Original Article

Comparison Between the Effect of Albumin and Fresh Frozen Plasma in the Cardiopulmonary Bypass Prime Solution on the Clinical and Laboratory Outcomes of Children Undergoing Congenital Cardiac Disease Surgery

Mazyar Gholampour Dehaki[1], MD; Farhad Gorjipour[2], MS; Mandana Hosseinzadeh[1*], MS; Naser Kachoueian[3], MD; Saeid Heydari Nia[1], MS; Ahmad Javanmard[4], MD

ABSTRACT

Background: A decrease in blood oncotic pressure following hemodilution due to cardiopulmonary bypass (CPB) in cardiac surgery results in fluid shift and organ dysfunction. The present comparative study evaluated the effects of adding albumin and fresh frozen plasma (FFP) to the priming solution of a CPB system on clinical and laboratory outcomes in pediatric congenital cardiac surgery candidates.

Methods: The present clinical trial study recruited 2 groups of 50 pediatric patients (weight<10 kg) scheduled for the elective surgical repair of congenital heart diseases. The study population was randomly assigned to 2 groups: FFP and albumin. The patients' hemodynamic parameters, diuresis, chest tube drainage, transfusion, and inotropic drugs, as well as laboratory tests, including the erythrocyte sedimentation rate (ESR), C-reactive protein, blood urea nitrogen, creatinine, lactate, hemoglobin, and hematocrit, were measured as the trial's primary outcome.

Results: ESR was significantly higher in the FFP group (P<0.05). Blood urea nitrogen and creatinine were remarkably lower in the albumin group (P<0.05). No significant differences in hemodynamic variables, the volume of the red blood cell transfusion, the volume of the inotropic infusion, and clinical outcomes were observed between the 2 groups.

Conclusions: In patients with FFP in the prime solution, a higher ESR value was observed. While there was no significant difference between the 2 groups regarding hemostasis, albumin offered the advantages of better kidney, liver, and cardiac functions. ***(Iranian Heart Journal 2022; 23(3): 33-41)***

KEYWORDS: Albumin, Cardiac surgery, Cardiopulmonary bypass, Fresh frozen plasma

[1] Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
[2] Iranian Scientific Society of Extracorporeal Technology, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
[3] Department of cardiac surgery, Imam Hossein Educational Hospital, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran.
[4] Shahid Beheshti University of Medical Sciences, Tehran, IR Iran.

***Corresponding Author:** Mandana Hosseinzadeh, MS; Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
Email: mandana6964@gmail.com **Tel:**+ 989124574301

Received: December 28, 2020 **Accepted:** April 14, 2021

Improvements in pediatric cardiac operation outcomes such as the cardiac output and the quality of patient care are highly demanded.[1] Little information exists on the outcome of pediatric cardiac surgery in developing countries such as Iran, and the focus is on mortality as an outcome indicator.[2] It appears that some other morbidities and postoperative complications should be screened as pediatric cardiac surgery outcomes.[2] Hemodynamic instability, bleeding, coagulation disorders, and multiple organ failure are known complications that may occur during cardiopulmonary bypass (CPB) for pediatric congenital heart disease surgery.[3-5] Indeed, the prime volume of pediatric CPB circuits exceeds the patient's total blood volume in many cases, causing the risk of hemodilution in CPB circuits in pediatric surgeries, which may persist even by adding blood to the prime solution.[6-9] The use of colloidal solutions such as albumin and fresh frozen plasma (FFP) as the main prime fluid can be effective in resolving this problem.[10]

Albumin is one of the major factors in determining oncotic blood pressure, the transfer of endogenous substances, the exertion of antithrombotic effects, and hemodynamic stability.[11] On the other hand, acute kidney injury (AKI) is common after cardiac surgery and is associated with an increased risk of postoperative mortality and morbidity.[12,13] The administration of albumin 20% immediately before cardiac surgery can increase the urine output and reduce the risk of postoperative AKI in patients.[14] FFP is a blood product that has coagulation factors, albumin, immunoglobulin, and antithrombin, and its consumption has been increasing worldwide over the past 2 decades.[15,16] It seems that the use of FFP as a prime solution for CPB in children undergoing congenital heart disease surgery can not only increase oncotic pressure but also reduce hemostatic abnormalities after CPB and heparin reversal by increasing fibrinogen levels.[17,18]

Considering the high prevalence of congenital heart abnormalities and the incidence of mortality, as well as the significance of modulating postoperative stress responses in children, reducing the length of stay in the intensive care unit (ICU), lessening patient costs, maintaining renal function, decreasing bleeding, and diminishing the need to intraoperative and postoperative blood transfusions, the present study aimed to compare clinical outcomes between the use of albumin and the use of FFP to determine their appropriate use in pediatric congenital heart disease surgery.

