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Preoperative Plasmapheresis in Patients Undergoing Cardiac Surgery Procedures

J. Boldt, M.D., B. von Bormann, M.D., D. Kling, M.D., M. Jacobi, R. Moosdorf, M.D., G. Hempelmann, M.D.

Donor plasmapheresis that is carried out weeks before the operation has proven to be of benefit in elective orthopedic patients with regard to reducing homologous blood consumption and preserving coagulation. In this study acute preoperatively performed plasmapheresis (APP) was investigated in cardiac surgery patients. Forty-five patients scheduled for elective aortocoronary bypass surgery were randomly divided into three groups of 15 patients each: 1) removal of platelet-poor plasma (PPP), 2) removal of platelet-rich plasma (PRP), and 3) no plasmapheresis (control group). Plasma volume removed was 10 ml/kg in all APP patients, and plasma was replaced by the same amount of low-molecular weight hydroxyethylstarch solution (6% HES 200/0.5). Various laboratory data were investigated before, during, and after extracorporeal circulation (ECC). Blood loss in control patients was more pronounced than in the two APP groups; two of the control patients needed packed red cells. APP itself did not affect coagulation variables, free hemoglobin, or polymorphonuclear (PMN) elastase. At the end of the operation, 5 h after ECC, and at the first postoperative day the number of platelets was significantly lower in the control group; PRP patients showed the highest values. Fibrinogen and AT-III levels were less compromised in APP patients than in the control group. Global coagulation parameters did not differ between the groups within the whole investigation period. PMN elastase increased significantly during ECC in all groups with the greatest increase in the control group (722%) and the smallest increase in PRP patients (280%), possibly due to the removal of cellular elements in this group. It is concluded that APP seems to be an additional approach to reduce blood consumption in cardiac surgery and to improve coagulation after ECC. Its positive influence on concentration of damaging substances (elastase) might be one of the important aspects of this procedure. (Key words: Blood, coagulation: PMN elastase. Surgery: cardiac. Transfusion: plasmapheresis.)

BLOOD CONSERVATION TECHNIQUES are gaining increasing importance due to the increasing risks from homologous blood transfusions.[1–6] Various techniques have been initiated to reduce the need for donor blood, such as controlled hypotension, acute normovolemic hemodilution, preoperative withdrawal, and storage of autologous blood.[7–9] The collection of autologous plasma has to be performed weeks or even months before the day of the operation, which is not always possible, particularly in patients undergoing cardiac surgery. Preoperative donor plasmapheresis not requiring additional time in the hospital is a newly developed technique, which has been proven to be effective in reducing use of homologous blood in patients undergoing elective orthopedic surgery.[10] The technique of acute plasmapheresis (APP) has also been used for minimizing use of homologous blood and blood products and for improving coagulation in cardiac surgery.[11,12]

The aim of this study was to investigate whether acute, preoperatively performed plasmapheresis is of benefit with regard to blood loss, the volume of blood products transfused, and various laboratory parameters in patients undergoing cardiac surgery and extracorporeal circulation.

Methods

PATIENTS

The study was performed in 45 patients scheduled for aortocoronary bypass surgery. Exclusion criteria were a preoperatively impaired myocardial function (ejection fraction [EF] < 50%; left ventricular end-diastolic pressure [LVEDP] > 20 mmHg), preoperative coagulation disorders, concomitant valvular disease, and medication with aspirin or other cyclooxygenase inhibitors. All patients gave their informed consent to participate in the investigation, and the study was approved by the local ethics committee.

GROUPING

The patients were randomly subdivided into three groups: 1) APP was performed harvesting autologous platelet-poor plasma (PPP); the volume of plasma removed was 10 ml/kg (n = 15); 2) APP was carried out harvesting platelet-rich plasma (PRP); the volume of plasma removed was 10 ml/kg (n = 15); and 3) no APP was performed (control group) (n = 15).

Plasmapheresis was started after induction of anesthesia, which consisted of weight-related doses of fentanyl, midazolam, and pancuronium bromide and was completed before the onset of surgery. In all APP patients the volume of plasma removed was replaced by an equal volume of low-molecular weight hydroxyethylstarch solution (6% HES 200/0.5).

