lactated Ringers) solutions, at a rate 1:1 of total blood volume removed. A post-PRP hematocrit was determined and a resultant CPB hematocrit calculated. If the resultant hematocrit was anticipated to drop below 20% then the red blood cell (RBC) volume was returned. Otherwise, the RBC was reinfused post-CPB. The PRP product was sampled for platelet count and fibrinogen levels, and stored at 37°C with gentle periodic agitation. Infusion of PRP commenced after heparin reversal with protamine as confirmed by return to preoperative activated clotting time (ACT) values, and was completed within 6 hours of sequestration.

Moderate hypothermic (28°C) cardiopulmonary bypass was conducted with a roller pump arterial drive system[b], membrane oxygenator[c], and closed venous system in all patients. Autotransfusion with a cell washing system[d] was employed and

a Plasma Saver, Haemonetics, Inc. Braintree, MA 02184
b Shiley Stockert, Sorin, Inc. Irvine, CA 92714
c Sarns Membrane Oxygenator, Sarns 3M Health Care, Ann Arbor, MI 48103
d Cell Saver 4, Haemonetics, Inc. Braintree, MA 02184

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ultrafiltration was included when deemed necessary by the perfusionist. Non-pulastile perfusion was carried out at cardiac indexes between 1.8 and 2.8 L/min/m^2 maintaining mean arterial pressures between 50 and 80 mmHg. Blood cardioplegia (4:1 blood to crystalloid) was utilized with an initial potassium concentration of 24-28 mEq/L, with consecutive doses at 10-14 mEq/L. ACT was maintained at or above 480 seconds and routinely measured (approximately every 30 minutes) throughout CPB.

One hundred and twelve parameters were measured for each patient. These included anthropometric, surgical and CPB factors. Patients were monitored in the intensive care unit for the first two postoperative days, and the following indices for hemorrhage recorded: chest tube drainage, intake and output volumes, and transfusion requirements.

Patients' perioperative minimum hemoglobin levels were maintained according to the following protocol: Patient age less then 70 years, 7 gm/dl, and greater then 70, 8 gm/dl. Patients were transfused with coagulation factors in the form of fresh frozen plasma (FFP), platelets (PLT), and cryoprecipitate (CRYO) only when bleeding was uncontrollable, according to the following protocol: FFP when prothrombin times (PT) were greater than 16 seconds, PLT when platelet counts were less then 100,000/ul, and CRYO when fibrinogen levels were less than 100 mg/dl. Red blood cells (RBC) were transfused postoperatively for a hematocrit less than 21%, except in the case of incomplete revascularization where RBC were given for a hematocrit less than 25%.

Coagulation profiles were performed on admission and included PT, PTT, template bleeding time (BT), PLT count, and fibrinogen levels. Once in the operating room, the patient had concurrent ACT[e] and thrombelastograph profiles (TEG)[f] measured at the following times: Pre-skin incision, post-skin incision, 10 minutes post-protamine, and 30 minutes post-protamine (PRP reinfusion occurred between these two time periods in the treatment group). The overall coagulative status of the patient was assessed via the use of combined discriminant analysis of the measured parameters of the TEG, according to the recommendations of the manufacturer.[f] The following equation for TEG index was calculated incorporating the nominal measurable parameters from native whole blood TEG profiles:

TEG Index = -0.0227 (R) + 0.0092 (K) + 0.1655 (MA) - 0.0241 (alpha angle) - 5.022

R = Reaction time, initial time for clot formation

K = Kinetic time, time from initial clot formation to development of clot of specific amplitude

MA = Maximum amplitude, the maximum strength of a clot

Alpha angle = the rate of clot development

A@60 = Amplitude measured 60 minutes after MA

Normal range of TEG indices were developed from linear modeling of normal patient TEG profiles as established by the manufacturer[f] and range from -2.0 to 2.0, representing a mean value ± 2 standard deviations from the mean. Values of -2 and lower represent hypocoaguable states, while greater than two are hypercoaguable.