METHODS

Trial Design

This study was a randomized clinical trial with a parallel design. The study protocol was reviewed and approved by the Ethics Committee Rajaie Cardiovascular Medical and Research Center, Tehran, Iran (code: IR.RHC.REC.1397.086). Guardian informed consent was obtained for the study subjects.

Trial Participants

The inclusion criteria were composed of weight below 10 kilograms, an ejection fraction above 40%, indications for congenital cardiac surgery, no history of infection, no previous cardiac surgery, no known inflammation 2 weeks preoperatively, no renal failure (serum levels of creatinine>1.5 mg/dL), no metabolic disorders, no liver failure and coagulation disorders, and serum levels of albumin of less than 4 g/dL. The parents of the recruited pediatrics signed an informed consent form for their children to participate in the study. Patients undergoing deep hypothermia and CPB duration below 1 hour or above 4 hours were excluded.

This study was performed in the Cardiac Surgery Operating Room of Rajaie Cardiovascular Medical and Research Center.

Participants were randomly selected based on the study's inclusion criteria and randomly assigned to 2 groups receiving albumin and FFP in their prime solution via the balanced block randomization method (n=50 per group). The trial participants, surgeons, and outcome assessors (nurses) were blinded to the prime solution of the trial participants. The prime solution was introduced by the perfusionist and the anesthesia team.

Intervention

The children in both groups received albumin 20% (1 g/kg) or FFP (15 mL/kg) in their prime solution. The participants were fully monitored, and the values of SPO_2, noninvasive blood pressure, heart rate, respiratory rate, end-tidal CO_2, central venous pressure, and cerebral oximetry were measured and recorded. The induction of anesthesia was carried out using intravenous anesthetics (ketamine, thiopental, or propofol) depending on the patient's conditions and the type of surgery. Additionally, the muscle relaxant used was pancuronium (0.1 mg/kg). A fentanyl infusion (0.03 µg/kg/min), followed by an atracurium infusion (2 µg/kg/min), was used to maintain anesthesia during the operation. Following intubation and mechanical ventilation, heparin was administered as an anticoagulant (300 units/kg). After a target activated clot time (ACT) of 480 seconds was achieved, bicaval cannulation and CPB were permitted. The prime solution content was equal for both groups and consisted of at most 1 whole blood unit to achieve a hematocrit level of between 25% and 30% on CPB, heparin (150 units/kg), bicarbonate (1 mL/kg), and Ringer lactate.

After moderate hypothermia (30–32 °C) and aortic cross-clamping, the Custodiol cardioplegia solution (50 mL/kg) was injected into the aortic root, and intermittent hemofiltration was established for all the patients from the beginning to the end of CPB to prevent severe hemodilution, to reduce the inflammatory side effects of CPB, and to prevent hyponatremia due to custodial solution. A non-pulsatile roller pump was used during CPB, and Alpha stat was the strategy needed to balance the acid-base state. Protamine was administered to reverse the heparin effect and establish appropriate coagulation activities after the end of CPB and the removal of arterial and venous cannulae.

Outcomes

The same care was offered to the patients perioperatively and in the ICU according to the protocol in our center. Right ventricular function was assessed by echocardiography postoperatively in the operating room and in the ICU. Patients with surgery-induced right ventricular dysfunction and increased central venous pressure were indicated for a milrinone infusion.

Checklists were drawn upon to collect necessary data from test sheets, anesthesia sheets, perfusion sheets, ICU sheets, and patient records. All the data were recorded directly. All the required information, including vital and hemodynamic symptoms, age, the type and duration of the operation, weight, the lactate level, the bleeding rate, the establishment of spontaneous respiration, the extubation time, the length of stay in the ICU, the urine output, and on-pump hemofiltration, as well as laboratory factors such as hemoglobin, hematocrit, albumin, blood urea nitrogen, creatinine, C-reactive protein, and the erythrocyte sedimentation rate (ESR), were measured and recorded at the preoperative time, after arterial catheter insertion, during CPB, after rewarming the patient, upon arrival to the ICU, and up to 24 hours after ICU admission.