PLASMAPHERESIS

APP was performed by means of the Haemonetics Plasma Collecting System (PCS) V 50® (Haemonetics,

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Address reprint requests to Dr. Boldt: Department of Anesthesiology and Intensive Care Medicine, Klinikstrasse 29, Justus-Liebig-University Giessen, D-6300 Giessen, Federal Republic of Germany.

Munich, FRG), which is based on a discontinuous flow centrifugation technique. This method involves drawing of blood into a centrifuge to separate it into plasma, white blood cells, platelets, and red blood cells. Using a single-needle technique blood was collected from the patient *via* a 14-G cannula from the external jugular vein, and anticoagulant solution (acid citrate dextrose [ACD-A]) was immediately added to the blood in a 12:1 ratio. Withdrawal flow was 60 ml/min and blood was centrifuged at either 5,650 U/min (PPP group) or 4,200 U/min (PRP group). After plasma separation was completed, the red cells were returned through the same needle. The process (withdraw and return) was continued until 10 ml/kg of plasma had been removed. The time required for this procedure ranged from 32 to 48 min.

Extracorporeal Circulation

All patients received 300 IU/kg heparin 5 min prior to the start of extracorporeal circulation (ECC), 1.5 h after start of ECC half of the initial dose was repeated. ECC was carried out with a nonpulsatile pump using membrane oxygenators (Sorin 41, Sorin, Turino, Italy). The circuit was primed with 1,000 ml 5% dextrose solution, 1,000 ml Ringer's solution, and 250 ml of albumin 5% and electrolytes (20 ml potassium [20 meq/l] 50 ml sodium 10%); a flow of $2.4\ l \cdot min^{-1} \cdot m^{-2}$ was maintained during moderate hypothermia (esophageal temperature 33.2 ± 1.0° C); 1,000 ml of Bretschneider's cardioplegic solution (based on low sodium [15 mM] and absence of calcium, contains mannitol [20 mM] and is buffered with histidine [180 mM]) was given initially followed by 200 ml every 20 min. A two-stage cannula was used for venous return into the circuit, and the operation was performed in partial bypass (monoatrial cannulation technique). This technique implies that all cardioplegic solution is returned to the extracorporeal circuit. Within 20 min after start of ECC, blood was concentrated using a cell saving system (cell saver IV®, Haemonetics, Munich, FRG; two cycles standardized). When necessary, Ringer's solution was added to the heart lung machine to maintain the filling volume of the circuit. When hemoglobin concentration was less than 7 g/dl, packed red cells were given. After termination of ECC, the residual blood of the circuit was concentrated by the use of the cell saver system, and washed erythrocytes and the preoperatively removed autologous plasma were retransfused before the end of the operation. To antagonize heparin effects, protamine sulfate was given in the same dosage as the initially administered heparin.

Laboratory Investigations and Data Points

The following parameters were measured from arterial blood samples: hemoglobin (Hb), hematocrit (Hct), number of red and white blood cells, number of platelets, free hemoglobin, haptoglobin (from removed plasma only), blood gas variables, colloid osmotic pressure (COP; Sartorius membrane, 20,000 dalton), total protein, albumin, coagulation parameters (thrombin time [TT], prothrombin time [PT], partial thromboplastin time [PTT]), activated clotting time (ACT), thromboelastogram (TEG), heparin, fibrinogen, AT-III, electrolytes (Na^+, K^+), and polymorphonuclear (PMN) elastase. Blood samples were taken after the induction of anesthesia (before the start of APP), after the termination of APP, before the start of ECC, 30 min after the start of ECC (after hemoconcentration with the cell saver), immediately after the termination of ECC (before the administration of washed erythrocytes, protamine, and autologous plasma), at the end of the operation, 5 h after the termination of ECC, and on the morning of the first postoperative day. Postoperatively, Ringer's solution was infused to maintain stable hemodynamic conditions, and packed red cells were administered when Hb concentration was less than 9 g/dl. Blood loss from the chest tube drainages, use of homologous blood or blood products, and duration until extubation were documented as well. Shed mediastinal blood was not collected and retransfused during the postoperative period.

