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Retrograde Autologous Priming for Opposing the Adverse Effects of Extracorporeal Circulation during Open Heart Surgery

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Abstract

The Cardiopulmonary Bypass circuit has to be primed before implementation for releasing the air inside the system. One of the most important techniques in order to avoid the hemodilution caused by priming solutions during Cardiopulmonary Bypass (CPB) is Retrograde Autologous Priming (ROP). Fifty patients operated at Medipol University, Department of cardiovascular surgery who fulfilled the criteria of Euroscore <6, ejection fraction >30%, hematocrit level between 25% to 45%, without and medical history of coagulopathy or hemorrhagic disorder, being operated electively for the first time for cardiac surgery were included in the study. The patient population was divided into two groups; the control group received standard priming solution whereas the study group received the ROP technique. Lesser amounts of intraoperative and postoperative blood and blood product transfusions as well as postoperative drainage were observed in the study (ROP) group.

Keywords: Hematocrit; Hemoglobin; Transfusion; Cardiopulmonary bypass; Retrograde autologous prime; Cardiac surgery

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Introduction

The functions of the heart and lungs are maintained by a device called heart-lung machine or "the pump" (Cardiopulmonary Bypass-CPB) during open heart surgery. Before initiating CPB, the lines between the patient and the pump have to be filled as well as the oxygenator and venous reservoir with a priming solution in order to create an air-free, closed circulation system to prevent embolism. The priming solutions, which have been previously prepared using high volume of isotonic solutions or colloids may lead to complications such as postoperative fluid overloading and dilutional anemia which deems postoperative blood transfusion mandatory in some cases. Hemodilution leads to a decrease in the formed elements of the blood, especially in erythrocytes, and the blood's oxygen transport capacity is reduced due to hemodilutional anemia. In an adult patient, a prime solution with an approximate volume of 1,650 ml is mixed with the blood, and this solution provides normovolemic hemodilution [1-3]. On the other hand, blood transfusions may lead to hemolytic, allergic, febrile reactions and besides it has a risk of transmission of infectious diseases such as hepatitis, cytomegalovirus and human immunodeficiency virus, as well as early and late complications such as causing immunosuppression and Transfusion-Related Acute Lung Injury (TRALI), it also has known and still unknown side effects [4,5]. Moreover, the use of blood and blood products also increases hospital costs. The Retrograde Autologous Priming (RAP) technique is the attempt of filling the lines with patient's own blood by delivering the prime solution into a bag in an amount allowed by the hemodynamic parameters before initiating CPB and reducing the hemodilution by lowering the prime solution to the lowest level possible [6]. In this study, we aimed to search for the effects of ROP in patients undergoing open heart surgery using CPB.

Materials and Methods

Fifty adult patients who underwent an open cardiac surgery using CPB in Istanbul Medipol University were enrolled into the study following the approval of institutional review board. The inclusion criteria were defined as i) Euroscore lower than 6; ii) Ejection fraction is above 30%; iii)

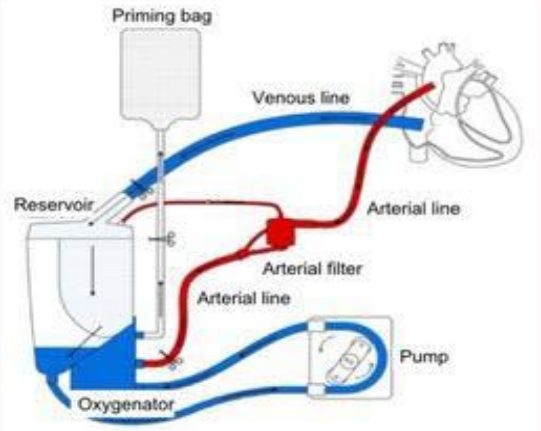

Figure 1: Blood and the prime solution to be reduced to the lowest level possible.