The degree of post-CPB fibrinolysis was determined by creating a fibrinolytic index according to the following formula:

Fibrinolytic Index = {1- (A@60 ÷ MA)} X 100

Normal fibrinolytic indices have been reported as being 15% or less at A@60 minutes.[f] Postoperative coagulation screens were performed immediately upon entry into the intensive care unit, routinely occurring within two hours of PRP administration.

Parametric data was analyzed using one way and two way analysis of variance. When significant f ratios were reached, additional multiple comparison tests were performed and included either Tukey's least significance difference or Duncan's

Table 1
Patient demographic data

Parameter	PRP Group	Control Group	p Value
Number	63	52	
Age (years)	60.4±10.0	61.8±10.8	NS
Sex (male/female)	54/9	45/7	NS
BSA (m2)	2.04±0.2	1.95±0.2	NS
Weight (kg)	87.1±13.7	82.0±18.7	NS
Height (cm)	174.8±12.9	174.1±10.0	NS
Preop Hct (%)	41.9±3.9	39.7±5.0	NS
Preop Plt. Meds. (%)	33	31	NS

All data are mean ± SD

Table 2
Plasmapheresis product

Parameter	
Platelet Count	167,500 ±63,000
Fibrinogen Count	260.1±91.3 mg/dl
Total Volume	659 ±100 ml
Platelet Yield	1.1 x 10^{11} platelets

All data are mean ± SD

e. Hemochron 800, International Technidyne Corp., Edison, NJ 08220

f. Thrombelastograph Model 2000 D, Haemoscope Corp., Morton Grove, IL 60053

Table 3
Operative data

Parameter	PRP Group	Control Group	p Value
Operation			
CABG (graft #)	2.6	2.9	NS
IMA usage (%)	80	73	NS
Valve Replacement (#)	3	5	NS
Combined CABG/Valve (#)	3	2	NS
CPB Time (min)	121.2±41.2	114.6±38.1	NS
Cross Clamp Time (min)	81.0±30.4	78.6±29.7	NS
High CPB ACT (sec)	621.0±92.7	627.2±80.3	NS
Low CPB ACT (sec)	441.7±67.1	425.5±44.5	NS
Low CPB Hct (%)	19.7±2.3	20.8±3.2	NS
Low CPB COP (mmHg)	10.8±1.5	11.0±1.5	NS
Prime Albumin (gms)	13.3±15.3	2.2±7.7	.0001
Anesthesia Vol. Replacement			
Colloid (ml)	1280±645.8	1084±559	NS
Crystalloid (ml)	5224±2290	4195±1148	.004

All data are mean ± SD

Table 4
Perioperative coagulation parameters

Parameter	Preop	Postop	p Value
PRP Group			
Prothrombin Time (sec)	12.0±0.8	14.9±1.0	.001
A. Part. Thrombplast. Time (sec)	28.5±6.6	36.9±10.9	.008
Thrombin Time (sec)	———	35.8±26.1	
Bleeding Time (sec)	5.4±2.1	———	
Fibrinogen (mg/dl)	412.4±135.8	164.4±60.1	.0001
Platelets (thousands)	246.6±62.6	112.6±37.8	.0001
Calcium (mg/dl)	———	7.0±0.7	
Control Group			
Prothrombin Time (sec)	12.0±0.7	15.5±1.6	.001
A. Part. Thrombplast. Time (secs)	26.9±4.0	35.3±7.8	.005
Thrombin Time (sec)	———	35.3±35.6	
Bleeding Time (secs)	5.5±3.0	———	
Fibrinogen (mg/dl)	414.2±118.1	159.5±67.4	.0001
Platelets (thousands)	249.2±68.4	110.4±34.2	.0001
Calcium (mg/dl)	———	7.0±.0.6	

All data are mean ± SD

test. Nonparametric data were analyzed by the Wilcoxon rank sign test. Statistical significance was accepted at the p<.05 level. All data represented as mean ± standard deviation of the mean (SDEV).