Statistics

Mean values (±SD) were calculated for each parameter. One- and two-factor analysis of variance (including multitesting analysis of variance) followed by the Scheffé test were used for statistical interpretation; P values < 0.05 were considered significant.

Results

The patients in the three groups were comparable with regard to demographic data and preoperative myocardial function; no significant differences could be seen in the duration of ECC and ischemia, and in hemoconcentration procedure during ECC; fluid balance after ECC was also without significant differences between the groups, although the control group tended to higher positive balance ($P = 0.08$) (table 1). Changes of laboratory variables from baseline values to values at the end of the operation are illustrated in figure 1.

Blood loss through the first postoperative day was significantly greatest in the control group (696 ± 130 ml), and two of these patients required transfusion of homologous packed red cells (two units each), whereas none of the APP patients received donor blood or blood derivatives. The amount of volume infused until the first postoperative day was without difference between the groups. Pulmonary gas exchange and time to extubation and maximal body temperature did not differ between the

TABLE 1. Demographic Data, Data from Preoperative Catheterization, ECC, and Postoperative Intensive Care

	PPP	PRP	Control
Age (yr)	62.8 ± 5.1	59.0 ± 3.3	63.7 ± 4.4
Height (cm)	171.2 ± 4.8	168 ± 6.6	175 ± 5.5
Weight (kg)	77.0 ± 5.9	78.7 ± 5.9	72.0 ± 6.1
LVEF (%)	62.3 ± 5.5	62.5 ± 3.6	69.5 ± 4.4
LVEDP (mmHg)	16.4 ± 3.3	14.6 ± 4.4	13.4 ± 6.6
ECC (min)	79.5 ± 12	78.6 ± 4.5	83.5 ± 17.0
Ischemia (min)	46.6 ± 4.8	42.9 ± 4.4	53.5 ± 16.4
Cardioplegia (ml)	1,450 ± 140	1,500 ± 180	1,340 ± 300
Discarded volume at ECC (ml)	845 ± 120	920 ± 140	930 ± 120
Fluid balance after ECC (ml)	812 ± 244	800 ± 210	918 ± 200
Extubation (min)	795 ± 213	790 ± 230	788 ± 202
Maximum temperature (° C)			
Day of operation	37.7 ± 0.8	37.2 ± 0.4	38.2 ± 0.4
First postoperative day	37.5 ± 1.0	37.4 ± 0.4	38.1 ± 0.6
Blood loss (ml)			
Day of operation	298 ± 130	348 ± 170	498 ± 100
First postoperative day	543 ± 230*	500 ± 210*	696 ± 130
Donor blood (patients/units)	0/0	0/0	2/2

Values are mean ± SD.

* $P < 0.05$, *versus* control group.

groups (table 1). The two types of autologous plasma produced by APP were significantly different only with regard to the number of platelets (table 2); *p*H was low in both types of plasma due to the anticoagulant solution added to the plasma. Plasmapheresis reduced albumin concentration significantly (PPP, −22%; PRP, −28%), whereas in any of the other measured variables APP itself caused no significant change or a change toward abnormal values (tables 3–5).

At the end of the operation, 5 h after ECC, and on the first postoperative day the number of platelets was significantly greater in the PRP patients than in the other two groups (table 4). After retransfusion of autologous plasma, concentrations of AT-III and fibrinogen were always significantly greater in both APP groups than in the control patients. Global coagulation parameters (TT, PT, PTT, ACT, and TEG) were not significantly different between the groups (table 4). Heparin concentration and Na^+, K^+, Hb, Hct, and red blood cells were comparable for all three groups within the whole investigation period. PMN elastase was not changed by the APP procedure but increased significantly in all three groups during ECC (table 3). This increase was most pronounced in the control group at the end of the operation (722%) and was lowest in PRP patients (maximum, 280%). In the control group elastase remained elevated until the first postoperative day (586%). In PPP patients elastase increased (maximum, 480%) but returned to lower values (380%) at the end of the investigation period. None of the investigated patients suffered from sequelae attributable to the study.

