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Original Article

Comparison of the Effects Between Ringer's and Ringer's Lactate Administration as the Prime Solution on Perioperative Acid-Base Status in Pediatric Patients With Non-Cyanotic Diseases Undergoing Cardiac Surgeries

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ABSTRACT

Background: The solutions used to prepare the cardiopulmonary bypass (CPB) circuit are known to constitute some of the potential causes of metabolic acidosis at the onset of CPB. Solutions containing lactate, acetate, and other anions have a buffering effect owing to the metabolism of these anions into bicarbonate ions. Hence, the administration of lactate-containing solutions to children may lead to elevated serum lactate levels.

Methods: The present double-blind randomized clinical trial evaluated 50 non-cyanotic pediatric patients (2 groups of 25 cases) aged between 12 and 48 months undergoing cardiac surgeries. Ringer's solution and Ringer's lactate solution were each used in 1 study group as the CPB prime solution. The levels of pH, bicarbonate, base excess (BE), lactate, calcium, glucose, chloride, and arterial blood gas were measured at 4 different time points: before the initiation of CPB (T0) and then 5 (T1), 30 (T2), and 60 (T3) minutes after bypass commencement.

Results: The levels of pH at T1 and T2 were statistically different between the 2 groups (P=0.029 and P=0.001, respectively). The 2 groups were also statistically meaningfully different concerning T2 BE (P<0.0001). The mean HCO^{-}_{3} levels at T2 and T3 were statistically different between the groups (P<0.0001 and P=0.039, respectively). Lactate levels at T1 and T2 statistically significantly differed between the 2 groups (P<0.0001 and P=0.017, respectively).

Conclusions: The current study showed that Ringer's lactate solution as the CPB prime solution was more effective than Ringer's solution in reducing CPB-induced acidosis without increasing the circulatory lactate level. ***(Iranian Heart Journal 2023; 24(3): 6-14)***

KEYWORDS: Cardiopulmonary bypass, Prime solution, Metabolic acidosis, Lactate

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Cardiopulmonary bypass (CPB) is required to repair numerous congenital heart defects and diseases in infants and children. CPB circuits should be prepared with solutions termed "prime solutions" so that by the initiation of CPB, appropriate blood flow is accomplished without the risk of air embolism. [1] The optimal combination of CPB preparation solutions is still a matter of debate. In the past, preparation solutions were fluids with electrolyte content and osmolality similar to intravascular fluids. The characteristics of current solutions are such that when mixed with blood, they preserve the ability to deliver oxygen, excrete carbon dioxide, and maintain physiological homeostasis. [2]

The solutions used to prepare CPB circuits are known to be one of the potential causes of pH disturbances, causing metabolic acidosis at the onset of CPB. Acid-base imbalance secondary to CPB is considered iatrogenic and is secondary to the effect of prime solutions. [3,4] Metabolic acidosis also depends on osmotic colloid pressure and blood buffering capacity. [3] Several causes have been reported for CPB-induced metabolic acidosis, including elevated serum levels of lactate, chloride, and non-measurable anions. [5,6] In medical centers, various crystalloid solutions, such as normal saline, and balanced electrolyte solutions, such as Ringer's, Plasma-Lyte, Isolyte, Normosol, Hartmann's, and Ringer's lactate solution, are used for priming. [7] Balanced electrolyte solutions contain bicarbonate precursors, such as lactate, acetate, gluconate, and other anions, which are utilized to correct acidosis. [8]

In 2012, Hassani et al [9] compared Ringer's solution and Ringer's lactate solution as primary extracorporeal solutions in terms of metabolic acidosis in patients undergoing coronary artery bypass graft surgery. The results showed that Ringer's lactate solution caused fewer acid/base disturbances during the surgery and CPB support.

In 2007, Alston et al [10] reported a slight increase in lactate levels up to 1 day post-surgery. They attributed this phenomenon to the use of Hartmann's solution as the prime solution for the CPB machine and, therefore, decided to use a non-lactate solution instead of Hartmann's. Nonetheless, their findings showed more acidosis during CPB.

On the other hand, in a study by Morgan et al [11] on the prime solution of the CPB machine, the researchers compared a normal saline-containing solution with a normal saline-containing solution plus sodium bicarbonate. They found that using an anion-free solution, such as normal saline to which sodium bicarbonate had been added, was more effective than the Plasma-Lyte solution containing acetate and gluconate anions in preventing and controlling metabolic acidosis during CPB. The researchers considered higher importance for the role of non-measurable anions and their accumulation in the blood, leading to the development of metabolic acidosis during CPB.

