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The Relationship of Hyperlactatemia Following Paediatric Open Heart Surgery with Mortality, Morbidity and Risk Factors

ORIGINAL INVESTIGATION

Sonay Oğuz[1], Orhan Bozoğlan[2], Faruk Serhatlıoğlu[3], Kemalettin Erdem[4], Hakan Ceyran[5]

ABSTRACT

Objective: In this present study, the association of hyperlactatemia frequency with probable risk factors, postoperative morbidity and mortality were investigated in patients undergoing paediatric open heart surgery.

Materials and Methods: The present study included 45 consecutive paediatric patients who had undergone open heart surgery with hypothermic cardiopulmonary bypass in the cardiovascular surgery clinic between January 2008 and July 2008. Four blood samples for lactate analysis were collected from each of the patients preoperatively, intraoperatively and at 1 and 12 hours postoperatively. The patients were divided into two groups according to blood lactate levels as the high lactate group (mean lactate level≥ 3 mmol/L) and the normal lactate group (mean lactate level <3 mmol/L). Hyperlactatemia frequency, associated risk factors, and the relationship with morbidity and mortality were statistically analysed.

Results: Of 45 cases, 33 (73.3%) were included in the normal lactate (NL) group, and 12 (26.7%) were included in the high lactate (HL) group. A borderline association was found between lactate levels and mortality in the HL group (p=0.052). Body surface area, age, low cardiac output syndrome, intraoperative and postoperative inotropic support requirement, duration of mechanical ventilation were determined as risk factors associated with mortality (p<0.05), and low cardiac output syndrome, urine output and metabolic acidosis were determined as risk factors associated with hyperlactatemia (p<0.05).

Conclusion: In patients followed up in the intensive care unit, lactate concentration is a good indicator for disease severity. Blood lactate levels seems to be a parameter that can be used in routine follow-up.

Key words: Pediatric open heart surgery, hyperlactatemia, congenital heart disease

[1]Sivas Anadolu Hospital, Cardiovascular Surgery Clinic, Sivas, Turkey

[2]Kahramanmaraş Sütçü İmam University Faculty of Medicine, Department of Cardiovascular Surgery, Kahramanmaraş, Turkey

[3]Erciyes University Faculty of Medicine, Department of Cardiovascular Surgery, Kayseri, Turkey

[4]Bolu Abant İzzet Baysal University Faculty of Medicine, Department of Cardiovascular Surgery, Bolu, Turkey

[5]Kartal Koşuyolu Training and Research Hospital, Cardiovascular Surgery Clinic, İstanbul, Turkey

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Correspondance
Orhan Bozoğlan MD, Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi, Kalp Damar Cerrahisi Anabilim Dalı, 46100, Kahramanmaraş, Türkiye
Phone: +90 344 221 23 37
e.mail: orhanbozoglan1975@hotmail.com

INTRODUCTION

Hyperlactatemia is a common metabolic abnormality after open heart surgery (1). As hyperlactatemia is the early indicator of hypoperfusion, which is fatal, monitoring blood lactate levels in critical patients may increase the chance of an early life-saving intervention (2). Metabolic acidosis with hyperlactatemia is the most important indicator of septic shock-related mortality (3). Hyperlactatemia can occur regardless of the presence of tissue hypoxia after cardiac surgery. It has been demonstrated that blood flow and oxygenation in the splanchnic region is decreased and there is a significant mucosal hypoperfusion during cardiopulmonary bypass (CPB). Due to the increased lactate production and decreased elimination in the splanchnic region, lactate levels are expected to increase in CPB; however, this increase normal and anlamlı kabul edilebilecek levels üzerinde yeterli çalışma yapılmamıştır (4). In patients undergoing paediatric open heart surgery, close follow-up of lactate levels in the preoperative, intraoperative and postoperative periods may be an early indicator of mortality (5, 6). In this present study, we aimed to evaluate hyperlactatemia frequency, risk factors that are probably related to hyperlactatemia and the relation between postoperative morbidity and mortality and hyperlactatemia in patients who had undergone paediatric cardiac surgery.

