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ORIGINAL ARTICLE / ÖZGÜN MAKALE

Effect of cardiopulmonary bypass on late-onset hyperlactatemia after pediatric cardiac surgery

Pediyatrik kardiyak cerrahi sonrası kardiyopulmoner baypasın geç başlangıçlı hiperlaktatemi üzerine etkisi

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ABSTRACT

Background: This study aimed to investigate the effect of operative and postoperative parameters on late-onset hyperlactatemia (LOHL) after cardiac surgery in the pediatric patient population.

Methods: One hundred fifty-nine ventricular septal defect patients (77 males, 82 females; mean age: 8.0±8.6 years; range, 1 to 48 years) were retrospectively examined between August 2020 and February 2023. Patients with the highest lactate value measured between 6 to 12 h postoperatively <3 mmol/L were defined as Group 1, and those with lactate values ≥3 mmol/L (LOHL) were included in Group 2.

Results: Cardiopulmonary bypass (CPB) time, aortic cross-clamp time, and CPB flow did not differ between groups (p=0.916, p=0.729, and p=0.699, respectively). The difference between partial oxygen pressure (PaO_2) in the first blood gas obtained after CPB was statistically significant (p=0.017). The lactate level measured in the first arterial blood gas obtained after CPB was 1.74±0.61 mmol/L in Group 1 and 3.01±1.63 mmol/L in Group 2 (p<0.001). The PaO_2 in the arterial blood gas measured at 6 h postoperatively was 129.22±61.20 mmHg in Group 1 and 156.07±64.49 mmHg in Group 2 (p=0.046).

Conclusion: The development of hyperlactatemia due to ischemia in the early post-CPB period may affect the development of LOHL. Microcirculatory changes at the tissue level may play a role in the etiology of LOHL.

Keywords: Late onset hyperlactatemia, pediatric cardiac surgery, ventricular septal defect.

ÖZ

Amaç: Bu çalışmada, pediatrik hasta popülasyonunda kardiyak cerrahi sonrası ameliyat sırası ve ameliyat sonrası parametrelerin geç başlangıçlı hiperlaktateminin (GBHL) üzerine etkisi araştırıldı.

Çalışma planı: Ağutsos 2020-Şubat 2023 tarihleri arasında ameliyat edilmiş 159 ventriküler septal defekt hastası (77 erkek, 82 kız; ort. yaş: 8.0±8.6 yıl; dağılım, 1-48 yıl) retrospektif olarak incelendi. Ameliyat sonrası 6-12 saatler arası ölçülen en yüksek laktat değeri <3 mmol/L olan hastalar Grup 1 olarak tanımlandı, ≥3 mmol/L (GBHL) olan hastalar Grup 2'ye dahil edildi.

Bulgular: Kardiyopulmoner baypas (KPB) zamanı, aortik kros klemp zamanı, KPB akımı açısından gruplar arası fark gözlenmedi (sırası ile p=0.916, p=0.729 ve p=0.699). Kardiyopulmoner baypas sonrası alınan ilk kan gazında parsiyel oksijen basıncı (PaO_2) arasında gruplar arası fark istatistiksel olarak anlamlı idi (p=0.017). Kardiyopulmoner baypas sonrası alınan ilk arteriyel kan gazında ölçülen laktat seviyesi Grup 1'de 1.74±0.61 mmol/L iken Grup 2'de 3.01±1.63 mmol/L idi (p<0.001). Ameliyat sonrası 6. saatte bakılan arteriyel kan gazındaki PaO_2 Grup 1'de 129.22±61.20 mmHg, Grup 2'de 156.07±64.49 mmHg olarak saptandı (p=0.046).

Sonuç: Erken dönemde iskemiye bağlı hiperlaktatemi gelişimi, KPB sonrasında LOHL gelişimini etkileyebilir. Doku seviyesinde mikrodolaşım değişiklikleri, LOHL etiyolojisinde bir rol oynayabilir.