Statistical Analysis

The data were coded and entered into the SPSS software. The normality of the distribution of variables was evaluated using the Kolmogorov–Smirnov or Shapiro–Wilk

tests. Quantitative data with normal and non-normal distributions were presented as the mean ± the standard deviation and the median (Q_1–Q_3), respectively. Normally distributed data were analyzed using parametric tests. Nonparametric tests were applied in the case of non-normal distributions. Repeated-measures ANOVA was employed to compare intragroup variables in successive measurements, an independent samples *t* test was used to compare the means between the groups, and the Mann–Whitney *U* test was utilized for the between-group comparisons of the non-normal data. Qualitative data were expressed as relative frequencies and percentages, and the frequencies of qualitative data between the 2 groups were compared using the χ^2 method. A *P* value of less than 0.05 was considered significant in all the statistical tests. The power of analysis was 0.8.

RESULTS

A total of 100 patients were evaluated in the present study. Albumin was randomly added to the prime solution of 50 patients and FFP to the prime solution of another 50 patients. Age, weight, body surface area, the aortic cross-clamp time, the CPB pump time, the length of mechanical ventilation, and ICU admission were not significantly different between the groups. The demographic characteristics, the cross-clamp time, the CPB time, the length of mechanical ventilation, and the length of ICU stay for each group are listed in Table 1.

There was no significant difference between the 2 groups in mean arterial pressure before anesthesia until the start of CPB. However, the use of these 2 products had a significant effect on changes in mean arterial pressure 1 hour after the onset of CPB until it was completed and 24 hours after ICU admission. Central venous pressure was evaluated in 2 the groups at 4 different time points, and no significant differences were observed between the 2 groups at any time (Table 2).

There was also no significant difference between the 2 groups regarding hemoglobin and hematocrit levels (Table 3).

Table 1: Demographic variables, cross-clamp times, cardiopulmonary bypass times, mechanical ventilation times, and ICU stay times among the study participants

Variables	Albumin Median (Q_1-Q_3)	Fresh Frozen Plasma Median (Q_1-Q_3)	*P* value
Age (d)	140 (57.5-360)	175 (80-440)	0.07
Weight (kg)	6 (3-8)	6.6 (4.3-9.12)	0.09
Body surface area (m^2)	0.33 (0.26-0.4)	0.36 (0.27-0.46)	0.07
Cardiopulmonary bypass time (min)	170 (128-217)	130 (103-184)	0.08
Cross-clamp time (min)	100 (87-145)	84 (63-126)	0.06
Mechanical ventilation (d)	3 (2-4)	2.5 (2-3.2)	0.06
Hospitalization (d)	13 (8-17)	10.2 (7.75-14)	0.73

Table 2: Mean arterial and central vein pressures among the study participants

Variables		Albumin Median (Q_1-Q_3)	Fresh Frozen Plasma Median (Q_1-Q_3)	*P* value
Mean Arterial Pressure (mm Hg)	Preoperative	50 (50-60)	56 (53-60)	0.10
	Anesthesia induction	53 (50-57)	54 (50-60)	0.38
	Start of bypass	46 (43-50)	47 (42-50)	0.23
	1 h after bypass	44 (41-46)	46 (42-50)	0.01
	Rewarming	49 (45-50)	51 (46-55)	0.01
	ICU entrance	53 (50-56)	56 (55-60)	0.006
	24 h after ICU entrance	55 (51-58)	56 (55-60)	0.03
Central Venous Pressure (mm Hg)	Preoperative	7 (6-9)	8 (6-9)	0.30
	Anesthesia induction	7 (6-8.5)	7 (6-9)	0.77
	ICU entrance	8 (7-9)	8 (7-9)	0.46
	24 h after ICU entrance	8 (7-9)	8 (7-9)	0.07