As evidenced by the results of most of these studies, Ringer's lactate solution as the prime solution for the CPB machine exerts a greater effect on the prevention and control of metabolic acidosis during CPB than Ringer's solution. As these studies were conducted on adults, in the present study, we investigated the effects of the use of these 2 solutions on acid-base status and lactate levels during CPB in pediatric patients.

METHODS

Trial Design

The study protocol was approved by the Institutional Review Board of Rajaie Cardiovascular Medical and Research Center (Tehran, Iran) (code: RHC.AC.IR.REC.1395.42). The study was registered in the Iranian Registry of Clinical

Trials (registration number: IRCT20184007039222N1) .

Sample Size and Randomization Sequences

Fifty eligible pediatric patients aged between 12 and 48 months who were candidates for cardiac surgeries due to previously diagnosed non-cyanotic diseases were recruited in the study. Informed consent was signed by the parents or legal guardians of the recruited patients. The inclusion criteria were elective surgery, informed consent, serum lactate levels lower than 2 mmol/L, weight between 6 kg and 18 kg, and hemoglobin levels above 10 mg. The exclusion criteria were acid-base imbalance, redo surgeries, coagulopathy, liver and renal dysfunction, and ultrafiltration during bypass. Fifty sealed envelopes, each indicating either Group I or Group II, were prepared. After the patients were screened for eligibility, 1 envelope was opened randomly, and the indicated group was recorded for the patient. Double blinding was accomplished by assigning a trained perfusionist, blind to the patients' assigned group and the solution type used for priming, to data gathering. Additionally, the principal researchers of the study were not involved in data gathering.

The preparation of the bypass device and circuit with the prime solution was performed by another trained perfusionist so that other perfusionists, anesthesiologists, and surgeons were unaware of the patients' assigned group. Efforts were made to ensure that all the patients had the same condition for anesthesia, surgery, and CPB support. The only difference between the groups was the prime solution, which was Ringer's in 1 group and Ringer's lactate in the other.

Interventions

Upon the patient's entrance into the operating room, primary monitoring, including electrocardiography and pulse oximetry, was started. A peripheral intravenous line was established with an angiocatheter commensurate with the patient's weight and age.

Before the start of open-heart surgery, all the patients received 10 mL/kg of crystalloid solution (Ringer's).

Anesthesia induction was performed using 10 to 15 µg/kg of fentanyl and 0.1 mg/kg of midazolam. In order to ease endotracheal intubation, we injected a muscle relaxant (pancuronium) as an intravenous bolus of 0.1 mg/kg and at intervals of 45 minutes to 60 minutes during surgery for the maintenance of muscle relaxation, if necessary. Anesthesia was maintained using fentanyl (5 µg/kg/h) and midazolam (1 µg/kg/min). Then, mechanical ventilation was started at 10 mL/kg tidal volume, set with the patient's respiration rate and age.

$PaCO_2$ was kept between 30 mm Hg and 35 mm Hg, and the mean arterial pressure was preserved between 45 mm Hg and 60 mm Hg. During bypass support, acid-base management was performed using the α-Stat Acid-Base Management Strategy, and $PaCO_2$ was kept between 35 mm Hg and 40 mm Hg. Hypotension and hypertension during CPB support were treated with epinephrine and TNG, respectively. In the case of inotrope or vasopressor use, the dosage was recorded in the patient's profile. Heparin (300 IU/kg) was used as an anticoagulant. After an active clotting time of higher than 480 seconds was achieved, cannulation and CPB initiation were allowed. The use of the prime solution caused blood thinning and decreased hematocrit levels. In the case of a significant decrease in hematocrit, packed cells were added to the circuit. In patients whose preoperative hemoglobin and hematocrit were low, fresh-packed cells were added to the prime solution, and the same blood product was used intraoperatively until hematocrit levels reached 25% to 30%. The

total amount of the added packed cell for each patient was recorded as mL/kg. During surgery, moderate hypothermia was induced up to 32 ℃. Other monitoring measures included arterial blood gasses, nasopharyngeal temperature, and urine output volume. Total $NaHCO_3$ (mL/kg) was used for the correction of acidosis. As room temperature can affect acidosis and lactate levels, mercury-in-glass thermometers were utilized. Any use of warming systems, such as forced-air warming blankets or warm touch systems, was recorded. At the end of surgery and after hemodynamic stability was confirmed, the patients were weaned from the CPB device, and heparin was reversed by protamine administration.

