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| of the rest of the second        | Original Research Paper Cardiovascular Surgery  |  |  |
|                                  | THE EFFECTS OF FILLING THE PERFUSION SYSTEM USED IN OPEN HEART<br>OPERATIONS WITH THE PATIENT'S OWN BLOOD ON HEMODILUTION AND<br>BLOOD TRANSFUSION                                    |  |  |
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ABSTRACT Prime solutions are used to fill the system in order to extract air from the existing lines in the heart-lung machine used in open heart surgery before starting the operation. These prime solutions cause hemodilution during cardiopulmonary bypass. Retrograde Autologous Prime (ROP) is one of the techniques developed to reduce hemodilution and blood transfusion. The aim of this study is to investigate the effects of ROP technique on hemoglobin values and transfusion applications. For this reason, 80 adult patients who underwent open heart surgery, with an ejection fraction of over 35%, will be operated for the first time, undergoing elective surgery, without hematological disease and a known bleeding pathology were included in the study. Standard prime solution (Control Group) was applied to one group during CPB, and ROP technique was applied to one group (Study Group). Standard CPB and perfusion techniques were used in all patients. Intraoperative and postoperative hemoglobin values were found to be higher in the patients in the ROP group. It was concluded that transfusion of blood and blood products was less in ROP group patients.

# KEYWORDS : Cardiopulmonary Bypass, Hemodilution, Hemoglobin, Retrograde Autologous Priming, Transfusion.

# **INTRODUCTION**

Cardiopulmonary bypass (CPB) is a technique that temporarily takes over the function of the heart and lungs in open heart surgery and maintains the body blood perfusion and oxygen supply. In doing so, it provides an inactive and bloodless environment during surgery.

The name of the device that allows this technique to be performed is the heart lung machine or also known as pump (1,2).

Components of heart lung machine consist of pump (artificial heart), plastic pipes circuits, cannulas, venous reservoir, filters, oxygenator (artificial lung) and heat modifier (2,3).

Venous blood is drained into the venous reservoir with the effect of gravity through cannulas placed in the right atrium. (3). Then the blood is sent from the reservoir to the oxygenator by roller pump or centrifugal pump. Here, blood is oxygenated and carbon dioxide is excreted. The blood leaving the oxygenator returns to the systemic circulation after passing through the arterial filter.(3).

The solution used to remove the air in the lines of the heartlung machine before cardiopulmonary bypass is called prime solution and this air removal process is called priming. (2). Prime solutions consist of liquids that contain crystalloid and balanced electrolytes. However the amount varies according to the set used in adult patients, an average of 1300 to 2000 cc of prime solution is used and this prime solution causes hemodilution in the blood. (4,5,6).

Hemodilution causes a reduction of erythrocytes and other shaped formations like thrombocytes. These effects give rise to anemia and complications like bleeding. (7,8). It is known that the minimum hematocrit level is of 20% and above to carry enough oxygen to the tissues during cardiopulmonary bypass. A low hematocrit value can cause tissue hypoxia and acidosis.(9). The hemodilution caused by the priming solutions used in CPB also lowers the colloid osmotic pressure and causes tissue edema. Tissue edema can gives rise to organ dysfunction like pulmonar,kidney or liver after the surgery (10,11).

Hepatitis, Human Immunodeficieny Virus (HIV), allergic and febrile reactions can be seen in people who receive blood transfusion. Along with the risk of transmission of infectious diseases, there are early and late complications such as acute lung injury syndrome. On the other hand, It is seen in studies that the use of the blood and blood product also increases hospital costs (9,12,13).

Blood protection techniques have been developed to decrease the hemodilution seen in CPB and the usage of blood and blood product amount. These developed methods include mini cardioplegia systems, acute normovolemic hemodilution (ANH), hemofiltration, autotransfusion (cell saver), venous vacum drainage systems, heparin-coated systems and retrograde autologous prime (14,15,16).