ICU, Intensive care unit

Table 3: Mean hemoglobin and hematocrit levels among the study participants

Variables	Measurement Time	Albumin Median (Q_1-Q_3)	Fresh Frozen Plasma Median (Q_1-Q_3)	*P* value
Hemoglobin (g/L)	Preoperative	13 (11-15)	11.9 (10.9-14)	0.12
	Anesthesia induction	12 (10.9-14)	11.2 (9.9-13.2)	0.15
	Start of bypass	10.2 (8.9-11)	9.2 (8.9-11)	0.43
	Rewarming	12 (11-12.8)	11.9 (11.2-12.9)	0.99
	ICU entrance	13 (12-14)	12.4 (12-13)	0.33
	24 h after ICU entrance	13 (12-12.5)	12.5 (12-13.5)	0.34
Hematocrit (%)	Preoperative	39 (33-44)	36 (33-42)	0.13
	Anesthesia induction	36 (32-41)	34 (30-40)	0.23
	Start of bypass	31 (27-32)	30 (27-32.6)	0.39
	Rewarming	36 (33-38)	36 (34-38)	0.73
	ICU entrance	38 (36-42)	37 (36-39)	0.40
	24 h after ICU entrance	38 (36-40.8)	37 (36-39)	0.18

ICU, Intensive care unit

Preoperative blood urea nitrogen levels were not significantly different between the albumin and FFP groups (9 [6.5-11.5] mg/dL vs 10 [8.7-11.2] mg/dL; *P*=0.77). Nonetheless, the post-ICU admission level of blood urea nitrogen in the albumin group was significantly lower than that in the FFP group (12 [9-16] mg/dL vs 16 [13-19] mg/dL; *P*<0.001), and the same trend was observed 24 hours after admission to the ICU (13 [9-14.5] mg/dL vs 16 [13-19] mg/dL; *P*<0.001). Preoperative creatinine levels were not significantly different between the albumin and FFP groups (0.5 [0.4-0.6] mg/dL vs 0.5 [0.4-0.6] mg/dL; *P*=0.77). Nevertheless, the post-ICU creatinine level in the albumin group was significantly lower than that in the FFP group (0.6 [0.5-0.7] mg/dL vs 0.8 [0.7-1.0] mg/dL; *P*<0.001), and there was no difference until 24 hours afterward (0.6 [0.5-0.7] mg/dL vs 0.8 [0.6-0.9] mg/dL; *P*<0.001). The changes in blood lactate and albumin levels were measured in the 2 groups at different time points. There was no significant difference between the 2 groups during these periods. Still, serum albumin levels were significantly increased in the group receiving the human albumin solution in their prime solution (Table 4).

Assessment of inflammatory factors showed that preoperative ESR was not significantly different between the albumin and FFP groups (3 [2-3.5] mm/h vs 2.9 [2.2-4.5] mm/h, respectively; *P*=0.34). After ICU admission, the ESR value was significantly lower in the albumin group than in the FFP recipients (4 [3-6] mm/h vs 6.2 [3.9-8] mm/h: *P*=0.008). The same conditions were also observed 1 hour after ICU admission (4.4 [3.5-5.5] mm/h vs 6 [3.8-7] mm/h; *P*=0.049). There was no significant difference between the albumin and FFP groups in terms of preoperative C-reactive protein levels (2.1 [1-4] mg/dL vs 3 [1-4] mg/dL, respectively; *P*=0.45). After ICU admission, the C-reactive protein level was similar in both groups (6 [4-9] mg/dL vs 5.6 [4.3-8] mg/dL; *P*=0.80). Similar conditions were observed 24 hours after ICU admission (5.8 [3.9-9.5] mg/dL vs 5.5 [4-8.5] mg/dL; *P*=0.61). Moreover, no difference was observed between the 2 groups in terms of red blood cell (RBC) transfusions in the operating room (200 vs 235; *P*=0.09), and the same conditions were present at ICU admission (100 vs 98; *P*=0.55). There was no significant difference between the 2 groups vis-à-vis chest tube drainage and the urinary output at the end of surgery, after ICU admission, and up to 24 hours after surgery, as well as hemofiltration during the pumping process (Table 5).

The results also showed no significant differences between the groups in terms of the need for inotropes in the operating room. However, only among the patients who received milrinone, the need for inotropes was significantly lower in the albumin recipients than in the FFP recipients during the first 24 hours of ICU admission (*P*=0.004) (Table 6).