Results

One hundred fifteen patients were included in the study with 63 PRP patients and 52 controls. Patient preoperative parameters are shown in Table 1. There were no significant differences among groups in preoperative status. Patient use of antiplatelet medications was evenly distributed with 33% of PRP and 31% of CTR patients on this preoperative therapy (p=ns). There were no significant differences between groups in regards to preoperative medication schedules with the major drug groups being antianginals, antihypertensives and calcium channel blockers. Total PRP volume and platelet yield are shown in Table 2.

To determine if the removal of a substantial portion of the patient's plasma volume would alter patient response to heparin, ACTs were measured and are reported in Table 3. There were no intergroup differences seen in this parameter. The PRP group received significantly more albumin on CPB to maintain predetermined colloid oncotic pressure, set according to protocol, as 11 mmHg or greater. Average PRP patient albumin administration was 13.1±15.3 grams while CTR patients received 2.3±7.7 grams (p<.0001). There were no differences between groups in the quantity of colloid administration, but the PRP group received significantly more crystalloid solution, 5224±2290 vs. 4195±1148 ml (p<.004).

Table 4 lists the coagulation screen data for both groups. Post-CPB PT and PTT were significantly elevated from baseline values but did not vary between groups. Fibrinogen concentration was reduced equally in each group by 61%, while platelet counts dropped by 54% in the PRP group, and 56% in CTR.

Chest tube drainage was similar between groups, and intake and output volumes for the first two postoperative days were not significantly different between groups (Table 5). Although red blood cell and fresh frozen plasma transfusions were reduced in the PRP group by 36% and 45%, respectively, statistical significance was not reached. Patients in the treatment group received an average of 1.58±4.5 platelet transfusions compared to 3.84±8.1 in the CTR group (p<.06). The CTR patients required significantly more cryoprecipitate than the PRP group, 0.80±3.3 vs. 3.14±7.4 units, (p<.03). Total homologous blood exposure rate was 1.41±3.2 units in the PRP group vs. 3.06± units in the CTR group (p<.0007).

TEG results are summarized in Table 6. Pre-skin incision

Table 5
Postoperative data

Parameter	PRP Group	Control Group	p Value
Postop CT Drain Day 1 (ml)	1166±513	1227±619	NS
Postop CT Drain Day 2 (ml)	334±250	304±409	NS
Postop Day 1 Intake (ml)	3521±1218	3652±1564	NS
Postop Day 1 Output (ml)	4767±1618	4755±1317	NS
Postop Day 2 Intake (ml)	1773±645	1663±583	NS
Postop Day 2 Output (ml)	2319±881	2344±1053	NS
PRBC Transfusions (U)	2.5±2.5	3.9±6.0	.10
FFP Transfusions (U)	0.7±.1.6	1.3±4.4	NS
Platelet Trans. (packs)	1.6±4.5	3.8±8.1	.06
Cryoprec. Trans. (packs)	0.8±3.3	3.3±7.4	.03
Total Homologous Exp. (U)	1.4±3.2	3.1±6.6	.0007
Discharge Hematocrit (%)	31.5±5.2	29.8±4.8	.07
Total Hospital Stay (days)	10.8±4.2	13.4±7.8	.02