MATERIAL and METHODS

Consecutive 45 paediatric cases that had undergone elective open heart surgery with hypothermic cardiopulmonary bypass in the cardiovascular surgery clinic between January 2008 and July 2008 were included in the study. Before the surgery, the legal representatives of the patients were informed about the study and informed consents were obtained. Patients who underwent emergency surgery and re-surgery were excluded from the study. Characteristics of the patients are presented in Table 1. After preoperative routine examinations were performed, the patients were taken to the surgery. After anaesthetic monitoring was completed, the first arterial blood sample for lactate analysis (preoperative) was taken. Necessary cardiac repairs were accomplished through a median sternotomy under CPB. During CPB, the mean arterial blood pressure (MABP) was maintained at 60 mmHg (50-70 mmHg), and the mean body temperature was maintained at 30°C (28-31°C). After the intervention, cardiac output was decreased and the patient was weaned from CPB. Four blood samples for lactate analysis were col-

Table 1. Characteristics of the cases

	Total n=45 (100%) mean (min-max)	NL Group n=33 (73.3%) mean (min-max)	HL Group n=12 (26.7%) mean (min-max)	p value (p<0.05)
Age (years)	6.31 (0.4-15)	6.63 (0.4-15)	5.4 (0.5-14)	p= 0.008
Gender (M/F)	(20/25)	(15/18)	(5/7)	NS
BSA, (m^2)	0.88 (0.33-1.95)	0.93 (0.35-1.95)	0.74 (0.33-1.62)	p<0.001

NL: Normal lactate, HL: High lactate, BSA: Body surface area, NS: Not significant

Table 2. Surgical parameters

	Total Mean (min-max)	NL Group Mean (min-max)	HL Group Mean(min-max)	p value (p<0.05)
Duration of CPB, minutes	80.1 (25-175)	75.81 (25-150)	91.91 (43-176)	NS
XCL time, minutes	48.2 (14-100)	44.60 (14-90)	58.16 (18-100)	NS
BP, mmHg	66.5 (54-75)	66.48 (58-75)	65.75 (54-70)	NS
VP requirement	1 (2.2%)	0	1 (8.3%)	NS
ISR	15 (33.3%)	8 (24.2%)	7 (58.3%)	p= 0.009
Volume supplementation	1 (2.2%)	1 (3.0%)	0	NS

CPB: Cardiopulmonary bypass, XCL: Cross clamp, BP: Blood pressure, VP: Vasopressor, ISR: Inotropic support requirement, NS: Not significant

lected from each of the patients preoperatively, intraoperatively and at 1 and 12 hours postoperatively. Additionally, body surface area (BSA), duration of CPB, cross clamp (XCL) time, degree of hypothermia during CPB, MABP, requirement of volume supplementation, intraoperative vasopressor (VP) and inotropic support requirement (ISR), length of stay in the intensive care unit (ICU), mechanical ventilation duration (MVD), postoperative ISR, low cardiac output syndrome (LCOS), urine output, metabolic acidosis, amount of tube drainage, revision requirement, increased glucose levels, hepatic dysfunction, renal failure, infection, fever, increased white blood cell (WBC) count, gastrointestinal (GIS) complications, β-agonist requirement were recorded in the follow-up forms. Criteria for starting inotropic support were determined as difficulty in weaning from CPB, post-CPB acute left heart and/or right heart failure, and low cardiac output in the postoperative period. The values obtained in the intraoperative period are presented in Table 2. The UV-160A Shimadzu visible recording spectrophotometer in the metabolism laboratory was used to determine lactate levels. In order to increase the accuracy of testing, the collected samples were immediately transferred to the laboratory in ice batteries in accordance with cold chain requirements. According to the laboratory results, patients with an arterial lactate concentration <3 mmol/L were included in the normal lactate (NL) group (group 1) and those with an arterial lactate concentration≥ 3 mmol/L were included in the high lactate (HL) group (group 2). A blood glucose level >150 mg/dl was considered as a high glucose level, a WBC count>15000/mm^3 was considered as leucocytosis, and body temperature≥ 38.0°C (100.4 F) was considered as fever. A postoperative alanine aminotransferase (ALT) level >100 IU/L was accepted as hepatic dysfunction. Urine output was calculated in ml/kg/h and recorded. The patients were monitored until discharge and all clinical and laboratory changes were recorded.