Table 4: Mean albumin and lactate levels among the study participants

Variables	Measurement Time	Albumin Median (Q_1-Q_3)	Fresh Frozen Plasma Median (Q_1-Q_3)	*P* value
Albumin (mg/dL)	Preoperative	3.6 (3.3-3.8)	3.6 (3.4-3.8)	0.94
	ICU entrance	4 (3.7-4.2)	3.4 (3.2-3.5)	<0.001
	24 h after ICU entrance	4 (3.8-4.1)	3.4 (3.1-3.5)	<0.001
Lactate (mg/dL)	Preoperative	0.8 (0.6-0.9)	0.7 (0.5-1)	0.24
	Anesthesia induction	0.9 (0.8-1.2)	0.9 (0.7-1.2)	0.75
	Start of bypass	1.5 (1.2-1.8)	1.5 (1.2-2)	0.82
	1 h after bypass	1.9 (1.5-2.7)	2.2 (1.5-3)	0.44
	Rewarming	2.2 (1.6-3)	2.5 (1.9-3.1)	0.28
	ICU entrance	2.4 (2-3.4)	2.5 (2-3.7)	0.47
	24 h after ICU entrance	2.3 (1.8-3)	2 (1.5-3)	0.30

ICU, Intensive care unit

Table 5: Chest tube derange, urine output, and hemofiltration among the study participants

Variables		Albumin Median (Q_1-Q_3)	Fresh Frozen Plasma Median (Q_1-Q_3)	*P* value
Chest tube derange (mL)	At the OR	20 (15-20)	20 (15-20)	0.62
	First day at the ICU	20 (15-20)	20 (15-20)	0.85
	Second day at the ICU	50 (45-60)	50 (40-70)	0.90
Urine output (mL)	Operating room on CPB	200 (150-275)	180 (127-230)	0.23
	ICU entrance	200 (155-280)	180 (138-242)	0.33
	24 h after ICU entrance	330 (250-400)	320 (270-400)	0.62
Hemofiltration (mL)	During CPB	500 (425-600)	600 (450-760)	0.08

OR, Operating room; CPB, Cardiopulmonary bypass; ICU, Intensive care unit

Table 6: Inotrope use frequency in the OR and the ICU among the study participants

Variables		Albumin Frequency (%)	Fresh Frozen Plasma Frequency (%)	*P* value
Epinephrine (n)	OR	50 (100%)	50 (100%)	<0.001
	ICU	50 (100%)	49 (98%)	0.32
Norepinephrine (n)	OR	1 (2%)	1 (2%)	0.98
	ICU	4 (8%)	3 (6%)	0.67
Dopamine (n)	OR	43 (87%)	37 (74%)	0.08
	ICU	35 (71%)	26 (52%)	0.47
Milrinone (n)	OR	15 (30%)	23 (46%)	0.08
	ICU	4 (8%)	15 (30%)	0.004
Dobutamine (n)	OR	2 (4%)	0 (0.0%)	0.14
	ICU	2 (4%)	1 (2%)	0.54
Phenylephrine (n)	OR	2 (4%)	3 (6%)	0.66
	ICU	0 (0.0%)	3 (6%)	0.08

ICU, Intensive care unit; OR, Operating room

There was no significant difference between the albumin and FFP groups apropos of preoperative PaO_2 (256.00±161.13 vs 191.91±148.78, respectively; *P*=0.091) and PaO_2 after CPB (285.37±111.95 vs 254.92±121.93, respectively; *P*=0.291). The same conditions were also observed 24 hours after ICU admission (203.82±104.78 vs 248.84±110.06, respectively; *P*=0.91).

DISCUSSION

Congenital heart diseases constitute one of the most common congenital abnormalities in children, most of whom need CPB for many related surgeries. Choosing an appropriate prime solution can largely prevent the unintended complications of these surgeries such as pulmonary problems, coagulation disorders, prolonged intubation, prolonged ICU admission, metabolic disorders, and acid-base state disorders in children, especially infants. On the other hand, colloidal solutions such as human albumin should be used due to decreased oncotic pressure during the dilution of blood owing to the use of the prime solution. Albumin can prevent platelet activation, the release of inflammatory factors, and the initiation of the complement cascade by covering the CPB system and reducing blood contact with the nonphysiological system. It can also prevent brain, tissue, and pulmonary edema, as well as renal failure, by maintaining colloidal pressure. FFP also contains a blood product that includes coagulation factors such as albumin, immunoglobulin, and antithrombin, and could not only prevent tissue edema and renal failure but also coagulation disorders and bleeding by maintaining oncotic pressure.