All data are mean ± SD

Table 6
Thrombelastograph data

	PRP Group		Control Group	
Parameter	Pre-Skin Inc.	Post Skin Inc.	Pre-Skin Inc.	Post Skin Inc.
R Time (min)	16.5±6.5	16.4±12.0	16.5±5.0	14.9±6.5
K Time (min)	7.5±4.1	6.8±11.9	7.8±5.1	6.7±4.3
MA (mm)	58.7±7.9	56.3±10.0	61.5±7.2	59.8±7.3
A @ 60 mins (mm)	52.8±8.4	50.3±9.6	55.7±7.2	54.1±7.6
Alpha Angle (degrees)	40.2±13.0	41.3±17.5	40.6±13.9	42.1±12.4
TEG Index	1.77±1.5	1.38±1.7	2.27±1.2	2.1±1.2
FIB Index	0.10±0.06	0.11±0.05	0.10±0.04	0.10±0.04
	PRP Group		Control Group	
Parameter	10′ Post Prot	30′ Post Prot.	10′ Post Prot	30′ Post Prot.
R Time (min)	13.2±6.7	12.9±4.7	16.7±7.9	17.4±9.0
K Time (min)	8.3±15.6	4.9±2.7	10.0±14.5	8.8±7.9
MA (mm)	46.0±13.7	52.6±7.7	50.8±11.9	49.8±10.0
A @ 60 mins (mm)	36.8±16.3	47.7±8.1	42.4±15.9	42.7±14.8
Alpha Angle (degrees)	44.3±16.0	48.4±12.9	40.7±16.6	37.6±15.8
TEG Index	-0.03±2.2	1.0±1.3	0.2±2.2	0.3±1.8
FIB Index	0.23±0.3	0.09±0.1	0.24±0.3	0.17±0.2

All data are mean ± SD

TEG indices in both groups tended to be more hypercoagulable, with the CTR group significantly higher than the PRP group. This relationship continued in the post-skin incision TEG from both groups (PRP was collected from the treatment patients in between these sampling points). Ten minutes following protamine administration both groups demonstrated highly significant reductions in TEG indices when compared to pre-CPB values. In the CTR group no TEG change was observed between 10 and 30 minutes post-protamine. Following PRP reinfusion in the treatment group, the TEG index rose significantly from the 10 minute post-protamine level, and was not significantly decreased when compared to the post-skin value.

The TEG parameters MA and alpha angle are thought to correlate with platelet and fibrin interaction, and affect the rate of clot formation and the overall strength of the clot. Both groups demonstrated significant reductions in these parameters following CPB. In the CTR patients neither factor increased during the post-protamine TEG measurements. MA increased significantly following PRP infusion, and alpha angle was significantly higher then pre-CPB values in the treatment group.

Clot dissolution is measured by the A@60 and is used as an indicator of fibrinolysis. The PRP group experienced the greatest drop in A@60 following CPB. However, following PRP infusion there was a significant amelioration of the lytic activity with the A@60 returning to near base line values. These effects were not seen in the CTR group. The calculated fibrinolytic index was almost identical between groups at the 10 minute post-protamine sample point. Following infusion of PRP the fibrinolytic index declined significantly in the treatment group to 0.09±0.1 ($p<.001$), but remained elevated in CTR.

DISCUSSION

Preoperative autologous blood donation was advocated as a panacea to patients involved in elective surgery but has not been widely accepted in treating cardiac patients. (17) Blood conservation methods are routinely practiced in various degrees in most hospitals performing major vascular and cardiovascular surgery.

Figure 1
Blood Component Utilization
CTR = Control. PRP = Platelet rich plasma

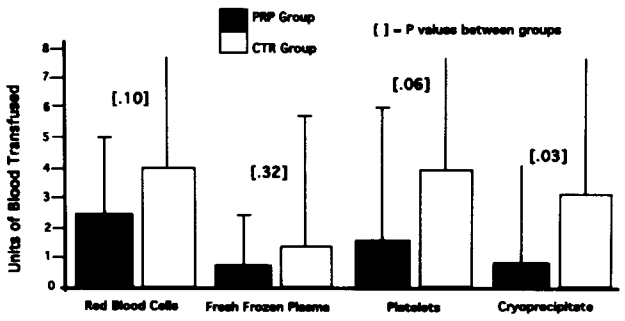


Figure 2
Total Homologous Blood Exposure
CTR = Control. PRP = Platelet rich plasma