Trial Outcomes

The levels of arterial blood gasses, pH, bicarbonate, BE, lactate, calcium, blood glucose, chloride, sodium, and potassium were measured at 4 different time points: before the initiation of CPB (T0) and then 5 (T1), 30 (T2), and 60 (T3) minutes after bypass commencement. The CARE diagnostica device was used to measure blood lactate and glucose levels, while the GASTAT-603ie device was employed to measure other variables.

Statistical Analysis

Data analysis was performed using the SPSS software, version 19 (IBM Corp, USA). Descriptive statistics, including measures of central tendency (mean and standard deviation), coefficients of dispersion, and frequencies, were used to describe the study's variables in both groups. Additionally, repeated measures of ANOVA, Mann–Whitney *U*, independent samples *t*, χ^2, and the Wilcoxon signed ranks tests were applied to compare the results. All *P* values less than 0.05 were assumed as significant results.

RESULTS

The demographic and intraoperative variables of the patients, including age, gender, type of the underlying disease, height, weight, body surface area, CPB duration, and aortic cross-clamp time, were compared and analyzed using the independent samples *t* test. The results showed no statistically significant differences between the 2 groups (*P*>0.05).

Comparisons of pH levels between the 2 groups at different time points (T0–T3) were performed using the independent samples *t* test. The level of pH was significantly higher in the Ringer's lactate solution group than in the Ringer's solution group at T1 (7.37±0.047 vs 7.34±0.040; *P*=0.029) and T2 (7.35±0.052 vs 7.30±0.054; *P*=0.001).

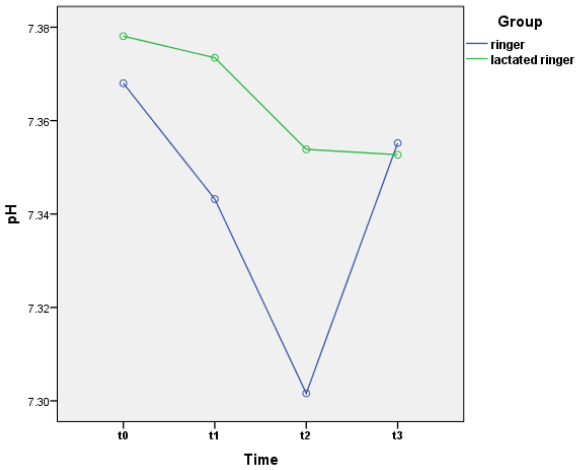

Figure 1: The image presents a comparison of pH levels between the 2 groups at different time points.

The statistical analyses of arterial blood gas elements between the 2 groups at different time points, from pre-bypass to 1 hour after bypass initiation, were performed. Furthermore, comparisons of base excess (BE) between the 2 groups at different time points (T0–T3) were made. BE levels were significantly higher in the Ringer's lactate solution group than in the Ringer's solution group at T2 (7-4.0 [-5~-3.0] vs -7.0 [-6~-7.5]; *P*=0.0001)

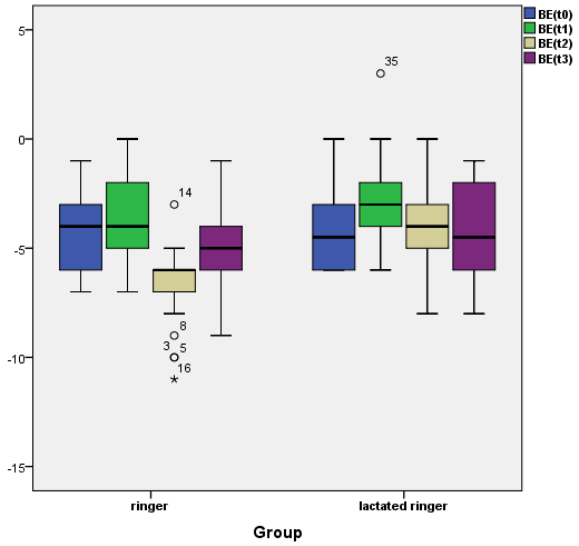

Figure 2: The image presents a comparison of base excess between the 2 groups at different time points.

The comparison of bicarbonate levels between the 2 groups at different time points (T0–T3) was performed. Bicarbonate levels were significantly higher in the Ringer's lactate solution group than in the Ringer's solution group at T2 (21 [20.0–21.0] vs 18 [17.0–20.0]; *P*=0.0001) and T3 (20 [19.0–21.25] vs 19 [18.0–20.0); *P*=0.039).