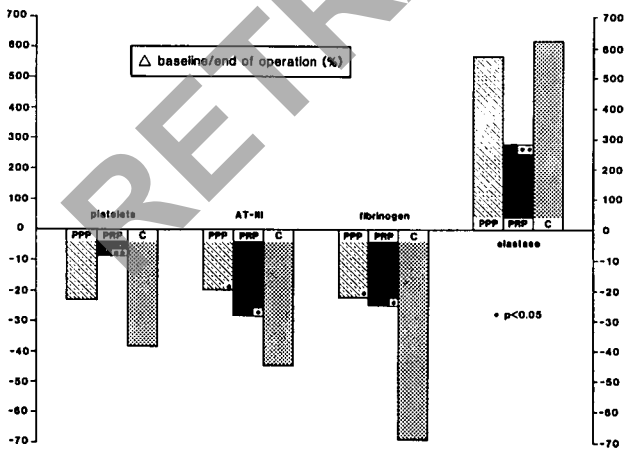

FIG. 1. Changes (Δ%) in laboratory variables from the end of the operation to baseline values. *$P < 0.05$, *versus* control. **$P < 0.05$, *versus* PPP and control.

Discussion

According to Estafanous,[13] every year blood transfusion is responsible for approximately 250,000 cases of post-

TABLE 2. Differences in the 2 Kinds of Autologous Plasma Produced by Acute Plasmapheresis

	PPP	PRP
Free Hb (mg/dl)	12.1 ± 4.4	18.3 ± 5.0
Haptoglobin (mg/dl)	1.82 ± 0.13	1.83 ± 0.11
Platelets (10^3/ml)	30 ± 4.2	301 ± 44*
COP (mmHg)	20.0 ± 2.2	20.2 ± 2.0
Na^+ (mmol/l)	140 ± 3.0	139 ± 2.5
K^+ (mmol/l)	4.55 ± 0.11	4.22 ± 0.44
*p*H	7.023 ± 0.022	7.011 ± 0.020
Volume (ml)	770 ± 50	800 ± 40
Duration of the procedure (min)	45.3 ± 4.0	38.5 ± 47.7

Values are mean ± SD.
* $P < 0.05$.

TABLE 3. Changes in Laboratory Values in the 3 Groups

	Group	Before Plasmapheresis	After Plasmapheresis	30 min ECC	After ECC	End of Operation	5 h after ECC	First Postoperative Day
Hb (g/dl)	PPP	13.1 ± 1.1	12.7 ± 1.0	8.5 ± 1.0	9.3 ± 0.9	11.1 ± 1.1	12.6 ± 1.3	12.1 ± 1.3
	PRP	12.9 ± 1.3	12.2 ± 0.9	8.1 ± 0.3	8.4 ± 0.9	10.9 ± 1.1	12.6 ± 1.1	12.5 ± 1.1
	Control	12.9 ± 0.5	—	8.4 ± 0.9	9.0 ± 0.7	11.9 ± 1.0	13.0 ± 1.2	12.5 ± 1.0
Hct (%)	PPP	40.3 ± 3.0	41.0 ± 4.0	26.2 ± 3.6	29.2 ± 3.6	33.7 ± 3.8	38.6 ± 4.1	37.5 ± 4.2
	PRP	39.9 ± 4.4	36.1 ± 3.3	23.9 ± 2.3	24.6 ± 2.0	31.5 ± 4.4	37.8 ± 3.3	38.1 ± 3.6
	Control	36.6 ± 2.6	—	26.0 ± 3.3	27.1 ± 2.3	36.0 ± 3.0	40.0 ± 3.6	38.6 ± 2.7
Red blood cells (10^6/ml)	PPP	4.79 ± 0.4	5.07 ± 0.8	3.35 ± 0.3	3.72 ± 0.3	4.08 ± 0.4	4.22 ± 0.5	4.00 ± 0.4
	PRP	4.95 ± 0.5	4.65 ± 0.4	3.13 ± 0.2	3.02 ± 0.2	3.70 ± 0.3	4.12 ± 0.3	3.98 ± 0.3
	Control	4.30 ± 0.3	—	3.07 ± 0.3	3.20 ± 0.2	4.03 ± 0.4	4.33 ± 0.2	4.20 ± 0.2
Platelets (10^3/ml)	PPP	193 ± 37	169 ± 40	146 ± 33	162 ± 34	149 ± 28	152 ± 25	154 ± 23
	PRP	200 ± 33	174 ± 44	153 ± 27	152 ± 29	186 ± 44†	186 ± 33†	195 ± 57†
	Control	211 ± 46	—	150 ± 46	172 ± 56	139 ± 45	151 ± 55	153 ± 55
Free Hb (mg/dl) (<40)	PPP	13.6 ± 4.0	20.3 ± 9.8	35.3 ± 10.4	67.2 ± 12.8	52.5 ± 13.0	32.2 ± 6.7	22.2 ± 6.6
	PRP	15.4 ± 3.0	23.2 ± 10.2	55.1 ± 20.1	68.2 ± 22.0	48.2 ± 17.3	27.1 ± 4.4	29.1 ± 9.3
	Control	14.2 ± 3.1	—	45.5 ± 12.8	66.8 ± 13.0	68.6 ± 13.3	29.3 ± 9.9	28.3 ± 5.7
Elastase (μg/l) (60–130)	PPP	69 ± 30	74 ± 33	401 ± 122	437 ± 233	401 ± 211	289 ± 133*	277 ± 111*
	PRP	88 ± 32	86 ± 22	211 ± 88†	261 ± 108†	262 ± 138†	244 ± 84*	250 ± 115*
	Control	72 ± 66	—	464 ± 97	520 ± 160	497 ± 180	444 ± 176	422 ± 133
White blood cells (10^3/ml)	PPP	6.02 ± 1.0	—	—	—	—	17.8 ± 2.2	19.1 ± 5.3
	PRP	5.88 ± 0.5	—	—	—	—	12.5 ± 3.0	14.1 ± 4.0
	Control	5.22 ± 0.8	—	—	—	—	16.4 ± 4.4	13.9 ± 3.6