Statistical analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) 15.0 statistical package program. A chi square test was used in the comparison of qualitative variables. Normality testing of data was performed using the Kolmogorov-Smirnov test. The independent two sample t test was used in variables with normal distribution, and the Mann Whitney U test was used in non-normally distributed variables. A p value <0.05 was considered statistically significant.

RESULTS

A total of 45 paediatric patients (25 boys, 20 girls) were included in the study. The reasons for surgery were as follows, ventricular septal defect (VSD) in 16 (35.5%) patients, Tetralogy of Fallot (TOF) in 11 (24.4%) patients, atrial septal defect (ASD) in 9 (20%) patients, aortic valve replacement (AVR) in 2 (4.4%) patients, transposition of the great arteries (TGA) in 2 (4.4%) patients, atrioventricular septal defect (AVSD) in 2 (4.4%) patients, subvalvular aortic stenosis (SVAS) in 2 (4.4%) patients, and pulmonary stenosis (PS) in 1 (2.2%) patient. Of the patients, 12 (26.7%) of them had hyperlactatemia (≥3 mmol/L). Normal lactate group (NL) included 33 cases (15 boys, 18 girls), and high lactate group included 12 cases (5 boys, 7 girls). While all values, other than those obtained in the preoperative period, were>3 mmol/L in the HL group, lactate levels >3 mmol/L was not observed at any time point including the preoperative period in the NL group. Mean lactate levels measured at the four time points were 2.22, 3.16, 3.72 and 3.48 mmol/L, respectively in the HL group, whereas the corresponding values in the NL group were 1.79, 2.23, 2.19 and 2.01 mmol/L, respectively. The mean age was 6.31±3.1 years; 6.63±3.6 years in the NL group and 5.4±2.1 years in the HL group. There was a significant relation between mean age and mortality (p=0.008). Mean

BSA was 0.88±0.4m² (0.33-1.95); 0.93±0.5 m² (0.35-1.95) in the NL group and 0.74±0.3 m² (0.33-1.62) in the HL group. The relation between low BSA and mortality was significant (p<0.001). Mean cardiopulmonary bypass duration was 80.1±22.4 (25-176) minutes; 75.81±26.4 (25-150) minutes in the NL group, and 91.91±25.6 (43-176) minutes in the HL group. Mean cross clamp time was 48.2±26.6 (14 -100) minutes; 44.60±22.6 (14 -90) minutes in the NL group, and 58.16±28.6 (18-100) minutes in the HL group. Inotropic support was required in 8 cases (24.2%) in the NL group and 7 cases (58.3%) in the HL group in the intraoperative period. There was a significant relation between intraoperative ISR and mortality (p=0.009). Mechanical ventilation duration was 8.06±4.8 (4-23) hours in the NL group and 12.0±6.8 (6-24) hours in the HL group. There was a significant relation between increased MVD and mortality (p=0.006). Length of stay in the intensive care unit was 3.09±2.8 (2-10) days in the NL group and 3.08±1.8 (1-6) days in the HL group. Inotropic support was required in 9 cases (27.2%) in the NL group and in 7 cases (58.3%) in the HL group in the ICU. ISR in the ICU was significantly related with mortality (p=0.012). Low cardiac output syndrome occurred in 3 cases (25%) in the HL group, and none of the cases in the NL group. LCOS was significantly related with both mortality and hyperlactatemia (p<0.001, p=0.016). Mean urine output was 1.84±0.8 (0.3-3.1) ml/kg/h in the NL group and 1.41±0.9 (0.3-2.7) ml/kg/h in the HL group. Decreased urine output was significantly related with hyperlactatemia (p=0.015). Metabolic acidosis occurred in 4 patients (12.1%) in the NL group and 8 (66.6%) patients in the HL group. There was a significant relation between metabolic acidosis and hyperlactatemia (p= 0.001). Of the 45 cases, 4 (8.8%) of them died in the postoperative period, 3 (25%) from the HL group and 1 (3%) from the NL group. The patients who died in the HL group died due to low cardiac output syndrome at the postoperative 20, 24 and 30 hours. Two of them were operated because of TOF and one of them was operated with a diagnosis of ventricular septal defect (VSD). The patient who died in the NL group had a diagnosis of VSD; he/she was intubated at postoperative 4 days due to sudden onset unconsciousness and respiratory failure, and was planned to be transferred to the ward as he/she was clinically and hemodynamically stable. This situation was probably suggestive of non-surgical mortality. Blood lactate levels of this patient were 1.07, 2.02, 2.07 and 2.24 mmol/L, respectively. Low BSA, low age, LCOS, ISR during the surgery and in ICU, and mechanical ventilation duration were found to be the risk factors related with mortality (p<0.05). LCOS, decreased urine output and metabolic acidosis were determined to be the risk factors related with hyperlactatemia (p<0.05). The risk factors associated with mortality and the risk factors associated with hyperlactatemia are shown in Table 3 and Table 4.