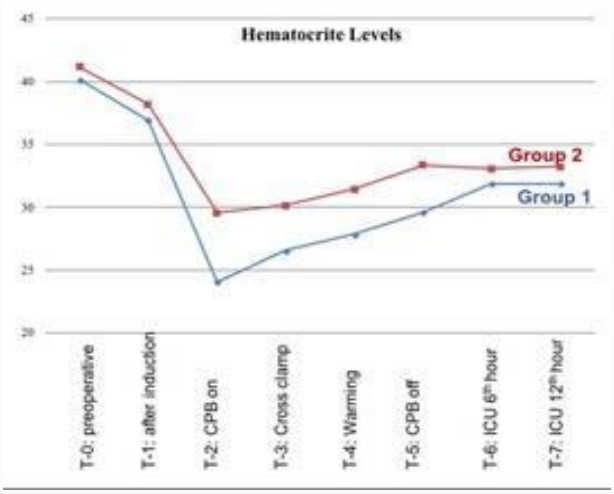

Figure 2: Rewarming and termination of CPB.

Hematocrit level between 25% to 45%; iv) Medical history without any underlying hematologic disease or any known hemorrhagic event; v) Undergoing Cardiac operation electively and for the first time (re-sternotomies were excluded).

The patients were randomly divided into two groups. Group 1 (n=25, the control group) received the standard priming during CPB (mean volume 1,650 cc: 1,000 cc balanced electrolyte solutions, 500 cc plasma volume expanders, 150 cc mannitol, 40 mEq bicarbonate and 5,000 IU heparin). Group 2 (n=25, the study group) received the retrograde autologous priming during CPB (attempt of filling the lines with patient's own blood by delivering the prime solution into a bag in an amount allowed by the hemodynamic parameters before initiating CPB and reducing the hemodilution by lowering the prime solution to the lowest level possible).

Standard CPB and perfusion techniques were carried out for all of the patients included in the study. All of the surgical procedures were performed using median sternotomy. In the control group, 1,000 cc balanced electrolyte solution; 500 cc plasma volume expanders, 20% 150 cc mannitol, 40 mEq bicarbonate and 5,000 IU heparin were used as the initial solution for CPB. Heparin was centrally administered at a dose of 300 IU/kg. After the systemic heparinization was completed and the Activated Clotting Time (ACT) value exceeded 480 sec, the cannulation procedure was initiated.

In the study (RAP) group, the RAP procedure was initiated after all setup for CPB were completed following cannulation. Before RAP, a ¼ prime bagging line was attached to the oxygenator and a prime bag was placed to the end of this line. Immediately before initiating cardiopulmonary bypass, the prime solution was delivered into a bag in an amount allowed by the hemodynamic parameters, providing the system to be filled with patient's own blood and the prime solution to be reduced to the lowest level possible (Figure 1). The procedure was slowly carried out within 5 min to 8 min. The systolic arterial pressure was not allowed to drop below 80 mmHg. The cardioplegia solution (1,000 mL) was prepared with 10 ml KCl (22.5%, 30 mEq), 10 ml Mg, 10 ml $NaHCO_3$ (10 mEq). During CPB, the flow rate of the pump was maintained at 2 L/m^2 min to 2.4 L/m^2 min and the mean arterial pressure was maintained between 50 mmHg to 80 mmHg. The hematocrit level was maintained at a value of 24% minimum. In both groups, erythrocyte suspension was used if hematocrit was below 24%.

Cardiopulmonary bypass was terminated when the warming procedure of the patients was completed and the esophagus temperature was 37°C. Following CPB, heparin was neutralized with protamine hydrochloride. ACT was targeted to be between 100 sec to 120 sec. Additional protamine was given in cases of continued bleeding and inadequate antagonism, however, fresh frozen plasma was used in cases where the targeted ACT value could not be achieved with proper amounts of protamine.