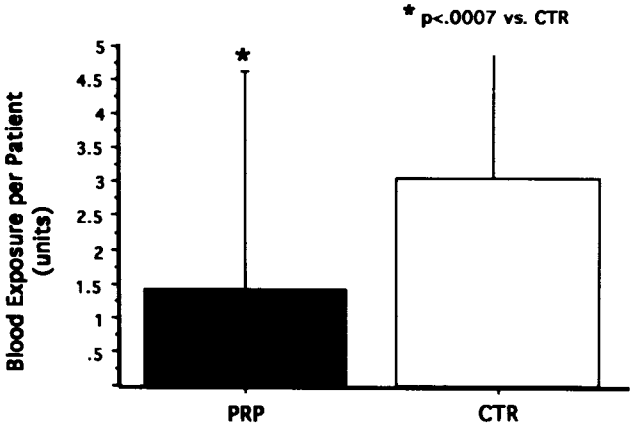


Figure 3
Thrombelastograph Index
CTR = Control. PRP = Platelet rich plasma. TEG = Thrombelastograph

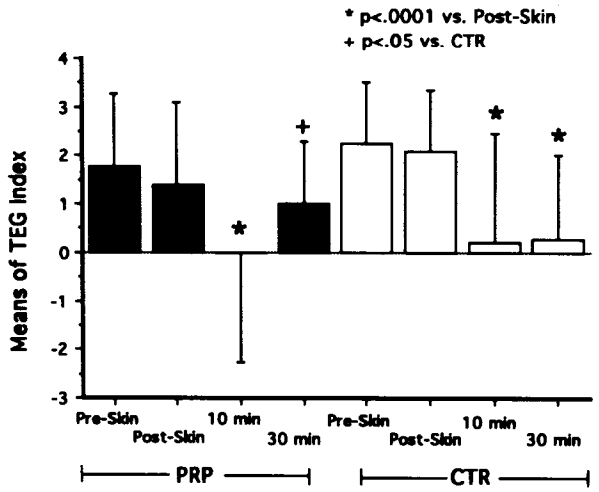
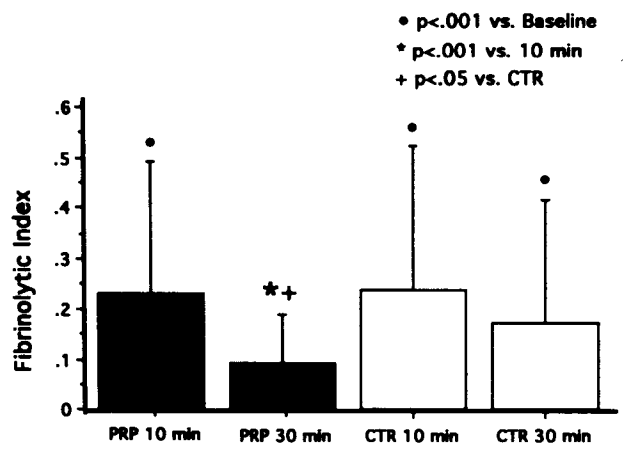


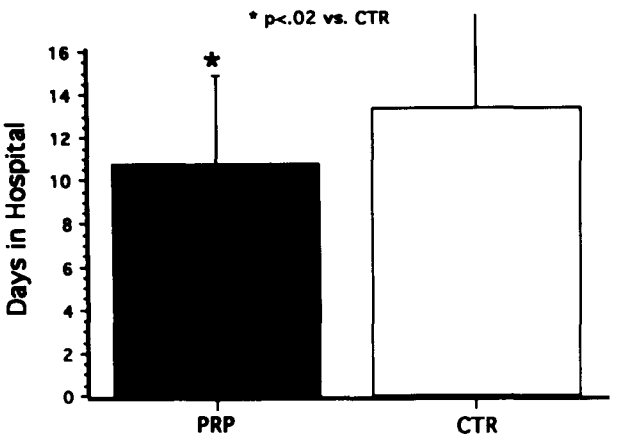
Figure 4
Post-CPB Fibrinolytic Index
CTR = Control. PRP = Platelet rich plasma