Retrograde autologous priming (ROP) technique, which is one of the blood preservation techniques, is based on reducing hemodilution by replacing the prime solutions in the perfusion system with the patient's own blood. The aim of this study is to examine the effects of ROP over hemoglobin values and the use of blood and blood products in intraoperative and postoperative periods.

## MATERIAL AND METHOD

This research was conducted as a quantitative research method and a prospective randomized controlled study. Our study was discussed at the meeting of Acıbadem University and Acıbadem Healthcare Institutions Medical Research Ethics Committee (ATADEK) dated 03.10.2019 and numbered 2019/15, and it was found appropriate in terms of medical ethics with the decision number 2019-15/33.

**Inclusion criteria;** Patients undergoing open heart surgery by being connected to a heart-lung machine are adult patients with an ejection fraction above 35%, who have no underlying hematological disease and known bleeding pathology.

40 patient were included in each patient group. The patients

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were divided into two groups by chosing random numbers between 1 and 80 via the computer program (random.org). Control group (n=40): Standard prime before CPB (mean prime volume 1500 cc: 1250cc gelofusine and 250cc mannitol and 5000 U heparin) administered patients and Study group (n=40, ROP); patients undergoing retrograde autologous priming before CPB, were determined.

After standard priming was applied to both groups, the first group continued with standard priming, while the second group was applied retrograde autologous priming. For applying the retrograde autologous prime method before starting the CPB, a bag with a capacity of 1000 ml was connected to the recirculation line (small circulation line: the line between the oxygenator and the reservoir) of the perfusion system, and the prime solution in the system was transferred to this bag. The system was filled with the patient's own blood through the arterial line as much as the hemodynamics allowed. ROP was performed in 5 to 10 minutes slowly because when it is perfored quickly it can cause hemodynamic deterioration. During the ROP it was not allowed the systemic tansion falling down below 80 mmHg. CPB was started after the ROP was completed.

CPB and aortic cross clamp times, 24-hour drainage amounts, extubation times, hemoglobin levels, use of blood and blood products, intensive care and hospital stays were recorded in the perioperative and post-operative period.

### RESULTS

Table 1: Comparison of Intergroup Demographic Datas and Pump Time (N=80)

|              | Group A            | Group B            | Test   | °p     |
|--------------|--------------------|--------------------|--------|--------|
|              | Mean±ss            | Mean±ss            | value  |        |
| Āge          | $64.08 \pm 10.32$  | 63.93±8.11         | 0.072  | 0.943  |
| Height       | $170.73 \pm 8.33$  | $172.55 \pm 6.34$  | -1.103 | 0.274  |
| Weight       | $82.48 \pm 15.05$  | $85.35 \pm 12.07$  | -0.943 | 0.349  |
| BMI          | $28.2 \pm 3.85$    | $28.67 \pm 3.87$   | -0.549 | 0.585  |
| Body surface | $1.97 \pm 0.21$    | 2±0.15             | -0.874 | 0.385  |
| area         |                    |                    |        |        |
| Ejection     | 49.95±7.18         | $53.75 \pm 6.58$   | -2.468 | 0.016* |
| Fraction     |                    |                    |        |        |
| CPB time     | $107.48 \pm 34.55$ | $115.63 \pm 44.39$ | -0.916 | 0.362  |
| Krossclamp   | $78.73 \pm 28.1$   | 89.55±34.13        | -1.549 | 0.125  |
| time         |                    |                    |        |        |
|              | n (%)              | n (%)              | Test   | bp     |
|              |                    |                    | değeri |        |
| Sex          |                    |                    | 5.952  | 0.015* |
| Male         | 34 (85)            | 33 (82.5)          |        |        |
| Female       | 6 (15)             | 7 (17.5)           |        |        |

<sup>A</sup>indipendent groups t test <sup>b</sup>Pearson chi-square test \*\*p<0.01 \*p<0.05