DISCUSSION

In open heart surgery, along with the expected effects of CPB, hyperlactatemia is a commonly encountered condition. Normal blood lactate concentrations is 0.5-1 mmol/L in unstressed patients and <2 mmol/L in critical patients. Hyperlactatemia is defined as blood lactate levels between 2 and 5 mmol/L, and lactic acidosis is defined as metabolic acidosis with blood lactate levels> 5 mmol/L (7). Many studies reported increased lactate levels above the normal range, which can be related with mortality. In the previous studies, it was demonstrated that hyperlactatemia occurs due to activation of anaerobic glycolysis before the parameters showing cardiac functions are impaired (BP, urine output, mixed venous oxygen saturation) when LCOS develops, and if identified early, there is a change of successful intervention (8, 9). Increase in lactate levels due to any reason and the resultant metabolic acidosis gains a particular importance as they will lead to suppression of cardiac functions (8). There may be significant elevation in blood lactate levels

Table 3. Risk factors related with mortality

	Alive mean±SD (median)	Exitus mean±SD (median)	p value (p<0.05 significant)
BSA	0.92±0.43 (0.83)	0.35±0.02 (0.35)	p<0.001
Age	6.80±4.55 (7.00)	1.27±0.86 (1.00)	p=0.008
LCOS	0	3 (25.0%)	p<0.001
ISR (intraoperative)	8 (24.2%)	7 (58.3%)	p=0.009
ISR (intensive care unit)	9 (27.2%)	7 (58.3%)	p=0.012
MVD	8.12±3.71 (8.00)	24.25±4.19 (23.50)	p=0.006

BSA: Body surface area, LCOS: Low cardiac output syndrome, ISR: Inotropic support requirement, MVD: Mechanical ventilation duration

Table 4. Risk factors related with hyperlactatemia

	NL group mean±SD (median)	HL group mean±SD (median)	p value (p<0.050)
LCOS	0	3 (25.0%)	p=0.016
Decreased urine output	(2.0±0.52) 2.1	(1.5±0.56) 1.4	p=0.015
Metabolic acidosis	4 (12.1%)	8 (66.6%)	p=0.001