Anahtar sözcükler: Geç başlangıçlı hiperlaktatemi, pediatrik kardiyak cerrahi, ventriküler septal defekt.

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Late-onset hyperlactatemia (LOHL) is known to be a benign phenomenon developing approximately 6 to 12 h after cardiac surgery, and unlike early-onset hyperlactatemia (EOHL) (0-6 hours), it is not associated with low cardiac output and ischemia and does not cause mortality and morbidity.[1] It occurs in approximately 10 to 20% of patients after cardiac surgery despite adequate cardiac output.[2-5] There are various hypotheses regarding the factors that cause the development of LOHL, including hyperglycemia, bleeding, glucogenesis due to stress response, and exogenous epinephrine.[1,6-11] There is limited data in the literature regarding the relationship between changes in operative parameters, particularly during cardiopulmonary bypass (CPB) and LOHL,[12] and the etiology of LOHL is not fully understood. The present study aimed to investigate the effect of operative and postoperative parameters on LOHL and whether LOHL causes mortality and morbidity in a pediatric patient population undergoing cardiac surgery.

PATIENTS AND METHODS

One hundred fifty-nine ventricular septal defect (VSD) patients (77 males, 82 females; mean age: 8.0±8.6 years; range, 1 to 48 years) operated at the Başakşehir Çam and Sakura City Hospital, Department of Pediatric Cardiovascular Surgery between August 2020 and February 2023 were retrospectively analyzed. Patients who underwent tricuspid valve repair, atrial septal defect (ASD) closure, and patent ductus arteriosus closure in addition to VSD closure were included in the study. Patients who underwent additional procedures apart from these procedures were excluded from the study. Patients with terminal intraoperative and early postoperative period (0 to 6 h) lactate values above 3 mmol/L were excluded. Patients with preoperative intubation, previous cardiopulmonary resuscitation, preoperative low cardiac output (need for preoperative inotropic support), known renal or hepatic insufficiency, diabetes mellitus, and history of preoperative catheterization due to delayed diagnosis were excluded. The study protocol was approved by the Başakşehir Çam and Sakura City Hospital Clinical Research Ethics Committee (date: 12.07.2023, no: 2023-286). Written informed consent was obtained from the parents of the patients included in the study. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Late-onset hyperlactatemia was defined as 6 to 12 h from intensive care unit (ICU) admission in some studies.[1,3] In our study, we defined LOHL as hyperlactatemia (HL) occurring after the 6 h postoperatively. Patients with the highest lactate value measured between 6 to 12 hours postoperatively <3 mmol/L were defined as Group 1, and those ≥3 mmol/L (LOHL) were included in Group 2.[4,13]

The arithmetic mean of the total mean arterial pressure values measured during aortic cross-clamping (ACC) was accepted as the mean blood pressure during ACC.

Vasoactive inotropic score (VIS) was calculated with the following formula: dopamine (μg/kg/min) + dobutamine (μg/kg/min) + 100 × epinephrine (μg/kg/min) + 100 × norepinephrine (μg/kg/min) +10 × milrinone (μg/kg/min) + 10,000 × vasopressin (units/kg/min).[14]

Major adverse events (MAEs) included complete atrioventricular block requiring pacemaker implantation, renal failure, diaphragmatic paralysis, neurological deficit, unplanned reoperation due to residual lesions, sudden circulatory arrest, need for postoperative mechanical circulation support, or death.[15] Renal failure was considered temporary or permanent depending on dialysis need.

Surgical techniques

All patients underwent CPB with bicaval venous and aortic arterial cannulation following standard median sternotomy. The diastolic arrest was achieved by administering antegrade del Nido cardioplegia, and the VSD was closed using an autologous pericardial patch treated with glutaraldehyde in all patients.

