Progress in Pediatric Cardiology 54 (2019) 101117

Contents lists available at ScienceDirect

Progress in Pediatric Cardiology

journal homepage: www.elsevier.com/locate/ppedcard

"Benign" lactic acidosis is common in adolescents and children following congenital heart surgery

Robert Horvath[a,b,*], Francis X. Moga[a,b], David A. Dassenko[b,c], Mark D. Lo Galbo[b], Shengxu Li[b], Alison E. Adams[b], David M. Overman[a,b]

[a] Children's Heart Clinic PA, 2530 Chicago Avenue Suite #500, Minneapolis, MN 55404, USA
[b] Children's Hospitals and Clinics of Minnesota, 2525 Chicago Avenue, Minneapolis, MN 55404, USA
[c] Pediatric Anesthesia PA, 2525 Chicago Avenue Suite #32-2613, Minneapolis, MN 55404, USA

ARTICLE INFO

Keywords:
Congenital heart surgery
Lactic acidosis
Postoperative
Inotrope score
Retrospective
Benign

ABSTRACT

Lactic acidosis is commonly observed in children following congenital heart surgery. Serum lactate is a surrogate measure of cardiac output and tissue oxygen delivery. Children and adolescents frequently have elevated lactate levels postoperatively without clinical signs of low cardiac output. Our objective was to evaluate children with postoperative lactic acidosis and to describe a distinct group of patients with lactic acidosis and low inotropic scores we named "benign" lactic acidosis. We conducted a retrospective chart review of 105 patients, 5 to 21 years old, who had undergone open-heart surgery from 05/2011 to 05/2013. Based on highest postoperative lactate levels (> 4.4 mmol/L or 40 mg/dl) and inotrope scores (≥15) in the first 48 postoperative hours we defined three groups: classic lactic acidosis (elevated lactate and inotrope score, n = 9), benign lactic acidosis (elevated lactate and low inotrope score, n = 25) and a control group (low lactate and low inotrope score, n = 71). Lactic acidosis in the benign group was less pronounced and resolved earlier than in the classic group. The classic and benign groups had significantly elevated serum glucose. The classic group had significantly longer cardiopulmonary bypass time, time to extubation and hospital length of stay compared to the benign and control groups. The classic group had significantly lower systolic blood pressure, higher heart rate and central venous pressure, and lower urine output than the benign and control groups. Benign lactic acidosis is clinically distinct from classic lactic acidosis. It has faster resolution and patients exhibit stable postoperative hemodynamics with similar clinical outcomes as patients in the control group.

1. Introduction

Lactic acidosis is commonly observed in children following congenital heart surgery [1]. Serum lactate serves as a surrogate measure of cardiac output and tissue oxygen delivery. Presence of lactic acidosis has been used as a marker of adverse outcome in postoperative cardiac patients [2]. Elevated lactic acid levels in critically ill patients with or without acidosis have been widely described in the literature with a subgroup of patients having preserved cardiac output and oxygen delivery [3]. Vernon et al. described in detail the physiology of type A and type B lactic acidosis and its clinical relevance in critical care medicine. **Type A lactic acidosis** occurs in the context of cellular (mitochondrial) hypoxia, as a result of lactate overproduction. It is usually associated with diminished oxygen delivery. **Type B lactic acidosis**, which is associated with normal cardiac output and oxygen delivery, in the postoperative cardiac surgical setting, is likely related to systemic inflammatory reaction from the cardiopulmonary bypass and endogenous catecholamine surge. Type A lactic acidosis is characterized by an elevated lactate:pyruvate ratio, as opposed to type B lactic acidosis, which has a normal lactate:pyruvate ratio [4]. Type B lactic acidosis has been well described following adult cardiac surgery and is associated with an excellent postoperative prognosis [5].