LCOS: Low cardiac output syndrome, NL: Normal lactate, HL: High lactate

due to severe hypoperfusion (without acidosis) (9-11). Increased lactate levels after paediatric open heart surgery show a parallelism with increased mortality and morbidity (12, 13). In the present study, four blood samples for lactate analysis were obtained from each of the patients undergoing paediatric open heart surgery preoperatively, intraoperatively and at 1 and 12 hours postoperatively. The mean preoperative lactate level was 1.91 mmol/L and the mean lactate level at postoperative 1 hour in the ICU was 2.67, there are differences in the upper range of lactate levels in numerous similar studies. In the HL group, which was formed according to a lactate threshold of 3 mmol/L, a borderline association was found between lactate levels and mortality (p=0,052). Of the 45 cases included in the study, 4 of them died; 3 of them were in the HL group and 1 was in the NL group; the patient who died in the NL group was intubated due to sudden onset unconsciousness and respiratory failure, and was planned to be taken to the ward as her/his hemodynamic and clinical status was stable. This situation was probably suggestive of non-surgical mortality. However, although this case had a remarkable effect on the statistical results, we determined a borderline relation between mortality and high lactate levels (p=0.052). When the lactate values obtained in the preoperative, intraoperative and at 1 and 12 hours in the postoperative period were evaluated separately, there was a significant relation between lactate values obtained at postoperative 12 hours and mortality (p=0.008). The lactate values obtained at postoperative 1 hour of the three cases who died in the HL group were 3.77, 5.4 and 3.85 mmol/L, respectively, and lactate values obtained at 12 hours were 5.42, 5.74 and 4.2 mmol/L, respectively. Başaran, Maullet, and Bolcal, in their studies emphasized the significant relation between mortality and increased lactate levels in the early period (8, 14, 15). According to the threshold value of ≥3mmol/L that we accepted, hyperlactatemia (≥3 mmol/L) frequency that developed in 12 of 45 cases was 26.7%. Risk factors related with hyperlactatemia were LCOS, decreased urine output, and metabolic acidosis (p<0.05). Low BSA, low age, LCOS, intraoperative inotrope requirement and ISR in ICU, and MVD were found to be the risk factors related with mortality (p<0.05). Different risk factors may be put forward according to different lactate thresholds. In the present study, risk factors were determined according to a lactate threshold of 3mmol/L. When hyperlactatemia threshold after open heart surgery is clarified, more reliable data can be collected and interpreted about the probable risk factors associated with mortality. In the present study that included 45 cases, LCOS is the only single risk factor related both with mortality and hyperlactatemia. As tissue perfusion is impaired in LCOS, development of hyperlactatemia is an expected situation. XCL time, CPB duration, VP, β agonist use and hyperglycaemia are considered as conditions leading to hyperlactatemia. These factors were not statistically significant in this limited patient group. In case of increased lactate levels after open heart surgery, Başaran et al. (8) recommended to evaluate cardiac functions using echocardiography, and in accordance with the results, to correct volume deficit according to central venous pressure (CVP), provide inotrope support if required, and to adjust ventilator settings in order to increase oxygenation and decrease carbon dioxide levels. Nevertheless, other than echocardiography all these procedures are routinely performed in the treatment and follow-up. In case of hyperlactatemia, at least determination of the reason of hyperlactatemia (cardiac or non-cardiac) will allow to intervene before low perfusion clinic develops or metabolic dysfunction leads to the impairment of cardiac performance. Early interventions will result in decreased mortality rates. Researchers put emphasize on early secondary markers of hypoperfusion before BP, urine output and mixed venous oxygen saturation that indicates cardiac performance is impaired. Many authors believe that hyperlactatemia can be an early indicator (5, 8, 16). Although there is a limited number of studies and no common consensus on this subject, in accordance with the current data, we think that follow-up of both intraoperative and postoperative lactate levels is beneficial as it allows early intervention before clinical symptoms of hypoperfusion develops.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Erciyes University Faculty of Medicine.

Informed Consent: Written informed consent was obtained from patients' parents who participated in this study.

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Authors' contributions: Conceived and designed the experiments or case: SO, FS, HC. Performed the experiments or case: SO, FS, HC. Analyzed the data: SO, FS. Wrote the paper: OB, KE, SO. All authors have read and approved the final manuscript.