Values are mean ± SD.
* $P < 0.05$, *versus* control group.
† $P < 0.05$, *versus* PPP and control groups.

transfusion hepatitis, 12,000 cases of cirrhosis, and several, but unknown in number, cases of AIDS in the United States. Furthermore, an increasing number of cardiac procedures in the last 10 yr has reduced the blood available for transfusion. Thus, several suggestions have been made to reduce the use of donor blood. Techniques, such as preoperative hemodilution, the use of red cell recovery devices (cell saver), nonhemic priming of the heart lung machine, and retransfusion of mediastinal blood, have been established in many institutions. A number of studies have reported the success of aggressive blood conservation methods, which permitted the patients to receive no blood transfusion during their hospital stay.[9] Some of these methods, however, are limited in patients undergoing coronary surgery. Preoperative acute hemodilution, for example, should not be performed in patients with severely depressed myocardial function or with already preoperatively reduced Hb concentrations because the margin of safety between myocardial oxygen requirements and the available subendocardial oxygen supply may be compromised.[14–16] However, bleeding after cardiac surgery still remains a problem despite the marked improvements in surgical technique and equipment of ECC.[17,18] The causes for postoperative bleeding appear to be multifactorial, including dilution of coagulation factors, excess protamine, inadequate reversal of heparin, fibrinolysis, reduction in platelets, or abnormal platelet function as well as activation of various mediator systems, such as complement cascade by contact with foreign materials.[19–23] This bleeding may necessitate the administration of platelets or homologous fresh frozen plasma (FFP) to correct the coagulopathy.[9,13] Preoperative donor plasmapheresis has been successfully used in orthopedic surgery patients, and reduced use of donor blood and improvement in coagulation have been reported in these patients.[10] Acute separation of platelets in cardiac surgery patients has been carried out by Harke *et al.*,[11] and a significant decrease in postoperative blood loss could be demonstrated in this study. Recently, Giordano *et al.*[12] reported a pilot study in a nonhomogeneous patient population undergoing cardiopulmonary bypass surgery in whom APP producing PRP was performed by means of the same plasma collecting system (PCS) that we used: patients with autologous PRP showed a decrease in blood usage compared with that in a nontreated control group. However, only few details with regard to laboratory data were published. Hemodynamics remain stable during APP as shown recently by our group,[24] provided normovolemia is maintained during the procedure.