The present study showed no significant differences between the 2 groups of albumin and FFP in terms of the cross-clamp time, the CPB time, the mechanical ventilation time, the length of stay in the ICU, the transfusion of blood and blood products, and the mortality rate. Both groups were also similar concerning clinical parameters, the intraoperative ultrafiltration rate, and the chest tube drainage rate. Blood parameters were similar between the groups except for urea and creatinine. Although serum urea and creatinine levels were similar in both groups before surgery, the urea and creatinine levels in the FFP recipients increased significantly compared with the albumin group after ICU admission. Nonetheless, there was no significant difference between the groups with respect to the urine output. However, an investigation of renal parameters showed a better renal function in the albumin group. Lee et al[14] in a prospective study examined the impact of albumin 20% on the incidence of postoperative AKI in patients undergoing off-pump coronary artery bypass graft surgery. They reported that the administration of human albumin 20% immediately preoperative could increase the rate of the urine output and reduce the risk of AKI after surgery. Patel et al[19] reported that the use of albumin in the CPB prime solution of children younger than 1 year did not significantly affect the urine output, serum urea, and creatinine in comparison with hydroxyethyl starch and the Ringer lactate solution when used as the priming fluid for CPB in pediatric cardiac surgery. Lee et al[14] identified serum albumin deficiency as the main cause of postoperative AKI.

The occurrence of inflammatory responses can affect systemic trends and sometimes lead to systemic disorders. These systemic trends include blood circulation, blood pressure, homeostasis, thrombosis, and renal, pulmonary, and hepatic disorders. Since postoperative immune stimulations can have devastating effects on different organs of the body and influence the postoperative recovery process, it seems that

the albumin solution is more appropriate than FFP because the present study also showed a further increase in ESR in the FFP group. We found concordant results in similar studies. The results of a systematic review study in 2015 showed a great risk of allergic reactions after the use of FFP in CPB operations.[20] However, Jong Wha Lee et al[18] used FFP in the CPB prime solution and examined its effects on coagulation factors in patients aged 1 month to 16 years scheduled for congenital heart surgery. The researchers noted that the addition of FFP to the prime solution in congenital and pediatric cardiac surgery reduced hemodilution-induced hemostatic complications immediately after CPB and improved the process of clot formation. Nevertheless, there was no significant difference between the groups in terms of the bleeding rate, chest tube drainage, and the need for blood products, and there were no similar results regarding the efficacy of FFP in reducing hemostatic complications.

The hemodynamic analysis of the patients in the 2 groups during the respective periods showed no significant differences between the 2 groups from before CPB to 1 hour afterward, while mean arterial pressure was significantly higher in the FFP group than in the albumin group during the time between the patients' warm-up until ICU admission and 24 hours afterward. However, the central venous pressure of the 2 groups was reported to be the same at all the time points. Examination of the patients in terms of the receipt of inotropes showed no significant differences between the groups, but the statistical results showed that milrinone was used in the FFP group more frequently than in the albumin group during the early hours of ICU admission. Since milrinone is an inotropic and vasodilator agent and is commonly used to reduce pulmonary hypertension and treat right ventricular failure after tetralogy of Fallot surgery, it appears that patients in the albumin group had a better right ventricular function.

Although higher mean arterial blood pressures in post-CPB time points were observed in the FFP group, a closer look at the difference between the 2 groups demonstrated minor changes, which could not be interpreted as clinically significant.

The interpretation of the results from the current study should be conservative. The limitations of the study include its relatively small population and the lack of a specific assay for cytokines and other inflammatory markers. Further studies with larger populations and assessments of more specific markers of the inflammatory response are warranted.

CONCLUSIONS

In our patients with FFP in their prime solution, a higher ESR value was observed. While there was no significant difference between the 2 groups concerning hemostasis, albumin offered the advantages of better kidney, liver, and cardiac functions.

REFERENCES

1. Eghtesady P, Brar AK and Hall M. Prioritizing quality improvement in pediatric cardiac surgery. *J Thorac Cardiovasc Surg* 2013; 145: 631-639; discussion 639-640. DOI: 10.1016/j.jtcvs2012.12.018.

2. Welke KF and Ungerleider RM. Mortality as an outcome parameter for pediatric heart surgery. *ASAIO journal* 2006; 52: 552-555.

3. Gorjipour F, Totonchi Z, Gholampour Dehaki M, et al. Serum levels of interleukin-6, interleukin-8, interleukin-10, and tumor necrosis factor-α, renal function biochemical parameters and clinical outcomes in pediatric cardiopulmonary bypass surgery. *Perfusion* 2019: 0267659119842470.