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REFERENCES

1. Civetta JM, Taylor RW, Kirby RR, eds. Postoperative management of the adult cardiac surgery patient. Critical care. 3rd ed. Philadelhia, PA: Lippincott Williams & Wilkins, 1997.p.1147-75.
2. Vincent JL, Dufaye P, Berré J, Leeman M, Degaute JP, Kahn RJ. Serial lactate determinations during circulatory shock. Critical Care Med 1983; 11(6): 449-51. [CrossRef]
3. Bakker J, Coffernils M, Leon M, Gris P, Vincent JL. Blood lactate levels are superior to oxygen derived variables in predicting outcome in human septic shock. Chest 1991; 99(4): 956-62. [CrossRef]
4. Landow L. Splanchnic lactate production in cardiac surgery patients. Crit Care Med 1993; 21(2): 84-91. [CrossRef]
5. Ranucci M, De Toffol B, Isgrò G, Romitti F, Conti D, Vicentini M. Hyperlactatemia during cardiopulmonary bypass: determinants and impact on postoperative outcome. Crit Care. 2006: 10(6): R167. [CrossRef]
6. Sheppard AP, Granger DN. Metabolic regulation of the intestinal circulation. In Sheppard A, Granger D, editors. Physiology of the intestinal circulation. New York: Raven Press; 1984.p.33-47.
7. Valenza F, Aletti G, Fossali T, Chevallard G, Sacconi F, Irace M, Gattinoni L. Lactate as a marker of energy failure in critically ill patients: hypothesis. Crit Care 2005; 9(6): 588-93. [CrossRef]
8. Basaran M, Sever K, Kafali E, Ugurlucan M, Sayin OA, Tansel T, et al. Serum Lactate Level Has Prognostic Significance After Pediatric Cardiac Surgery. J Cardiothorac Vasc Anesth 2006; 20(1): 43-7. [CrossRef]
9. Meregalli A, Oliveira RP, Friedman G. Occult hypoperfusion is associated with increased mortality in hemodynamically stable, high-risk, surgical patients. Crit Care 2004; 8(2): 60-5. [CrossRef]
10. Friedman G, Berlot G, Kahn RJ, Vincent JL. Combined measurements of blood lactate concentrations and gastric intramuco-

sal pH in patients with severe sepsis. Crit Care Med 1995; 23(7): 1184-93. [CrossRef]
11. Claridge JA, Crabtree TD, Pelletier SJ, Butler K, Sawyer RG, Young JS. Persistent occult hypoperfusion is associated with a significant increase in infection rate and mortality in major trauma patients. J Trauma 2000; 48(1): 8-14. [CrossRef]
12. Jeng JC, Jablonski K, Bridgeman A, Jordan MH. Serum lactate, not base deficit, rapidly predicts survival after major burns. Burns 2002; 28(2): 161-6. [CrossRef]
13. Mikulaschek A, Henry SM, Donovan R, Scalea TM. Serum lactate is not predicted by anion gap or base excess after trauma resuscitation. J Trauma 1996; 40(2): 218-22. [CrossRef]
14. Maillet JM, Le Besnerais P, Cantoni M, Nataf P, Ruffenach A, Lessana A, et al. Frequency, risk factors, and outcome of hyperlactatemia after cardiac surgery. Chest 2003; 123(5): 1361-6. [CrossRef]
15. Bolcal C, Doğancı S, Demirkılıç U, Tatar H. Koroner Bypass Cerrahisi Sonrası Görülen Hiperlaktateminin Sıklığı, Risk Faktörleri Ve Sonuçları. Turkiye Klinikleri J Cardiovasc Sci 2007; 19(1): 27-31.
16. Park SJ, Kim HS, Byon HJ, Kim CS, Cheong IY, Kim JT. Intraoperative plasma lactate as an early indicator of major postoperative events in pediatric cardiac patients. Tohoku J Exp Med 2012; 228(3): 239-45. [CrossRef]