The combined use of multiple techniques for blood conservation has been exploited in an effort to reduce patient exposure to homologous blood products. (1-3) The utilization of intraoperative autotransfusion devices and postoperative collection of chest tube drainage have had a profound effect on salvaging and reinfusion of shed blood. (18-20) Methods of hemoconcentration include ultrafiltration and have been used successfully to reduce hypervolemia associated with cardiac surgery. (21) Autotransfusion with cell washing devices has proven efficacious in reducing blood loss during surgical procedures. (18) Plasmapheresis has been recently introduced as a conservation application for cardiovascular surgery, but is a well accepted blood banking method. (4-6,11) The combination of a changing population of cardiac patients and more difficult operative and reoperative procedures, require that techniques and practices which could potentially reduce operative dependency on non-autologous sources for blood products be examined.

The benefits of PRP are derived from the apheresis of autologous blood products, which, due to the separation into specific components, can be administered to treat deficiencies

Figure 5
Total Hospital Length of Stay
CTR = Control. PRP = Platelet rich plasma



related to the patient's hemostatic needs. The effects of PRP infusion have been shown to reduce patient exposure to homologous blood products (4,6,11) and supplant the logistical steps involved in autologous predonation through blood banks, increase the patient pool not otherwise suitable for predonation, preserve platelets and protein factions from exposure to the extracorporeal circuit during cardiopulmonary bypass, reduce activation of polymorphonuclear neutrophils and avoid exposure to artificial surfaces (6,9) resulting in the generation of toxins implicated in post pump pulmonary dysfunction.

The results of plasmapheresis in thoracic surgery are thus far very encouraging. When the use of autotransfusion alone has been compared to plasmapheresis, the patients treated with PRP reinfusion have lower positive fluid balances than patients who had cell washing utilized as a method of hemoconcentration. (6) Several clinical trials have shown a decreased usage of homologous blood products, including plasma and platelets, during the hospitalization of patients treated with PRP. (6,7,12) Following the reinfusion of autologous PRP, patients have responded with higher operative platelet counts, (6) decreased postoperative bleeding, (4) and higher fibrinogen and antithrombin III concentrations. (22) Giordano has reported that the concomitant use of autotransfusion and plasmapheresis has reduced transfusions from 13.67 to 6.32 homologous blood exposures per patient. (11)

The effects of platelet altering drugs on the quality of the plasmapheresis product is germane since a substantial number of cardiac patients are exposed to these medications prior to surgery. In the present study a third of all patients had received aspirin up to the day before surgery. Giordano studied patients who received the anticoagulants coumadin, heparin, and/or nonsteroidal antiinflammatory agents up to the day prior to surgery. (12) He was unable to detect differences in postoperative bleeding between medicated patients and patients not on platelet inhibitors.

The results of the present study are in general agreement with those of others. However, we were unable to demonstrate a reduction in postoperative chest tube drainage between control and treatment patients. Although PRP patients had individual blood component utilization rates approximately half that required by control patients, statistical significance was achieved only modestly. The PRP patients, however, received significantly less total blood product exposure than controls, despite having similar chest tube and output volumes. This led us to question during what time period the majority of bleeding was occurring, and whether this corresponded with replacement therapy. Our results indicate that the major reduction in bleeding observed in the plasmapheresis group must be occurring while the patient is still in the operating room. Therefore, the benefits of PRP infusion must be manifested in the period immediately following the reversal of heparin, when the patient is most susceptible to continued hemorrhage. (10) It would have been fortuitous to measure sponge weights, and autotransfusion and waste sucker volumes during this time to confirm this hypothesis. Similarly, noting of the time of component transfusion would aid in determining when the majority of hemorrhage occurred.