We have observed in our postoperative cardiovascular unit, that children and adolescents frequently have elevated lactate levels following congenital heart surgery without clinical signs of low cardiac output. The aim of our study was to evaluate this particular group of patients. In a prospective cohort study, Shinde et al. described that lower lactate:pyruvate ratio in the first 48 postoperative hours was an indicator of a good clinical outcome [6]. Hosein et al. prospectively studied 10 Fontan patients during the first 12 postoperative hours and found that patients had parallel rise in their lactate and pyruvate and it was not associated with decreased oxygen delivery or decrease in their

* Corresponding author at: 1314 Marquette Ave, Apt 1308, Minneapolis, MN 55403, USA.
E-mail address: rhorvath@chc-pa.org (R. Horvath).

https://doi.org/10.1016/j.ppedcard.2019.04.001
Received 10 December 2018; Received in revised form 30 March 2019; Accepted 5 April 2019
Available online 13 April 2019
1058-9813/ Published by Elsevier B.V.

cardiac output [7]. Toda et al. reported that bloodless cardiopulmonary bypass prime and older age (> 4 years) was associated with elevated lactate, compared to a blood prime and younger age group, but had good clinical outcomes.

In our institution we frequently observe elevated lactate levels in our postoperative children and adolescents. The aim of our retrospective study was to describe the clinical characteristics of patients, who underwent congenital heart surgery and developed lactic acidosis without any other clinical evidence of low cardiac output or decreased oxygen delivery. We named this clinical phenomenon "benign lactic acidosis".

2. Materials and methods

The study was approved by the Children's Hospitals and Clinics of Minnesota Institutional Review Board. A retrospective chart review was conducted on patients 5 to 21 years of age at time of cardiac surgery between May 1, 2011 and May 1, 2013. We selected this age group for two reasons: we observed this type of lactic acidosis in this age group more frequently than in younger patients and in the pediatric literature this phenomenon was described in the corresponding age group [7]. Patients whose surgery did not require cardiopulmonary bypass were excluded. All patients were admitted to the Children's Hospitals and Clinics of Minnesota Cardiovascular Care Center, a 19 bed pediatric cardiac intensive care unit for postoperative care.

One hundred and five patients were identified. 1.) Demographic data including gender, height, weight, body mass index, history of diabetes and cyanotic heart disease were abstracted. 2.) Intraoperative data such as weight at surgery, operative procedure, risk adjustment for congenital heart surgery (RACHS) score, cardiopulmonary bypass time and aortic cross-clamp time were recorded. 3.) Postoperative data including lactate, glucose, pH, carbon dioxide partial pressure (pCO2), heart rate, systolic blood pressure, diastolic blood pressure and urine output were collected for 48 h following surgery.

As part of postoperative care, all patients were cared for in the cardiac intensive care unit postoperatively. They received inotropic infusions, which were titrated as per the attending physician's discretion. Blood products and crystalloid fluid boluses were administered as deemed necessary by the provider. Routinely, patients got extubated once awake and weaned off the mechanical ventilatory support in the cardiac intensive care unit. Postoperative sedation and analgesia were used and adjusted routinely by the cardiac intensive care team.

Patients were divided into three groups based on highest post-operative lactate value and inotropic score within the first 48 post-operative hours: benign lactic acidosis (elevated lactate and low inotrope score), classic lactic acidosis (elevated lactate and elevated inotrope score), and control (normal lactate and low inotrope score) (Fig. 1). Based on previous pediatric literature, a highest post-operative lactate level of 4.4 mmol/L (40 mg/dl) was used to identify significant lactic acidosis [8]. Inotrope score is comprised of a previously well described composite score [9]. In our study for inotrope score, we have used the Vasoactive Inotrope Score (VIS), which consisted of: VIS = Dopamine dose (mcg/kg/min) + 100 × Epinephrine dose (mcg/kg/min) + 10 × Milrinone dose (mcg/kg/min) + 10,000 × Vasopressin dose (units/kg/min) + 100 × Norepinephrine dose (mcg/kg/min) [10].