The Cobe-Stockert S5 heart-lung machine (Sorin Group Italia, Mirandola, Italy) was used in all patients. Terumo Capiox FX05 (Terumo Cardiovascular Systems Corporation, Tokyo, Japan) oxygenator was used for patients with a calculated CPB flow of 0 to 1200 mL/kg/min, and Terumo Capiox FX15 (Terumo Cardiovascular Systems Corporation, Tokyo, Japan) oxygenator was used for patients with a CPB flow above 1200 mL/kg/min. All operations were performed under mild hypothermia (32 to 34°C). During CPB, blood pH level was aimed to be 7.35 to 7.40, partial oxygen pressure (PaO_2) >200 mmHg, partial carbon dioxide pressure 35 to 40 mmHg, and mixed venous oxygen saturation >75%. Sets were washed with the prime solution. The prime solution consisted of Isolyte S (Koçak Farma, İstanbul, Türkiye), erythrocyte suspension, fresh frozen

plasma, sodium bicarbonate (1 mL/kg), heparin (250 IU/kg), prednisolone (10 mg/kg), cefazolin (25 mg/kg), and mannitol (250 mg/kg).

Postoperative treatment protocol

A one-third saline solution or normal saline solution was routinely used in the postoperative period. Ringer lactate solution was not used for maintenance fluid or volume replacement in any patient preoperatively, operatively, or postoperatively. We routinely used milrinone (0.5 mcg/kg/min), cefazolin (4×20 mg/kg/dose), pantoprazole (1 mg/kg), paracetamol (4×10 mg/kg/dose), and acetylcysteine (20 mg/kg/day) in all patients. Morphine (0.1 mg/kg/dose) was administered as needed for pain control. In patients requiring inotropic support in addition to milrinone, norepinephrine was started at a dose of 0.03 mcg/kg/min as the first choice.

Statistical analysis

Statistical analyzes were performed using IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). The normal distribution of variables was evaluated visual (histogram and probability graphs) and analytical (Kolmogorov-Smirnov/Shapiro-Wilk tests) methods. Descriptive analysis was performed using frequency tables for categorical variables and mean ± standard deviations (SD) for normally distributed variables. Whether the obtained quantitative variables demonstrated significant differences according to the groups was analyzed by the independent samples t-test, and the relationship between categorical variables and study groups was analyzed by the chi-square test. Analyzes were performed with IBM SPSS version 20.0 software at a 95% confidence level. The level of statistical significance was set at $p<0.05$.

RESULTS

Lactate levels measured between 6 to 12 h were ≥3 mmol/L in 33 (20.7%) patients. No statistically significant difference was determined between the groups in terms of age, weight, body surface area, sex, and genetic anomaly incidence (p=0.978, p=0.215, p=0.834, p=0.426, and p=0.499, respectively; Table 1).

No statistically significant difference was determined between the groups in terms of CPB flow, duration of ACC, CPB time, lowest body temperature, ultrafiltration volume, and the mean arterial pressure during ACC (p=0.699, p=0.69, p=0.56, p=0.752, p=0.166, and p=0.272, respectively; Table 2, Figure 1). However, in the first blood gas after CPB, the PaO_2 measured in arterial blood gas was 131.67±81.10 mmHg in Group 1 and 171.44±91.52 mmHg in Group 2, and the difference between the groups was statistically significant (p=0.017; Figure 2). The lactate level measured in the first arterial blood gas following CPB was 1.74±0.61 mmol/L in Group 1 and 3.01±1.63 mmol/L in Group 2 ($p<0.001$). The highest lactate value measured between the 6 and 12 h was 1.87±0.52 mmol/L in Group 1 and 4.45±1.93 mmol/L in Group 2 (Table 2).

There was no statistically significant difference between the groups regarding PaO_2, saturation of oxygen (SaO_2), and glucose levels in the first arterial blood gas obtained at 1 h postoperatively (p=0.270, p=0.253, and p=0.239, respectively; Table 2). The PaO_2 in the arterial blood gas measured at 6 h postoperatively was 129.22±61.20 mmHg

Table 1. Demographic data

	Group 1			Group 2			
Variables	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (month)			7.9±9.2			8.0±8.0	0.978
Weight (kg)			6.06±3.2			6.5±3.3	0.215
Body surface area (m^2)			0.3±0.1			0.3±0.1	0.834
Sex							0.426
Female	64	50.8		18	54.5		
Male	62	49.2		15	45.5		
Syndrome							0.499
No	89	70.6		24	72.7		
Yes	37	29.4		9	27.3		

SD: Standard deviation.