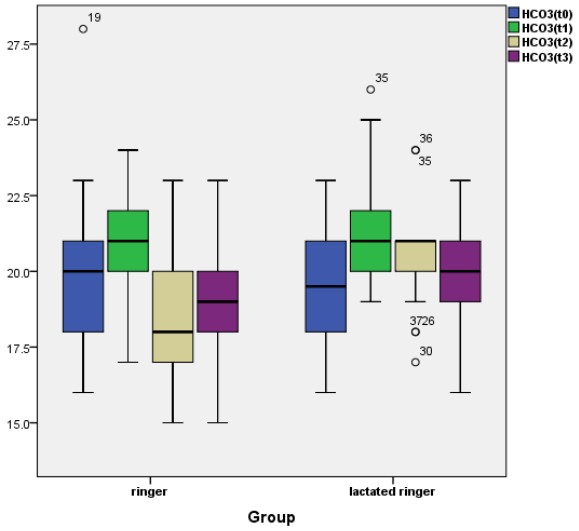

Figure 3: The image presents a comparison of bicarbonate levels between the 2 groups at different time points.

Comparisons of lactate levels between the 2 groups at different time points (T0–T3) were performed. Lactate levels at T1 and T2 were significantly higher in the Ringer's lactate solution group than in the Ringer's solution group (2.40 [1.85–3.50] vs 1.10 [0.80–1.45]; *P*=0.0001 and 1.70 [1.17–2.20] vs 1.20 [0.85–1.75]; *P*=0.017). Nevertheless, at T3, lactate levels were higher in the Ringer's solution group than in the Ringer's lactate solution group, although the difference was not statistically significant (1.40 [1.07–2.02] vs 1.60 [1.20–1.90; *P*=0.777).

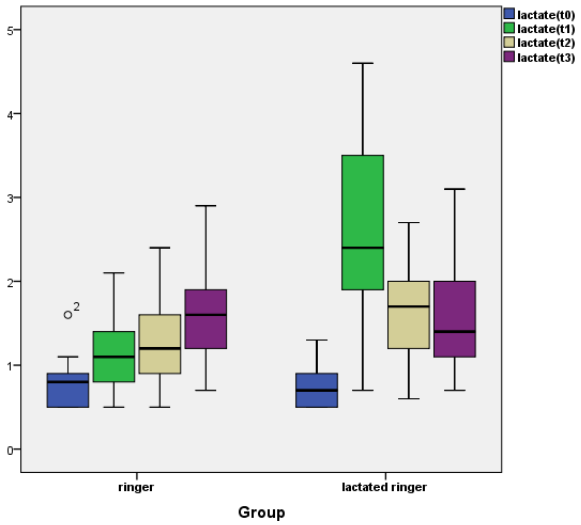

Figure 4: The image presents a comparison of lactate levels between the 2 groups at different time points.

Table 1: Comparisons of demographic and intraoperative measures between the 2 study groups

Variable	Ringer's Lactate (n=25) Frequency or Mean± SD	Ringer's (n=25) Frequency or Mean± SD	*P* value	Statistical Test
Gender, %			0.331	X^2
male	15 (60)	12 (48)		
female	10	13		
Type of Disease				
ASD	4	2	0.682	
VSD	18	17		
ASD+VSD	1	2		
AV canal	2	3		
AS	0	1		
Age, mon	34.6 ±9.7	31.4±11.9	0.249	Independent *t* test
Weight, kg	10.9 ±2.1	11.1±2.3	0.735	
Height, cm	88.6±8.5	84.4±9.3	0.070	
Body mass, m^2	0.51 ±0.06	0.5±0.07	0.707	
CPB time, min	76.7±20.0	86.3±19.7	0.92	
Aortic cross-clamp time, min	49.4±14.5	55.7±14.8	0.132	

ASD, Atrial septal defect; VSD, Ventricular septal defect; AV, Atrioventricular; CPB, Cardiopulmonary bypass

Table 2: Comparisons of arterial blood gas between the 2 study groups at different time points