Arterial blood gas analysis records at eight different phases were evaluated for each patient:

1. Preoperative,
2. Post-anesthesia induction,
3. At the 10th min of cardiopulmonary bypass,
4. At the 5th min after cross-clamping,
5. After the warming is completed,
6. 10 minutes after termination of cardiopulmonary bypass,
7. At the 6th hr of intensive care unit follow-up,
8. At the 12th hr of intensive care unit follow-up.

Statistical analysis

While the results obtained from the study were evaluated, the SPSS version 18 (SPSS Inc, Chicago, Il, USA) was used for statistical analyses. The Pearson Chi-square test and the Fisher's exact test were used to compare the categorical data. In the comparison of the quantitative data, the Mann Whitney U test was used for the intergroup comparison of parameters in the case of two groups. In the intra-group comparisons, the Wilcoxon sign test was used. The results were evaluated at a confidence interval of 95%, a significance level of $p<0.05$ and an advanced significance level of $p<0.001$.

Results

There was no statistically significant difference in terms of demographic parameters between two groups (Table 1). The incidence of diabetes mellitus and hypertension among the groups was statistically insignificant, as well. None of the cases had chronic renal failure.

Table 1: The demographical parameters among two groups are presented.

		Group 1		Group 2		P
		n	%	n	%	
Gender	Male	19	76%	20	80%	> 0.05
	Female	6	24%	5	20%	
		Mean	Standard Deviation	Mean	Standard Deviation	
Age		57,68	11,43	55,72	12,40	> 0.05
Height (cm)		170,36	9,00	168,12	6,21	> 0.05
Body weight (kg)		77,72	10,66	79,80	8,70	> 0.05
Body mass index		26,99	4,83	28,29	3,33	> 0.05
Body surface area (m^2)		1,91	0,15	1,91	0,11	> 0.05
Ejection fraction (%)		50,80	6,32	54,04	6,93	> 0.05
EuroScore		2,42	1,81	1,48	1,38	> 0.05

Table 2: The surgical procedures performed in two groups are presented.

Surgical Procedure	Group 1		Group 2	
	n	%	n	%
Atrial septal defect closure, valvular plasty	0	0%	1	4%
Aortic valve replacement	4	16%	0	0%
Aortic root replacement (Bentall procedure)	2	8%	0	0%
CABG	15	60%	16	64%
CABG and aortic valve replacement	1	4%	0	0%
CABG and mitral valve replacement	0	0%	1	4%
CABG and atrial septal defect closure	0	0%	1	4%
CABG and mitral valve plasty	1	4%	0	0%
Mitral valve replacement	2	8%	2	8%
Mitral valve replacement and ablation for AF	0	0%	1	4%
Mitral and aortic valve replacement	0	0%	1	4%
Mitral valve replacement and tricuspid plasty	0	0%	2	8%

*CABG: Coronary Artery Bypass Graft; AF: Atrial Fibrillation

When the underlying cardiac pathologies that constituted the indications for surgical interventions were considered; in Group I, 2 patients (8%) had ascending aortic aneurysm with associated aortic regurgitation, 2 patients had (8%) aortic stenosis, 2 patients (8%) had pure aortic regurgitation, 15 patients (60%) had ischemic coronary artery disease, 1 patient (4%) had ischemic coronary artery disease with concomitant mitral stenosis and had ischemic coronary artery disease, 1 patient (4%) had mitral regurgitation. In Group II, 1 patient (4%) had atrial septal defect with concomitant mitral and tricuspid regurgitation, 16 patients (64%) had ischemic coronary artery disease, 1 patient (4%) had ischemic coronary artery disease and atrial septal defect, 1 patient (4%) had ischemic coronary artery disease and mitral regurgitation, 1 patient (4%) had pure mitral stenosis, 1 patient (4%) had mitral stenosis and chronic atrial fibrillation, 1 patient (4%) had mitral regurgitation, 1 patient (4%) had mitral and aortic regurgitation, 2 patients (8%) had mitral and tricuspid regurgitation. Table 2 presents the surgical procedures that were performed in both groups. The aortic cross clamp durations in groups 1 and 2 were 110 ± 35 minutes and 107 ± 39 minutes, respectively (p>0.05). The CPB durations in groups 1 and 2 were 158 ± 36 minutes and 148 ± 41 minutes, respectively (p>0.05).