Table 2. Operative and postoperative parameters

	Group 1	Group 2	
Variables	Mean±SD	Mean±SD	*p*
ACC time (min)	59.32±20.28	57.91±22.45	0.729
CPB time (min)	78.09±25.64	77.55±28.78	0.916
Operation time (min)	207.30±42.46	206.67±70.01	0.948
Anesthesia time (min)	298.15±53.19	291.82±79.63	0.589
UF volume (mL/kg)	77.79±61.50	61.94±37.08	0.166
Mean ABP	55.80±9.02	53.76±10.78	0.272
Flow (mL/dk)	845.34±341.29	869.06±329.00	0.722
Flow (mL/dk/kg)	140.04±21.4	140.4±25.9	0.699
Temperature (°C)	32.94±1.40	33.03±1.33	0.752
ES usage (mL/kg)	43.76±25.90	40.03±21.67	0.448
FFP usage (mL/kg)	27.33±18.37	22.36±16.18	0.159
After CPB PaO_2 (mmHg)	131.67±81.10	171.44±91.52	**0.017***
After CPB SaO_2 (%)	97.54±4.05	96.08±8.44	0.159
After CPB ABG Hb (g/dL)	11.19±1.33	10.89±1.48	0.260
After CPB ABG Htc (%)	34.33±4.10	33.38±4.56	0.255
After CPB ABG glucose (mg/dL)	184.44±97.67	200.75±41.45	0.358
After CPB ABG lactate (mmol/L)	1.74±0.61	3.01±1.63	**0.000***
After CPB VBG $PmvO_2$ (mmHg)	47.11±25.51	47.75±17.55	0.894
After CPB VBG $SmvO_2$ (%)	77.23±13.78	76.82±19.00	0.892
Postoperative 1st h glucose (mg/dL)	169.27±47.74	158.10±40.31	0.239
Postoperative 1st h ABG SaO_2 (%)	97.57±4.31	98.50±2.00	0.253
Postoperative 1st h ABG PaO_2 (mmHg)	154.87±90.82	135.24±68.68	0.270
Postoperative 1st h VBG $SmvO_2$ (%)	70.18±17.24	75.71±15.16	0.110
Postoperative 1st h VBG $PmvO_2$ (mmHg)	39.65±12.50	43.34±13.22	0.154
Postoperative 6th h glucose (mg/dL)	161.54±57.91	163.41±51.12	0.868
Postoperative 6th h ABG saturation (%)	97.07±4.27	98.84±1.50	**0.036***
Postoperative 6th h ABG PaO_2 (mmHg)	129.22±61.20	156.07±64.49	**0.046***
Postoperative 6th h VBG $SmvO_2$ (%)	67.22±11.21	66.67±15.50	0.923
Postoperative 6th h VBG $PmvO_2$ (mmHg)	34.99±6.91	37.40±9.38	0.495
Drainage postoperative 6th h (mL/kg)	4.71±6.20	4.48±3.27	0.843
Drainage postoperative 12th h (mL/kg)	8.13±7.63	7.61±5.00	0.711
Drainage postoperative 24th h (mL/kg)	14.13±10.43	15.48±11.89	0.519
Drainage postoperative 48th h (mL/kg)	17.39±12.08	19.45±14.33	0.402

SD: Standard deviation; ACC: Aortic cross clamp; CPB: Cardiopulmonary bypass; UF: Ultrafiltration, ABP: Arterial blood pressure; ES: Erythrocyte suspension; FFP: Fresh frozen plasma; ABG: Arterial blood gas; VBG: Venous blood gas; Hb: Hemoglobin; Htc: Hematocrit.