Variable/Time	Ringer's Lactate (n=25) Mean ± SD or Median (IQR_1–IQR_3)	Ringer's (n=25) Mean ± SD or Median (IQR_1–IQR_3)	*P* value
pH levels / T0	7.37 ±0.047	7.36 ±0.058	0.507
pH levels / T1	7.37 ±0.047	7.34 ±0.040	0.029
pH levels / T2	7.35 ±0.052	7.30 ±0.054	0.001
pH levels / T3	7.35 ±0.042	7.35 ±0.059	0.865
PaO_2 (mm Hg) /T0	216 (142-262)	179 (165-200)	0.159
PaO_2 (mm Hg) /T1	252 (226-294)	267 (167-298)	0.478
PaO_2 (mm Hg) /T2	245 (220-274)	262 (237-297)	0.069
PaO_2 (mm Hg) /T3	191 (144-268)	114 (186-286)	0.173
Base excess/T0	-4.5 (-6~-3)	-4.0 (-6~-3.5)	0.763
Base excess/T1	-3.0 (-4~-2.0)	-4.0 (-2~-5.5)	0.111
Base excess/T2	-4.0 (-5~-3.0)	-7.0 (-6~-7.5)	0.0001>
Base excess/T3	-4.5 (-6~-2.0)	-6.0 (-4.5~-6.0)	0.051
HCO^-_3 (mmol/L) /T0	19.5 (18-21)	20 (18.5-21)	0.511
HCO^-_3 (mmol/L) /T1	21 (20.5-22.25)	21 (20.0-22.5)	0.286
HCO^-_3 (mmol/L) /T2	21 (20.0-21.0)	18 (17.0-20.0)	0.0001>
HCO^-_3 (mmol/L) /T3	20 (19.0-21.25)	19 (18.0-20.-0)	0.039
Lactate levels (mmol/L) /T0	0.70 (0.50.92)	0.80 (0.50-0.90)	0.802
Lactate levels (mmol/L) /T1	2.40 (1.85-3.50)	1.10 (0.80-1.45)	0.0001
Lactate levels (mmol/L) /T2	1.70 (1.17-2.20)	1.20 (0.85-1.75)	0.017
Lactate levels (mmol/L)/ T3	1.40 (1.07-2.02)	1.60 (1.20-1.90)	0.777
$PaCO_2$ (mm Hg)/T0	34 (30.5-38.5)	34 (30.5-37.5)	0.521
$PaCO_2$ (mm Hg)/T1	38 (33.75-40.0)	34 (33.0-41.0)	0.602
$PaCO_2$ (mm Hg)/T2	38 (32.0-40.0)	37 (32.0-40.0)	0.921
$PaCO_2$ (mm Hg)/T3	38 (34.75-39.25)	35 (3.0-39.0	0.147

DISCUSSION

In the present study, we evaluated the administration of Ringer's lactate solution and Ringer's solution as CPB prime solutions in pediatric patients with non-cyanotic diseases undergoing cardiac surgeries. We compared the effects of the 2 solutions on acid-base status as well as lactate levels between a Ringer's solution group and a Ringer's lactate solution group. Our results yielded no statistically significant differences between the 2 groups concerning PaO_2, PcO_2, potassium, calcium, blood glucose, total administered packed cells, urine output, and inotropic support at different time points (before the initiation of CPB [T0] and then 5 [T1], 30 [T2], and 60 [T3] minutes after bypass initiation). As these variables affect the acid-base balance and serum lactate levels, it can be assumed that no significant differences existed between the administration of Ringer's solution and Ringer's lactate solution. In the Ringer's lactate solution group, pH levels at T1 remained unchanged compared with their pre-bypass levels. The results in the same time interval showed a significant increase in $PaCO_2$, HCO^-_3, BE, and lactate levels, while the level of chloride was unchanged. A significant decrease in hematocrit during this time interval indicated blood dilution at the beginning of CPB, although this phenomenon is unavoidable and can be predicted. Despite the significant rise in $PaCO_2$ and blood thinning at the beginning of the bypass, pH levels remained unchanged at T1. This finding can be explained by the presence of sodium bicarbonate in the prime solution, causing elevated BE and HCO^-_3. The same condition (although slighter) was noted in the other study group. In the Ringer's solution group and after the initiation of CPB, pH levels decreased compared with their pre-bypass levels, although this drop was not statistically significant. At the same time interval, $PaCO_2$ levels rose significantly. The levels of BE also exhibited an increase, but this rise was not statistically meaningful, while HCO^-_3 levels remained unchanged. Still, immediately after the initiation of CPB, a significant rise in chloride levels was noted. Given the elevation in $PaCO_2$ levels in both groups at T1 and the absence of a significant difference in $PaCO_2$ levels between the 2 groups at this time point, the effects of respiratory status on pH levels can be considered to be the same in both study groups. Regarding the significantly higher level of chloride in the Ringer's solution group and the higher level of BE in the Ringer's lactate solution group during this time interval, the significant decrease in pH levels in the Ringer's solution group can be attributed to the increase in chlorine levels and metabolic and hyperchloremic acidosis. However, sodium bicarbonate in the prime solution caused a reduction in the severity of this acidosis.