4. Gorjipour F, Dehaki MG, Totonchi Z, et al. Inflammatory cytokine response and cardiac troponin I changes in cardiopulmonary bypass using two cardioplegia solutions; del

Nido and modified St. Thomas': a randomized controlled trial. Perfusion 2017; 32: 394-402. DOI:10.1177/0267659117691119.

5. Farsad BF, Janipour M, Totonchi Z, et al. Effects of dexmedetomidine on surgical stress responses at patients under CABG. *Biosciences Biotechnology Research Asia* 2016; 13: 1537-1545.

6. Cholette JM, Faraoni D, Goobie SM, et al. Patient blood management in pediatric cardiac surgery: a review. *Anesthesia & Analgesia* 2018; 127: 1002-1016.

7. Richmond ME, Charette K, Chen JM, et al. The effect of cardiopulmonary bypass prime volume on the need for blood transfusion after pediatric cardiac surgery. *J Thorac Cardiovasc Surg* 2013; 145: 1058-1064. DOI: 10.1016/j.jtcvs2012.07.016.

8. Gorjipour F, Saeedzadeh T, Toloueitabar Y, et al. Remote ischemic preconditioning effects on inflammatory markers and myocardial protection in coronary artery bypass graft surgery. *Perfusion* 2020: 0267659120979293. DOI:10.1177/0267659120979293.

9. Sadeghpour Tabaei A, Mortazian M, Yaghoubi A ,et al. Modified Ultrafiltration in Coronary Artery Bypass Grafting: A Randomized, Double-Blinded, Controlled Clinical Trial. *Iranian Red Crescent medical journal* 2018; 20: e66187. Research Article 2018-09-01. DOI: 10.5812/ircmj.66187.

10. Liumbruno G, Bennardello F, Lattanzio A, et al. Recommendations for the use of albumin and immunoglobulins. *Blood transfusion* 2009; 7: 216.

11. Evans T. albumin as a drug—biological effects of albumin unrelated to oncotic pressure. *Alimentary pharmacology & therapeutics* 2002; 16: 6-11.

12. Hobson CE, Yavas SMS, D. SJ, et al. Acute kidney injury is associated with increased long-term mortality after cardiothoracic surgery. . *Circulation* 2012; 119: 2444-2453.

13. Lee E-H, Baek S-H, Chin J-H, et al. Preoperative hypoalbuminemia is a major risk factor for acute kidney injury following off-pump coronary artery bypass surgery. *Intensive care medicine* 2012; 38: 1478-1486.

14. Lee E-H, Kim W-J, Kim J-Y, et al. Effect of exogenous albumin on the incidence of postoperative acute kidney injury in patients undergoing off-pump coronary artery bypass surgery with a preoperative albumin level of less than 4.0 g/dl. *Anesthesiology: The Journal of the American Society of Anesthesiologists* 2016; 124: 1001-1011.

15. Stanworth SJ, Grant-Casey J, Lowe D, et al. The use of fresh-frozen plasma in England: high levels of inappropriate use in adults and children. *Transfusion* 2011; 51: 62-70.

16. Wallis JP and Dzik S. Is fresh frozen plasma overtransfused in the United States? *Transfusion* 2004;.1675-1674 :44

17. Wang T, Wang X, Liu J, et al. Substitution of artificial colloids for fresh frozen plasma in pediatric cardiopulmonary bypass surgery. *Paediatr Anaesth* 2018; 28: 914-923. DOI: 10.1111/pan.13473.

18. Lee JW, Yoo Y-C, Park HK, et al. Fresh frozen plasma in pump priming for congenital heart surgery: evaluation of effects on postoperative coagulation profiles using a fibrinogen assay and rotational thromboelastometry. *Yonsei Med J* 2013; 54: 752-762. DOI: 10.3349/ymj.2013.54.3.752.

19. Patel J, Prajapati M, Solanki A, et al. Comparison of albumin, hydroxyethyl starch and ringer lactate solution as priming fluid for cardiopulmonary bypass in paediatric cardiac surgery. *Journal of clinical and diagnostic research: JCDR* 2016; 10: UC01.

20. Desborough M, Sandu R, Brunskill SJ, et al. Fresh frozen plasma for cardiovascular surgery. *Cochrane Database of Systematic Reviews* 2015. DOI:10.1002/14651858.CD007614.pub2.