in Group 1 and 156.07±64.49 mmHg in Group 2 (p=0.046). Additionally, SaO_2 in the arterial blood gas measured at the 6 h postoperatively was 97.07±4.27 in Group 1 and 98.84±1.50 in Group 2 (p=0.036; Table 2, Figure 3). No statistically significant difference was detected between the groups regarding the amount of drainage at 6, 12, 24, and 48 h postoperatively (p=0.843, p=0.711, p=0.519,

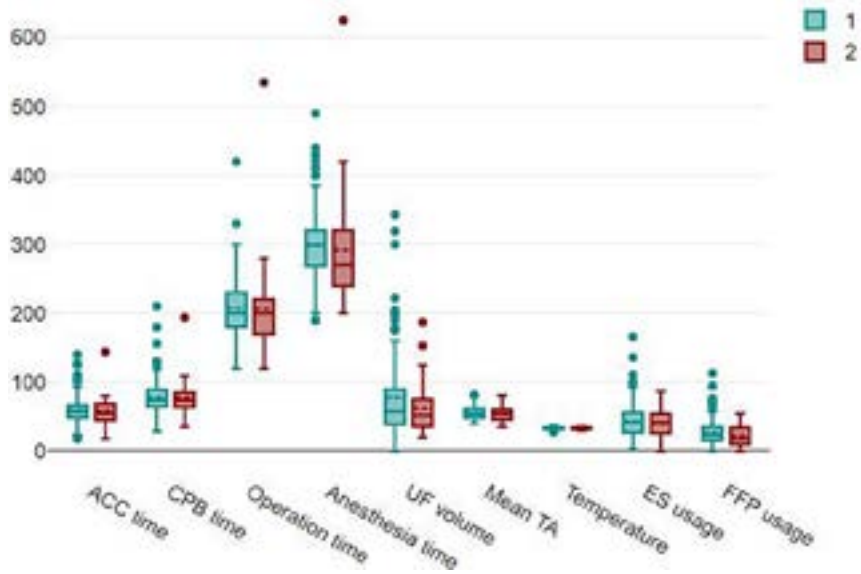

Figure 1. Operative parameters.

ACC: Aortic cross-clamping; CPB: Cardiopulmonary bypass; UF: Ultrafiltration; TA: Arterial blood pressure; ES: Erythrocyte suspension; FFP: Fresh frozen plasma.

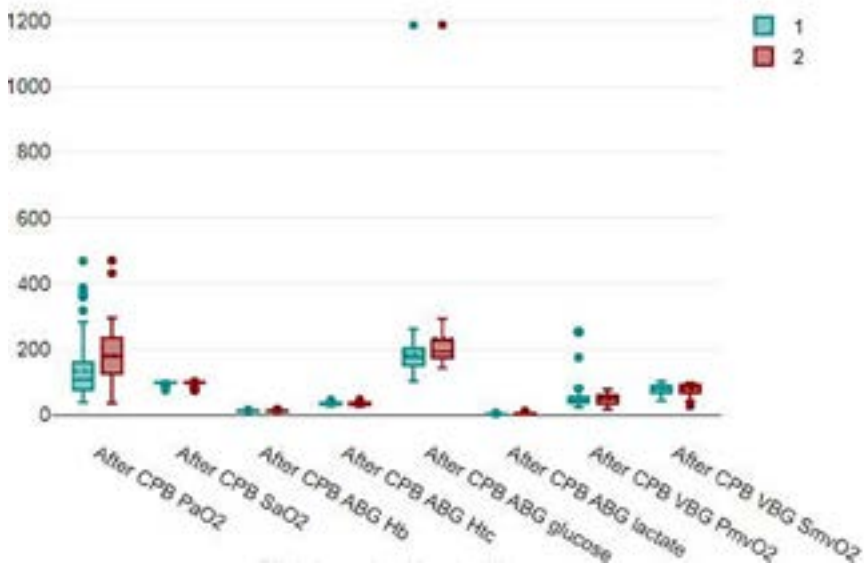

Figure 2. Postcardiopulmonary bypass blood gas parameters.CPB: Cardiopulmonary bypass; ABG: Arterial blood gas; VBG: Venous blood gas; Hb: Hemoglobin; Htc: Hematocrit; PaO_2: Partial oxygen pressure; SaO_2: Saturation of oxygen; $SmvO_2$: Mixed venous oxygen saturation; $PmvO_2$: Partial mixed venous oxygen.

and p=0.402, respectively; Table 2). The mean VIS was 6.93±5.4 in Group 1 and 6.36±3.13 in Group 2 (p=0.566).