There was no statistically significant difference between the groups in terms of age, height, weight, BMI, body surface area, pump time and cross-clamp time values and gender distribution (p>0.05). Avarage ejection fraction of study group subjects were higher than the values of the subjects in the control group. (p=0.016)

| Table | 2: | Intergroup | Hemoglobin | Assessments | by | Time |
|-------|----|------------|------------|-------------|----|------|
| (N=80 | )  |            |            |             |    |      |

|              | Group A          | Group B          | Test   | °p        |
|--------------|------------------|------------------|--------|-----------|
|              | Mean±ss          | Mean±ss          | value  |           |
| Preop (P)    | $13.45 \pm 1.36$ | $14.01 \pm 1.26$ | -1.926 | 0.058     |
| After first  | 8.25±1.19        | $10.05 \pm 1.23$ | -6.666 | <0.001**  |
| cardioplegia |                  |                  |        |           |
| After        | $8.54 \pm 0.94$  | $10.13 \pm 1.15$ | -6.774 | < 0.001** |
| Crossklamp   |                  |                  |        |           |
| Post CPB     | 9.1±1.13         | $10.1\pm1$       | -4.203 | <0.001**  |

- 10.73±1.09 11.19±1.19 -1.775 c Analysis of variance in repeated measures \*p<0.05
- d Binary comparisons with Bonferroni correction \*\*p < 0.01

0.080

Hemoglobine values of the subjects in the study group and control group were found 10.05±1.23 g/dL, 8.25±1.19 g/dL (p<0.001) after first cardioplegia,  $10.13\pm1.15$  g/dL,  $8.54\pm0.94$ g/dL (p<0.001) after cross clamp removal, 10.1±1 g/dL, 9.1±1.13 g/dL (p<0.001) after CPB. It was determined that hemoglobin values were statistically high in the ROP group.

|                 | Group A          | Group B                 | Test   | °p        |  |
|-----------------|------------------|-------------------------|--------|-----------|--|
|                 | Mean±sh          | Mean±sh                 | value  |           |  |
| Urine<br>volume | 872.5±<br>317.23 | 990±407.49              | -1.439 | 0.154     |  |
| Drenage         | 490±116.68       | $406.25 \!\pm\! 142.86$ | 2.872  | 0.005**   |  |
| Total           | $3669.5\pm$      | $2531.55 \pm$           | 9.463  | < 0.001** |  |
| volume          | 650.05           | 394.87                  |        |           |  |
| input           |                  |                         |        |           |  |
| Total           | 1360±            | $507.2 \pm 245.93$      | 12686  | < 0.001** |  |
| balance         | 346.82           |                         |        |           |  |
| Eritrocyte      | $0.23 \pm 0.58$  | $0\pm0$                 | 2.467  | 0.018*    |  |
| suspention      |                  |                         |        |           |  |
| given at CPB    |                  |                         |        |           |  |
| İntraoperati    | $1.2 \pm 0.79$   | $0.2 \pm 0.46$          | 6.896  | < 0.001** |  |
| ve Eritrocyte   |                  |                         |        |           |  |
| suspention      |                  |                         |        |           |  |
| Intraoperati    | $0.55 \pm 0.64$  | $0.15 \pm 0.48$         | 3.160  | 0.002**   |  |
| ve Plasma       |                  |                         |        |           |  |
| İntraoperati    | $0.23 \pm 0.48$  | $0.03 \pm 0.16$         | 2.504  | 0.016*    |  |
| ve Platelet     |                  |                         |        |           |  |
| ICU             | $0.78 \pm 0.77$  | $0.38 \pm 0.54$         | 2.696  | 0.009**   |  |
| Eritrocyte      |                  |                         |        |           |  |
| suspention      |                  |                         |        |           |  |
| ICU Plasma      | $1.38 \pm 0.95$  | 0.78±1                  | 2.748  | 0.007**   |  |
| ICU Platelet    | $0.08 \pm 0.27$  | $0.08 \pm 0.35$         | 0.000  | 0.999     |  |
| Total           | $2.37 \pm 1.55$  | $0.72 \pm 1.04$         | 5.602  | < 0.001** |  |
| Eritrocyte      |                  |                         |        |           |  |
| suspention      |                  |                         |        |           |  |
| Total           | 1.95±1.13        | $0.95 \pm 1.24$         | 3.769  | < 0.001** |  |
| Plasma          |                  |                         |        |           |  |
| Total           | $0.30 \pm 0.52$  | 0.10±0.38               | 1.975  | 0.052     |  |
| Platelet        |                  |                         |        |           |  |

## Table 3: Comparisons of Volume Amounts and Use of Blood and Blood Product Values Between Groups

Results adjusted for gender and body surface area are presented.