The mean volume of retrograde autologous priming in the study group was 762 ± 96 mlt (622-994). The hematocrit levels at different time intervals are presented at Table 3. In group 1, the reduction in the hematocrit values after induction was statistically significant compared to the preoperative status (p<0.05). The reduction in the hematocrit value during CPB initiation was statistically significant compared to the hematocrit value after induction and the reduction in the hematocrit value after cross-clamping was statistically significant (p<0.05) compared to the hematocrit value during CPB initiation. The increase in the warming hematocrit value was statistically significant compared to the hematocrit value after cross-clamping (p<0.05). The increase in the hematocrit value after CPB was statistically significant compared to the warming hematocrit value (p<0.05). The increase in the ICU 6^{th} hour hematocrit value was statistically significant compared to the hematocrit value after CPB (p<0.05). However, the increase of hematocritin the ICU at the 12^{th} postoperative hour was not statistically significant compared to the values at 6^{th} postoperative value (p>0.05). In Group 2, the reduction in the hematocrit value after induction was statistically significant compared to the preoperative hematocrit value (p<0.05). The reduction in the hematocrit value during CPB initiation was statistically significant compared to the hematocrit value after induction (p<0.05), however the increase in the hematocrit value after cross-clamping was not statistically significant compared to the hematocrit value during CPB initiation (p<0.05). The increase in the warming, hematocrit value was statistically significant compared to

Table 3: The hematocrit levels at different times of the perioperative period.

	Group 1		Group 2		P
	Mean	Standard Deviation	Mean	Standard Deviation	
Preoperative	40,14	5,12	41,17	4,25	0,497
Following induction of anesthesia	36,92	5,70	38,21	4,64	0,388
Initiation of CPB	24,05	3,50	29,56	4,52	0,001
Following aortic cross-clamping	26,55	3,41	30,13	4,03	0,002
Warming	27,84	3,24	31,42	3,95	0,002
Termination of CPB	29,58	3,21	33,35	3,26	0,001
ICU-6th postoperative hour	31,86	2,70	33,07	2,76	0,165
ICU-12th postoperative hour	31,88	2,27	33,24	2,96	0,135

*CPB: Cardiopulmonary Bypass; ICU: Intensive Care Unit

Table 4: The amount of transfusion of the blood and blood products (units).

	Group 1		Group 2		P
	Mean	Standard Deviation	Mean	Standard Deviation	
ES during CPB	0,32	0,69	0,04	0,20	0,077
ES by anesthesiologist	2,76	1,33	1,72	1,54	0,008
FFP by anesthesiologist	1,84	1,1	1,44	0,91	0,142
ES in ICU	2,32	1,65	0,80	1,11	0,001
FFP in ICU	2,16	1,90	1,40	1,68	0,128
Platelet suspension in ICU	0,12	0,44	0,04	0,20	0,540
ES at the ward	0,16	0,37	0,16	0,47	0,735

the hematocrit value after cross-clamping ($p<0.05$). The increase in the hematocrit value after CPB was statistically significant compared to the warming hematocrit value ($p<0.05$). On the other hand, the reduction in the 6th postoperative hour hematocrit value was not statistically significant compared to the hematocrit value after CPB ($p<0.05$). The increase in the 12th postoperative hour hematocrit value was not statistically significant compared to the 6th hour hematocrit value ($p>0.05$). When the two groups were compared between each other, statistically significant difference was encountered when the hematocrit levels at the following states were considered: initiation of CPB, following aortic cross clamping, following rewarming and termination of CPB. Figure 2 demonstrates the course of hematocrit levels at different states of the perioperative period.