There was no statistically significant difference between the groups in terms of MAEs and mortality (p=0.148 and p=0.792, respectively; Table 3). No statistically significant difference was observed between the groups in terms of duration of mechanical ventilation and ICU or hospital stays (p=0.439, p=0.381, and p=0.743, respectively; Table 4).

DISCUSSION

This study examined the relationship between CPB and LOHL and whether LOHL causes mortality

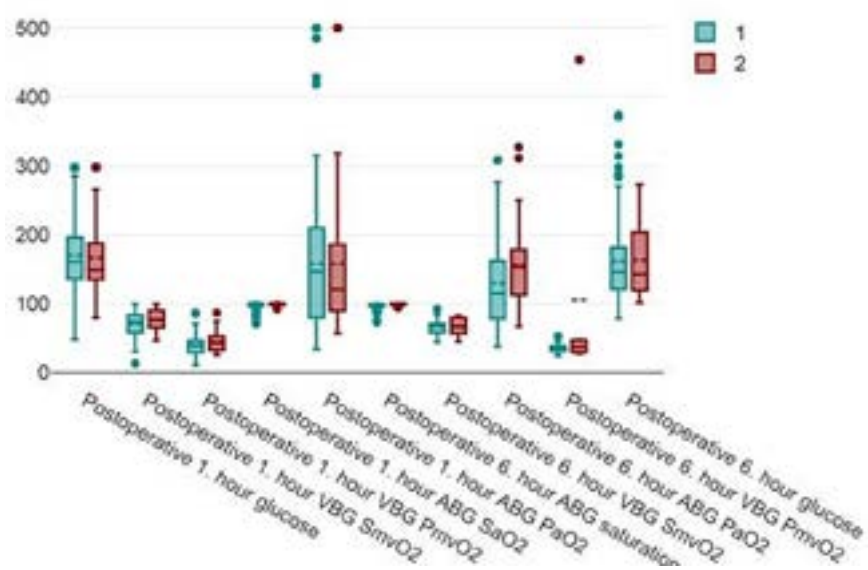

Figure 3. Postoperative parameters.

VBG: Venous blood gas; $SmvO_2$: Mixed venous oxygen saturation; $PmvO_2$: Partial mixed venous oxygen; ABG: Arterial blood gas; PaO_2: Partial oxygen pressure.

Table 3. Postoperative complications

	All (n=159)		Group 1 (n=126)		Group 2 (n=33)		
Variables	n	%	n	%	n	%	*p*
Extracorporeal membrane oxygenator	1	0.6	1	0.8	0	0	0.792
Cardiopulmonary resuscitation	4	2.5	4	3.2	0	0	0.39
Renal dysfunction	2	1.2	2	1.6	0	0	0.627
Neurological complication	2	1.2	2	1.6	0	0	0.627
Mortality	1	0.6	1	0.8	0	0	0.792
Major adverse event	8	5	8	6.3	0	0	0.148
Sternum left open	4	2.5	4	3.2	0	0	0.39
Infection	10	6.2	10	7.9	0	0	0.090
Arrhythmia	10	6.2	7	5.6	3	9.1	0.344
Wound infection	1	0.6	1	0.8	0	0	0.792
Pulmonary complication	7	4.4	7	5.6	0	0	0.189
Extubation in operation room	41	25.7	30	23.8	11	33.3	0.186
Reintubation	11	6.9	9	7.1	2	6.1	0.592