Covariance analysis \*\*p<0.01 \*p<0.05

In both groups, blood transfusion was performed when hemoglobin fell below 7 (g/dL) in the intraoperative period and when hemoglobin fell below 9 (g/dL) in the postoperative period. Platelet transfusion was performed in patients with platelet count below 70 thousand in both groups. Fresh frozen plasma (FDP) was transfused to both patient groups when the international normalized ratio (INR) was greater than 1.5 and there was more than 100cc per hour drainage.

Total ES in the study (ROP) group and control group were found  $0.72\pm1.04$ ,  $2.37\pm1.55$ ; (p<0.001) and total FFP in the study group and control group were found  $0.95 \pm 1.24$ ,  $1.95\pm1.13$ ; (p<0.001). There was a statistically significant difference between the two groups in terms of the use of fresh frozen plasma and erythrocyte suspension.

### Table 4: Comparison of intensive care unit stay, intubation time and ward length of stay between groups

|                 | Group A          | Group B   | Test  | °p    |
|-----------------|------------------|-----------|-------|-------|
|                 | Mean±sh          | Mean±sh   | value |       |
| ICU stay (hour) | $24.15 \pm 6.65$ | 23.78±5.6 | 0.273 | 0.786 |

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| Entübation time | $8.8 {\pm} 2.47$   | 8.95±3.39          | -0.226 | 0.822 |
|-----------------|--------------------|--------------------|--------|-------|
| (hour)          |                    |                    |        |       |
| Ward length of  | $131.45 \pm 29.57$ | $126.33 \pm 22.79$ | 0.868  | 0.388 |
| stay (hour)     |                    |                    |        |       |

"Independent groups t-test

There was no statistically significant difference between the groups in terms of length of stay in the intensive care unit, intubation time and length of stay in the service (p>0.05).

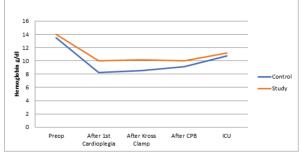


Figure 1: Change of Hemoglobin Values According to Stages

## DISCUSSION

Today, among the most discussed topics about CPB are the type and amount of the prime solutions used, the advantage and disadvantage of the hemodilution created by the prime solution, the need for blood and blood products resulting from the hemodilution that occurs, and the complications arising from the transfusions. Although blood transfusion is not performed as much as in the early years of CPB, open heart surgery has higher blood transfusion rates compared to other surgeries. Blood and blood product transfusions may cause transmission of diseases, inflammatory response, development of allergic reactions and increased risk of infection, as well as increase hospital stay and hospital costs.

(13,16). For these reasons, blood transfusion should be avoided unless necessary, and it should be used considering not only blood hemoglobin level but also other clinical and laboratory parameters. (9,17,18).

Studies have revealed that the decrease in hemoglobin and hematocrit values caused by the prime solutions used during CPB and the resulting hemodilutional effect are associated with morbidity and mortality during the operation. (9,19)

The ROP method, which is one of the techniques that can be routinely applied in open heart surgeries and has the potential to reduce blood transfusion, is a low-cost, reliable method that does not need extra equipment in its application and does not have side effects when followed carefully and closely. It is a practical and simple technique that can be prepared in 5-10 minutes, does not cause serious loss of time, tries to prevent hemodilution before it occurs, not after it occured (20,21).

In this study, how extend the ROP method reduces hemodilution compared to conventional priming solution application and its effects on blood and blood product use during CPB were investigated. Most of the other blood preservation techniques that have been developed have been shown to reduce blood transfusion, but they require extra equipment and/or high costs. Ameliyat öncesi otolog kan donasyonu, normovolemik hemodilusyon, ototransfüzyon (cell saver) ve vakumlu venöz drenaj kan koruma tekniklerinden bazılarıdır (22,23).