Two different types of plasma have been produced by plasmapheresis in our study: PPP containing noncellular plasma fraction and PRP including platelets and other cellular elements of the plasma. With regard to the coagulation process, significant differences in the number of platelets and the *r* value of the TEG could be demonstrated between PRP patients and the control and the

TABLE 4. Changes in Coagulation Values in the 3 Groups

	Group	Before Plasmapheresis	After Plasmapheresis	30 min ECC	After ECC	End of Operation	5 h after ECC	First Postoperative Day
Heparin (IU/ml)	PPP	0.13 ± 0.06	0.13 ± 0.04	1.77 ± 0.61	1.47 ± 0.33	0.12 ± 0.02	0.14 ± 0.03	0.25 ± 0.08
	PRP	0.13 ± 0.07	0.15 ± 0.11	1.65 ± 0.82	1.22 ± 0.50	0.13 ± 0.07	0.14 ± 0.06	0.27 ± 0.10
	Control	0.13 ± 0.05	—	1.82 ± 0.75	1.34 ± 0.44	0.15 ± 0.08	0.14 ± 0.06	0.29 ± 0.06
AT-III (%) (80–120)	PPP	120 ± 10	112 ± 18	68 ± 18	63 ± 21	96 ± 22*	95 ± 30*	97 ± 27*
	PRP	126 ± 19	99 ± 17	65 ± 14	66 ± 14	87 ± 15*	100 ± 23*	103 ± 17*
	Control	115 ± 16	—	58 ± 18	59 ± 14	70 ± 18	77 ± 22	80 ± 20
Fibrinogen (g/l) (1.5–4.5)	PPP	3.62 ± 0.75	3.43 ± 0.51	1.83 ± 0.57	1.70 ± 0.67	2.45 ± 0.80*	2.71 ± 0.98*	3.59 ± 0.69*
	PRP	3.39 ± 0.99	2.95 ± 0.73	1.63 ± 0.41	1.56 ± 0.40	2.21 ± 0.41*	2.78 ± 0.88*	3.82 ± 0.88*
	Control	3.98 ± 0.99	—	1.53 ± 0.47	1.40 ± 0.38	1.50 ± 0.59	1.89 ± 0.90	2.83 ± 0.99
Thrombin time (s) (16–24)	PPP	17.8 ± 3.0	24.6 ± 6.6	—	—	20.1 ± 3.3	17.9 ± 3.2	18.6 ± 5.1
	PRP	18.4 ± 1.5	18.9 ± 5.5	—	—	25.0 ± 3.7	22.1 ± 3.7	25.4 ± 9.9
	Control	18.4 ± 2.2	—	—	—	19.4 ± 3.6	17.8 ± 2.4	24.9 ± 8.6
Prothrombin time (%) (70–100)	PPP	72.0 ± 10	75.2 ± 7.7	—	—	41.6 ± 7.3	60.4 ± 9.1	63.8 ± 11.1
	PRP	80.7 ± 11	72.4 ± 9.8	—	—	38.8 ± 9.2	66.9 ± 9.0	73.5 ± 19.4
	Control	80.5 ± 13	—	—	—	55.5 ± 4.7	61.5 ± 9.8	76.5 ± 12.2
Partial thromboplastin time (30–40 s)	PPP	42.5 ± 4.0	46.5 ± 4.4	—	—	67.4 ± 19.2	51.5 ± 6.6	70.1 ± 19
	PRP	40.4 ± 4.0	47.2 ± 3.9	—	—	70.5 ± 20.1	52.5 ± 9.9	69.5 ± 13
	Control	37.6 ± 3.3	—	—	—	64.4 ± 26.0	45.2 ± 8.1	57.0 ± 21
ACT (s) (<150)	PPP	139 ± 10	—	455 ± 40	411 ± 33	136 ± 10	—	—
	PRP	155 ± 12	—	499 ± 33	400 ± 40	130 ± 16	—	—
	Control	128 ± 13	—	433 ± 45	401 ± 31	128 ± 11	—	—
TEG								
r-value (min) (normal 8–14)	PPP					9.07 ± 1.1		
	PRP					6.85 ± 0.6†		
	Control					9.98 ± 1.6		
k value (min) (normal 4–6)	PPP					7.00 ± 1.5		
	PRP					6.30 ± 1.5		
	Control					8.38 ± 1.2		
ma value (mm) (normal 47–60)	PPP					47.8 ± 8.4		
	PRP					45.9 ± 7.8		
	Control					43.6 ± 7.2		

Values are mean ± SD.
* $P < 0.05$ *versus* control group.
† $P < 0.05$ *versus* PPP and control groups.