The postoperative 24-hr chest tube drainage was significantly less in the study group (733 ± 599 mlt *vs.* 1,207 ± 704 mlt; $p<0.001$). Accordingly, when the transfusion of blood and blood products were compared, the units of erythrocyte suspensions were significantly lower in the study groups (Table 4). The intraoperative and postoperative transfusion of erythrocyte suspensions were significantly lower in the study group (1.7 ± 1.6 units *vs.* 3 ± 1.6 units and 0.9 ± 1.5 units *vs.* 2.4 *vs.* 1.6 units, respectively) ($p<0.001$).

The extubation times in group 1 and 2 were 7.5 ± 5 and 6.8 ± 4, respectively ($p>0.05$). The ICU and discharge periods were 2.4 ± 0.9 and 5.4 ± 2.1 days for group 1 whereas 2.3 ± 1.1 and 4.4 ± 1.3 days for group 2, respectively ($p>0.05$).

Discussion

The ultimate equilibrium of peroperative bleeding, the necessity of blood/blood product transfusions and prevention of transfusion associated complications is still debated in the current era of cardiac surgery. Preoperative and peroperative anemia may lead to untoward results in patients undergoing cardiac surgery, such as increased risks for wound infections, renal and pulmonary function impairment, prolonged hospitalization and costs [7,8]. Hemodilution results in a reduction in the oxygen delivery to the tissues [9]. The allowed limits for anemia are considered as 8 gr/100 ml over 70 years of age and as 7 gr/100 ml under 70 years of age [10,11]. In our study, we did not allow hemoglobin to drop below these limits in both groups. The lowest hemoglobin values were 7.79 ± 1.26 mg/dL and 9.67 ± 1.55 mg/dL in Groups 1 and 2 respectively.

The risks posed by homologous blood transfusion have prompted researchers to develop techniques that are cheap, reliable, and reduce the use of blood. The use of the techniques to prevent blood loss and its use considerably reduces the requirement for blood transfusion [12]. The principal of this study was based on investigating the effects of RAP procedure on the hemoglobin, hematocrit rates and the use of blood and blood products compared to the use of the standard prime solution. Other techniques for blood preservation in cardiac surgery are cell savers, ultrafiltration protocols and minimized circuits in the CPB set up [13,14]. On the other hand, simplicity and cost-effectiveness is as an important advantage of RAP. Several studies have reported the safe and effective utilization of RAP in order to prevent hemodilution and decrease the amount of blood transfusions [15-21].

Hofmann and colleagues [15] defined the independent factors in-hospital blood transfusion after elective cardiac surgery which were stated as a body mass index over 29 kg/m^2, a preoperative hematocrit value of ≤ 36% and a 12-hour postoperative blood loss of over 450 mL. They suggest a RAP volume of at least 350 mL in order to be effective in avoiding in-hospital blood transfusion.

Neurological complication following CPB and cardiac surgery is still an important problem. Another beneficial effect of RAP is

thought to be an incremental effect on cerebral oxygenation. Hwang and colleagues [22] reported an increased cerebral oxygenation and improved postoperative neurocognitive functions when RAP is implemented. Moreover, in a large patient series reported by Murphy et al. [23], incidence of cardiac arrest seemed to be lower in RAP group.

A couple of untoward effects of RAP include hypotension associated with hypovolemia, hypovolemia leading to lower reservoir volumes during CPB and insufficient de-airing of venous returned blood, and higher hematocrit levels (due to less hemodilution) during CPB that might increase hemolysis [24].

Conclusion

Our study showed that RAP is a safe, cost-effective and simple way of blood preservation in cardiac surgery. Intraoperative hemoglobin and hematocrit levels were higher, hemodilution was less, and intraoperative and postoperative blood transfusion was lower by carrying out the RAP procedure. Not only the side effects and complications of blood transfusion were reduced with the utilization of the RAP procedure, the amount of postoperative drainage also decreased significantly. More large-scale multicenter randomized clinical trials are deemed mandatory in order to evaluate the efficacy, safety and side effects of blood preservation strategies.

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