Himpe et al [12] also showed that although non-buffering solutions, such as Ringer's, are expected to increase serum chlorine levels besides reducing SID and subsequent dropping of pH levels, at the beginning of CPB, the level of pH did not significantly decrease. They attributed this phenomenon to the buffer (OH-) added to the prime solution. In the Ringer's solution group and at T1 and T2 (5 and 30 minutes after the initiation of CPB), pH levels were significantly lower than those in the Ringer's lactate solution group. At T3, pH levels were the same in the 2 groups, and there was no significant difference. Additionally, at all 3 time points (T1, T2, and T3), BE levels in the Ringer's solution group were lower than those in the other group, and this difference was statistically significant at T2. Serum bicarbonate levels before the initiation of the bypass were higher in the Ringer's solution group than in the Ringer's lactate group, but this

difference was not significant. Nonetheless, at time points of T2 and T3, bicarbonate levels were higher in the Ringer's lactate group, which was statistically significant. Additionally, the total amount of sodium bicarbonate used to correct acidosis during CPB was higher in the Ringer's solution group at all 3 time points. This difference was significant at T2 and T3. As the comparison of the study variables, including pH, BE, HCO^{-}_{3}, and the total amount of sodium bicarbonate intake, between the 2 groups indicated, fewer fluctuations in acidosis status were noted in the Ringer's lactate solution group. In addition, the results showed that in the Ringer's solution group, the amount of lactate was higher and the amount of chloride was lower. Lactate levels were similar in both groups before the start of CPB; however, after the initiation of CPB, a significant increase in serum lactate levels in both groups was noted, which was significantly higher in the Ringer's lactate solution group than in the Ringer's solution group at T1 and T2. This rise at the beginning of CPB can be explained by the presence of exogenous lactate in the Ringer's lactate solution group compared with the Ringer's solution group. In a study by Svenmarker et al [13] on the effects of the prime solution on serum lactate concentrations, it was noted that the administration of lactate-containing solutions significantly increased blood lactate levels. Serum lactate levels in the Ringer's lactate solution group decreased at T3 (60 minutes after the initiation of the bypass). On the other hand, in the Ringer's solution group, serum lactate levels rose, such that lactate levels were slightly higher than those in the Ringer's lactate solution group, although this difference was not significant. This finding may be explained by the metabolism of exogenous lactate and its conversion to bicarbonate in the Ringer's lactate solution group. Further, based on previous studies, including a study by Kim et al [14] in 2013, a gradual increase in serum lactate levels in the Ringer's solution group can be attributed to the greater amount of sodium bicarbonate injected for the correction of acidosis.

Hasani et al [9] compared Ringer's solution and Ringer's lactate solution as CPB prime solutions in adults and reported similar results. In their study, the pH level of the Ringer's solution group during bypass was significantly lower than that of the Ringer's lactate solution group. The researchers attributed this finding to a significant rise in chlorine concentrations in the Ringer's solution group and the attenuating effect of exogenous lactate on metabolic acidosis.

Liskaser et al [15] investigated the effects of the prime solution on CPB-induced acidosis during cardiac surgeries in adults and achieved similar results. In their study, standard BE levels and acidosis incidence were higher in the Ringer's lactate solution group than in the Ringer's solution group. Be that as it may, since the level of SID was not significantly different between the 2 groups, the researchers highlighted the effects of non-measurable anions on the state of acidosis during bypass.

CONCLUSIONS

Based on the findings of the present study, and chiming in with most similar studies in adults, it can be concluded that Ringer's lactate solution as the prime solution in pediatric CPB has a greater effect on the prevention of metabolic acidosis than Ringer's solution. This phenomenon can be attributed to the debilitating effect of exogenous lactate on metabolic acidosis and the role of chloride in the development of acidosis. In addition, in patients for whom exogenous lactate was administered, serum lactate levels decreased to the normal range after an initial increase at the beginning of the bypass, as in adult studies. According to

these results, it can be concluded that normal metabolism and the clearance of exogenous lactate in our pediatric patients prevented lactate accumulation and raised its serum level.

Conflict of Interest: There is no conflict of interest.
Ethics Committee's Code:
(RHC.AC.IR.REC.1395.42)
Registration number:
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