PPP groups. Although TEG is a global coagulation test and not a method for testing platelet function in detail, it is influenced by platelet function as well. Plasma concentration of fibrinogen and AT-III were closer to normal in both APP groups with significant differences from the control patients. These differences were most obvious at the end of the operation after autologous plasma had been retransfused. In the course of the investigation, coagulation variables approached normal values in all groups, but the number of platelets (PRP group only), AT-III concentration, and fibrinogen concentration were significantly better maintained in both APP groups compared with the control patients.

The lack of change in plasma Hb, a traditional marker of blood trauma generated by ECC components and procedures,[20] indicates that APP can be performed without the risk of additional trauma to blood. Maximum increase in free Hb in our study agrees with other investigations reporting a typical change toward 30–80 mg/dl during ECC.[20]

ECC has profound effects upon blood platelets.[17,21] The decrease in platelets during extracorporeal oxygenation procedures may play an important role in postoperative bleeding.[20] However, in addition to a reduction in the number of platelets following hemodilution and blood loss, an alteration in platelet function contributes to coagulation abnormalities as well.[25,26] Although no specific tests of platelet function have been performed in this study, "rescue" of platelets by preoperative PRP plasmapheresis seems to be an attractive feature of this method offering the opportunity to prevent bleeding mediated by platelet reduction.

Impaired coagulation in cardiac surgery is highly dependent on the duration of extracorporeal oxygenation procedures.[18,20] The total period of ECC in our study was short (mean = 80 min) and coagulation variables are expected to be impaired only slightly. In none of the control patients were global coagulation parameters dramatically changed, and even the most pronounced decreases in platelets, fibrinogen, and AT-III did not force us to ad-

TABLE 5. Changes in Laboratory Parameters in the 3 Groups

	Group	Before Plasmapheresis	After Plasmapheresis	30 min ECC	After ECC	End of Operation	5 h after ECC	First Postoperative Day
COP (mmHg) (18–24)	PPP	20.4 ± 2.1	20.3 ± 1.9	10.4 ± 0.9	12.0 ± 1.0	15.9 ± 2.0	21.6 ± 2.3	22.2 ± 3.0
	PRP	20.7 ± 1.8	20.1 ± 2.2	10.3 ± 2.0	11.1 ± 2.5	15.8 ± 2.0	22.2 ± 2.0	22.4 ± 1.7
	Control	19.9 ± 2.0	—	9.0 ± 1.2	11.1 ± 1.0	13.3 ± 1.6	20.0 ± 2.2	21.4 ± 2.1
Albumin (g/dl) (3.4–4.4)	PPP	3.57 ± 0.33	2.82 ± 0.44	1.81 ± 0.45*	2.02 ± 0.28	2.46 ± 0.32	2.95 ± 0.33	3.00 ± 0.22
	PRP	3.62 ± 0.30	2.62 ± 0.34	1.80 ± 0.27*	1.93 ± 0.38	2.40 ± 0.27	2.86 ± 0.27	3.01 ± 0.34
	Control	3.47 ± 0.21	—	2.44 ± 0.51	2.40 ± 0.28	2.99 ± 0.29	3.47 ± 0.23	3.46 ± 0.35
Total protein (g/dl) (5.5–8.0)	PPP	5.98 ± 0.56	4.96 ± 0.66	3.04 ± 0.27*	3.55 ± 0.43	4.30 ± 0.33	4.96 ± 0.42	4.95 ± 0.77
	PRP	5.82 ± 0.70	4.57 ± 0.39	3.01 ± 0.39*	3.12 ± 0.44	3.82 ± 0.46	4.53 ± 0.56	4.82 ± 0.55
	Control	5.56 ± 0.61	—	3.59 ± 0.49	3.57 ± 0.51	3.91 ± 0.50	5.07 ± 0.45	4.93 ± 0.27
Na^+ (mM)	PPP	143 ± 1.6	143 ± 0.7	133 ± 3.2	137 ± 2.0	142 ± 2.8	137 ± 4.7	136 ± 4.3
	PRP	141 ± 2.9	140 ± 2.3	132 ± 3.9	136 ± 3.2	140 ± 2.8	139 ± 2.9	138 ± 3.2
	Control	139 ± 2.2	—	135 ± 2.1	138 ± 2.2	140 ± 2.7	140 ± 2.6	139 ± 2.0
K (mM)	PPP	4.08 ± 0.2	4.18 ± 0.3	5.34 ± 0.8	5.93 ± 0.8	4.72 ± 0.3	4.79 ± 0.6	4.76 ± 0.4
	PRP	4.06 ± 0.3	4.00 ± 0.4	5.40 ± 0.8	4.84 ± 0.3	4.64 ± 0.5	4.36 ± 0.1	4.66 ± 0.3
	Control	4.25 ± 0.4	—	5.58 ± 0.6	5.30 ± 0.7	4.40 ± 0.4	5.02 ± 0.6	4.92 ± 0.4
PaO_2/FIO_2 (mmHg)	PPP	397 ± 89	383 ± 65	239 ± 40	385 ± 158	355 ± 127	351 ± 88	524 ± 223
	PRP	392 ± 57	423 ± 51	233 ± 44	389 ± 88	360 ± 74	450 ± 111	494 ± 178
	Control	429 ± 55	—	228 ± 70	409 ± 66	349 ± 83	346 ± 96	533 ± 183