Rosengart et al. (24) in their study of 60 people in 1998, applied an average of  $880\pm150$  ml retrograde prime to 30 people to

whom ROP was applied, and they found the lowest hemoglobin value as 6.6 g/dL in the control group and 7.3 g/dL in the ROP group.

They have reported that hemodilution and transfusion need was decreased in the ROP applied group and that ROP was an effective and safe technique. After this study by Rosengart et al., the interest in ROP technique has increased.

80 patients were included in our study, and ROP was applied in the 40-person group. In the blood gas controls taken after the first cardioplegia, the mean hemoglobin value was found o be  $10.05 \pm 1.23$  g/dL in the ROP group and  $8.25 \pm 1.19$  g/dL in the control group. Hemoglobin values, which were checked again after the cross clamp was removed and after the CPB, were also found to be significantly higher in the patients in the ROP group.

In addition, while no red blood cell suspension was used in any patient in the ROP group during CPB, an average of  $0.23\pm0.58$  units (p=0.018) was used in the control group. ES transfusion given post CPB by anesthesia in the ROP group was  $0.2\pm0.46$  units,while it was $1.2\pm0.79$  units in the control group. In this study, not only ES but also the use of other blood products were found to be significantly different between the two groups. The mean amount of FFP given by anesthesia after CPB in the ROP group was  $0.15\pm0.48$  units, it was  $0.55\pm0.64$  units in the control group and the mean platelet amount given after CPB in the ROP group was  $0.03\pm0.16$ units, while it was  $0.23\pm0.48$  units in the control group.

Koçoğlu et al. (25) included 50 patients in a study they conducted in 2018 and applied ROP to 25 of them. In both groups, the mean hemoglobin value after the onset of CPB was found to be  $7.79\pm1.26$  g/dL in the control group and  $9.67\pm1.55$  g/dL in the ROP group. In the postoperative period, they found the amount of drainage 1207.60 $\pm$ 704.90 cc in the control group and  $733.40\pm599.05$  cc in the ROP group, showing the priming effect on hemostasis.

Similarly, in our study, the amount of drainage in the postoperative period was  $406.25\pm142.86$  ml in ROP group patients and  $490\pm116.68$  ml in control group patients. (p=0.005). This difference in the amount of drainage may be associated with changes in coagulation factor concentrations and an absolute decrease in coagulation factor concentrations in the control group (26).

In 2013, Vandewielea et al. (27) published a literature review of 753 patients, 498 of whom received an average of 475  $\pm$ 221 ml of ROP technique. They found the mean amount of blood transfusion during the operation to be  $0.58\pm1.11$  units in the ROP group and  $0.89\pm1.42$  units in the control group. They reported that ROP technique reduces the amount of blood transfusion in CPB and helps to protect from the negative effects of hemodilution.

In the literature some studies has been showed that the use of blood and blood products increases the cost, and blood preservation methods reduce the cost (13). Kearsey et al. (21) applied the ROP technique to 101 people in a study that included 193 people in 2013, and found the mean hemoglobin value 9.1 g/dL in patients in the ROP group and 7.8 g/dL in patients in the control group. They found that the length of hospital stay was significantly lower in the ROP group and suggested that shortening the hospital stay would protect patients from nosocomial infections and reduce hospital costs. In our study, extubation times, intensive care and service hospitalization times were followed in two groups and no significant difference was detected.Altough no cost analysis was performed in our study, considering the amount of blood use between groups, the cost in the ROP group may be lower.

In our study, it was found that hemodilution was less, intraoperative hematocrit and hemoglobin values were higher, and blood and blood product transfusion rates were lower in intraoperative and postoperative processes with the ROP technique during CPB. ROP is an easy and cost effective technique that can be safely applied if used with care. ROP can be easily and routinely used in all open heart surgery centers with an extra bag modified to the CPB circuit.

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