Mohr and associates have recently stated that whole blood separation into PRP failed to match the benefits of sequestered packed cell fractions, because of platelet retention in the red cell layers. (13) We have also recently examined differential centrifugation as a means of procuring a superior PRP product, (16) and have found an inverse relationship with platelet yield and centrifugal speed. A laboratory investigation by Denfors has found a similar relationship. (23) The benefits of PRP seen in our study may reflect Mohr's findings in that the majority of our PRP patients had the sequestered RBC fraction reinfused following CPB, which may have preserved platelet number and function. Davies has recently reported the collection of superior yields of platelet-leukocyte product with the use of alternating centrifugal speeds and varying rates of collection, with a resultant improved clinical outcome in such treated patients. (24)

Patients treated by plasmapheresis had significantly shorter hospital stays than non-treated patients. Undoubtedly, a substantial number of factors go into the determination of hospital stay for cardiac patients, and it would be difficult, if not impossible, to isolate a single variable responsible for this finding. Bleeding remains a prominent pathological event associated with increased morbidity following cardiac surgery, (10,25) with the primary cause identified as alterations in platelet function and/or number. (10,26) Boldt has shown that plasmapheresis reduces the circulating levels of pulmonary elastase, a proteolytic enzyme released by polymorphonuclear neutrophils, (22) which has been implicated as a cause of post-CPB pulmonary dysfunction. (27) The transfusion of blood products, specifically platelets, alters pulmonary function adversely, influencing postoperative convalescence and recovery. Although pulmonary function analysis was not measured in this study, it is tempting to speculate

that both these effects influenced the differences seen in hospital stay.

There was a significant change in coagulation status when comparing pre and postoperative platelet and fibrinogen levels, and in intrinsic and extrinsic measures of the clotting cascade. These plasmatic tests reflect individual concentrations of isolated factors, but do not take into consideration interactions between the cellular and acellular coagulation components. The thrombelastograph is a viscoelastic measuring device that reflects the interaction between platelets and fibrin in whole blood samples. The increase in TEG parameters seen following PRP infusion were substantially greater than the offset in coagulation status seen by removing a quantity of PRP volume. The preservation of platelet function was well demonstrated by the TEG, despite no differences in platelet count as assessed through routine laboratory methods.

When pre-skin incision TEG data are combined from both groups the calculated TEG index for all patients is on the high end of normal. This hypercoagulable state is seen prior to surgery despite having a large percentage of patients present on antiplatelet medications. Although all preoperative coagulation screens were within normal laboratory values for our hospital, the fibrinogen levels were also on the high end of normal. (This serendipitous finding is interesting and may reflect characteristics of this patient population that have only previously been speculated.) We have previously shown that fibrinogen levels correlate well with the TEG maximum amplitude, alpha angle, and amplitude 60 minutes beyond maximum. (28) Removal of 20% of the circulating plasma volume reduced the TEG index by 22%, while control patients had only an 8% reduction over the same time period. Undoubtedly, this reflects the combined treatment of volume removal and replenishment with colloid and crystalloid solutions.

CPB has been shown to generate factors associated with the production of plasmin leading to excessive fibrinolysis. (29) Excessive stimulation of serine proteases by extracorporeal circuits has been well established, and inhibitors of this class of compounds are being actively pursued by many investigators. (30,31) Since fibrinolytic activity is stimulated by CPB, efforts to prevent or treat this condition would be enhanced by rapidly restoring the balance between thrombin and plasmin generation. The degree of fibrinolysis was monitored by the TEG and reflected in the dissolution of the clot 60 minutes beyond maximum amplitude. The PRP treated patients had significantly improved fibrinolytic indices post-infusion, and the total reduction in clot dissolution was significantly greater than the control group. To our knowledge, the antithrombolytic qualities of PRP have not been previously described. Fibrin degradation products and D-dimers were not routinely measured in our patients, and it would have been interesting to have measured these substances in this study to quantify changes in these widely accepted indicators of fibrinolysis.

In conclusion, the present study confirms the efficacy of plasmapheresis as a blood conservation technique in reducing patient homologous blood exposure. This is evident in spite of similar postoperative chest tube outputs between groups. The benefits of this technique are most likely seen in the immediate post-infusion period and can be related to an overall reduction in fibrinolytic tendency, and procurement of hemostatic stability, despite alterations in routine laboratory coagulation tests.

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