Values are mean ± SD.

* $P < 0.05$, *versus* control group.

minister blood derivatives. Thus, the advantages of APP might be expected to be more pronounced in longer-lasting ECC procedures, redo-operations and complex cardiac surgery procedures where important changes in the coagulation system may occur.

Cardiopulmonary bypass causes an alteration in structure and function of the blood due to trauma by the pumps or due to foreign surface contact. The mechanics of ECC may result in an activation of various humoral cascades with resulting cellular damages.[19,22,27–30] Elastase is a proteolytic enzyme released by PMN neutrophils and is assumed to be an important mediator in the development of organ failure, particularly in pulmonary dysfunction (postperfusion lung syndrome).[28,31] The APP procedure, which might be suspected to change elastase as well, did not affect its concentration significantly. ECC, however, increased PMN elastase, most pronounced in the control group (maximum 722%). Elimination of cellular elements of the plasma from the patient's circuit may be an explanation for the lowest increase in the PRP group. The increase in elastase in the control group was comparable to that found in investigations from Rommelsheim *et al.*,[31] who also documented a marked increase in elastase during ECC using membrane oxygenators. None of our patients suffered from severe organ dysfunction, and pulmonary gas exchange was without differences between the groups after termination of bypass until the first postoperative day, indicating an intact pulmonary system. The increase in elastase was moderate compared with that in septic shock patients with severe pulmonary dysfunction (elastase > 2,000 μg/ml).[32] In complex cardiovascular procedures with long-lasting extracorporeal oxygenation in which a much more pronounced activation of several mediators is to be expected, APP, particularly producing PRP, might be beneficial by reducing cellular components from the plasma, thus limiting the production of toxic substances. Harke *et al.*,[11] performing preoperative separation of platelets in his study, speculated that a reduced risk of alteration in lung function might occur due to the decreased extent of microembolism during cardiopulmonary bypass.

One aspect of APP that should be mentioned is the cost, although cost comparisons are difficult due to the different medical systems of the different countries. Preparing about 700–800 ml of autologous plasma is significantly less expensive than transfusion of an equal amount of homologous FFP (twice the cost) or platelets (5 times the costs). Moreover, transmission of viral infections by homologous blood or blood products would result in a dramatic increase in costs.

It can be concluded that APP in cardiac surgery patients might contribute to the attempt to reduce donor blood application and improve coagulation management in these patients. It can be performed even in patients with decreased Hb concentrations in whom the use of acute normovolemic hemodilution is limited. Collection of autologous plasma including cellular elements (PRP) may additionally offer the opportunity to reduce destruction and loss of platelets as well as the release of toxic products. The findings from our study warrants further investigation to elucidate the effects of APP under various conditions in cardiac surgery patients.

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