Table 4. Vasoactive inotropic score and durations

	Group 1	Group 2	
Variables	Mean±SD	Mean±SD	*p*
VIS	6.93±5.40	6.36±3.13	0.566
MV time (h)	47.26±138.70	28.21±45.54	0.439
ICU time (day)	6.44±9.48	4.94±4.64	0.381
LOHS (day)	12.55±11.39	11.82±11.26	0.743

SD: Standard deviation; VIS: Vasoactive inotrope score; MV: Mechanichal ventilation; ICU: Intensive care unit; LOHS: Length of hospital stay.

and morbidity. The study was designed with a patient group undergoing VSD closure, which is a more homogeneous patient group that causes relatively less mortality and morbidity. It was observed that high PaO_2 levels and high lactate levels after CPB, high PaO_2, and SaO_2 values in arterial blood gas at 6 h postoperatively affected the development of LOHL, and LOHL was not associated with morbidity. Furthermore, CPB flow, CPB duration, and duration of ACC did not have an impact on LOHL.

The incidence of LOHL is reported to be approximately 14 to 25% after cardiac surgery and even higher in pediatric patients.[1,3-5,8,16] There are various hypotheses regarding the etiology of LOHL. However, the number of studies on the subject in the pediatric patient population is limited. In a study by Abraham et al.,[13] where 68 patients with isolated ASD closure were analyzed, all patients who developed early and late hyperlactatemia postoperatively between 0 to 12 h were defined as the high lactate group. In their results, they reported that 38% of patients developed HL, and they retrospectively found that lower CPB flows were used in the HL group leading to lower oxygen delivery during CPB and higher blood glucose values in the early postoperative period. They also reported that low CPB flows (<100 mL/kg/min) and mean arterial blood pressure values during CPB were risk factors for HL. Only patients with LOHL (6 to 12 h) were included in our study. None of our patients had a target CPB flow below 100 mL/kg/min. We did not observe a statistically significant difference between Groups 1 and 2 regarding CPB flows (140.04 mL/min/m^2 *vs*. 140.4 mL/min/m^2). However, the lactate level after CPB was higher in the LOHL group. Therefore, we believe that the development of HL due to ischemia in the early post-CPB period may have affected the development of LOHL. Klee et al.[12] reported in a more complex post-CPB pediatric patient group that lactate values measured at 4 h after pediatric ICU admission were high (>2 mmol/L) in 62% of patients, but oxygen extraction was normal in 55% of these patients. They reported that HL at the 4 h postoperatively was associated with hyperglycemia and a high lactate-to-pyruvate ratio and was not associated with parameters such as oxygen extraction, patient body weight, severity of cardiac lesion, and CPB duration. They also indicated that HL at 12 h postoperatively was not associated with oxygen extraction but with hyperglycemia. In our study, no difference was observed between the groups in CPB duration, duration of ACC, CBP flows, and hematocrit levels after CPB and in the postoperative period. No difference was determined between the groups in terms of mixed venous oxygen saturation ($SmvO_2$) and partial mixed venous oxygen ($PmvO_2$), both after CPB and in the early postoperative period. However, arterial PaO_2 values after CPB and arterial PaO_2 values at 6 h postoperatively were higher in the LOHL group. Moreover, arterial SaO_2 measured at the 6 h postoperatively was higher in the LOHL group. However, $SmvO_2$ levels were similar in the two groups. $SmvO_2$ is used as an indicator of adequate oxygen delivery. Although oxygen delivery was sufficient in both groups, the high PaO_2 in the LOHL group means that the arteriovenous saturation range was higher in this group. This result may indicate a need for higher oxygen utilization at the tissue level in the LOHL group, or, as in septic shock, functional shunts may occur due to the deleterious effects of CPB on the microcirculation. Although oxygen delivery is sufficient and sometimes even higher than necessary, oxygenated blood may bypass the capillary bed and cause ischemia at the tissue level despite high $SmvO_2$.[17-19] Klee et al.[12] reported that they did not observe a relationship between oxygen extraction and LOHL. However, some studies conducted in the adult patient population have shown that high oxygen levels during CPB are associated with increased systemic vascular resistance and increased microcirculatory perfusion heterogeneity.[20-22] We believe pathological oxygen use at the tissue level may play a role in the etiology of LOHL. However, further prospective studies are needed on this subject.

Hemodilution during CPB is considered to play a role in the etiology of LOHL. Nonetheless, in our study, no statistically significant difference was revealed between the groups in terms of ultrafiltration volumes and operative and postoperative hematocrit levels. Exogenous epinephrine is another cause of HL. Furthermore, stress-related endogenous epinephrine release has a role in the etiology of HL by increasing glucose uptake into the cell and causing increased glycolysis.[9,23,24] In a study comparing epinephrine and norepinephrine after cardiac surgery, the incidence of HL was reported to be lower in the norepinephrine group.[9] In our study, no statistical difference was detected between the groups in terms of VIS. However, since we conducted the study in a patient group with simple cardiac pathology, the incidence of inotrope use was quite low. Additionally, our inotrope strategy was to use norepinephrine in the first line in addition to milrinone. Therefore, the number of patients receiving epinephrine infusion was limited.

Another critical factor in the development of LOHL is glucogenesis due to hyperglycemia and stress response.[1,25,26] Palermo et al.[6] included 132 (10%) patients who developed HL despite adequate tissue perfusion in their pediatric patient population and examined the relationship between HL and hyperglycemia. The median time to development of HL after CPB was reported as 4.4 h, and the time to development of hyperglycemia was reported as 4.9 h. They reported that lactate and blood glucose levels rise and fall simultaneously. The present study demonstrated no statistically significant difference in terms of blood glucose levels measured after CPB and at 1 and 6 h postoperatively.

Various studies in the literature have examined factors related to the etiology of LOHL. In a study by Auborg et al.,[7] 432 adult patients were examined after cardiac surgery, and LOHL was detected in 8.5%. Bleeding amounts of >300 mL at the 6 h postoperatively and fluid loading >250 mL at the 6 h postoperatively were reported as risk factors for LOHL. The study did not report the fluid that was used for fluid loading. In our study, no statistical difference was observed between groups in terms of bleeding.

There are various studies in the literature regarding the effect of LOHL on mortality and morbidity. It was reported that LOHL generally has a benign course.[3,5] Maillet et al.,[4] in their study examining low lactate, EOHL, and LOHL reported that the mortality rate was 1.5% in the low lactate group, 3.6% in the LOHL group, and 14.9% in the EOHL group. However, Auborg et al.[7] observed that complications such as the need for mechanical ventilation for longer than 24 h, acute renal failure, blood transfusion, and postoperative bleeding were higher in the LOHL group and reported that LOHL may be related to inadequate tissue oxygenation. In the present study, we did not determine a statistically significant difference between the groups in terms of MAEs and mortality.

The major limitation of our study was that it was a single-center retrospective study. In addition, since our study was retrospective, parameters such as oxygen extraction ratio, indexed oxygen delivery, and oxygen consumption could not be calculated. Instead, values such as PaO_2 and mixed venous $SmvO_2$ were considered, and CPB flows calculated according to the routine CPB strategy applied in our clinic were investigated. Therefore, it was not possible to evaluate the effect of oxygen delivery and oxygen consumption on LOHL in our study.

In conclusion, the present study demonstrated that LOHL was not associated with mortality and MAEs, and LOHL was frequently observed following pediatric cardiac surgery. The lactate level after CPB was higher in the LOHL group. Therefore, we believe that the development of HL due to ischemia in the early post-CPB period may have affected the development of LOHL. In addition, higher arterial PaO_2 levels were determined in the LOHL group despite normal mixed venous $PmvO_2$ both in the early post-CPB period and the early postoperative period. Therefore, we believe that microcirculatory changes at the tissue level may play a role in the etiology of LOHL. Further prospective studies are needed.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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