Descriptive statistics were used to describe the frequency for categorical data, and mean (standard deviation) or median (range) for continuous variables. Analysis of variance (ANOVA) was used to compare continuous clinical outcomes between patients with benign lactic acidosis, classic lactic acidosis and patients without lactic acidosis. Chi-square test or Fisher's exact test was used to compare categorical variables between patients with benign and classic lactic acidosis and patients without lactic acidosis. Linear mixed model was used to compare the repeated measures.

All analyses were done using Statistical Package for Social Science 20.0. An alpha level of 0.05 was used as the significance level.

3. Results

Table 1 summarizes the surgical interventions in our patients. Of the 105 patients included in our study, 34 patients had significantly elevated lactate levels (25 patients with benign lactic acidosis and 9 patients with classic lactic acidosis) while 71 patients had normal lactate levels and were part of the control group. We identified two patients with inotrope score of 15 and a highest lactate level below 4.4 mmol/L (40 mg/dl) in the control group. The following inotrope medications were utilized: milrinone, dopamine, epinephrine.

The three groups were similar in their age, weight and RACHS scores. The classic group had significantly longer cardiopulmonary bypass time, time to extubation and hospital length of stay compared to the benign and control groups (Table 2).

The classic group had significantly lower systolic blood pressure (mean of 89 (+/−9) versus 98 (+/−9.2) mm Hg, p = 0.009), higher average heart rate (mean of 110 (± 14.1) versus 93 (+/−14.3) bpm, p = 0.001) and elevated central venous pressure (11 (+/−3.1) versus 7 (+/−3.4) mm Hg, p = 0.001) than the control group. These hemodynamic variables did not show any significant difference between the benign and the control group for systolic blood pressure (mean of 101 (+/−9) versus 98 (+/−9.3) mm Hg, p = 0.15), average heart rate (mean of 91 (+/−14) versus 93 (+/−14.3) bpm, p = 0.52) and average central venous pressure (mean of 8 (+/−3) versus 7 (+/−3.4) mm Hg, p = 0.16). There was no significant difference between arterial pH (7.34 (+/−0.05) versus 7.33 (+/−0.03), p = 0.85) and pCO2 (43 (+/−3.5) versus 43 (+/−3.2) mm Hg, p = 0.97) in the benign and classic groups. All three groups showed mild metabolic acidosis. The classic group had significantly lower urine output for the first 6 h (p = 0.04), than the benign and control groups (Fig. 2).

Postoperative length of stay, inotrope use, operative and post-operative variables showed no significant difference in the benign group compared to the control group (Table 2).

3.1. Lactic acidosis

Lactate levels were significantly different between the three groups (Fig. 3). The mean lactate level was 1.90 mmol/L (17.13 (+/−11) mg/dl) in the control group, while the classic group had significantly higher mean lactate, 4.59 mmol/L (41.32 (+/−9.3) mg/dl) (p < 0.001) compared with 3.56 mmol/L (32.07 (+/−10) mg/dl) mean lactate level in the benign group (p = 0.013). The time to resolution, defined as mean lactate level < 2.44 mmol/L (22 mg/dl), was longer in the classic group than in the benign group (23.6 vs.16.5 h, p < 0.001).

3.2. Serum glucose

All 3 groups had elevated blood glucose levels, but the classic and the benign group had more pronounced hyperglycemia, when compared to the control group (Fig. 4). Mean glucose levels were 160.28 (+/−28.6) mg/dL in the control group, 173.84 (+/−28) mg/dL in the benign group (p = 0.04) and 209.27 (+/−26) mg/dL in the classic group (p = 0.001). When comparing the resolution of the hyperglycemia we documented resolution in the benign group at 13.2 h (same time as the control group) and 27.8 h in the classic group (p < 0.001). In the benign group 6 patients (24%) had intravenous fluid switched to glucose-free intravenous fluid. This did result in a trend toward earlier resolution of hyperglycemia (12.5 versus 17 h, p = 0.26), but did not impact the duration of lactic acidosis (16.4 versus 18.5 h, p = 0.83). Insulin was used in three patients (one in classic and two in benign group).

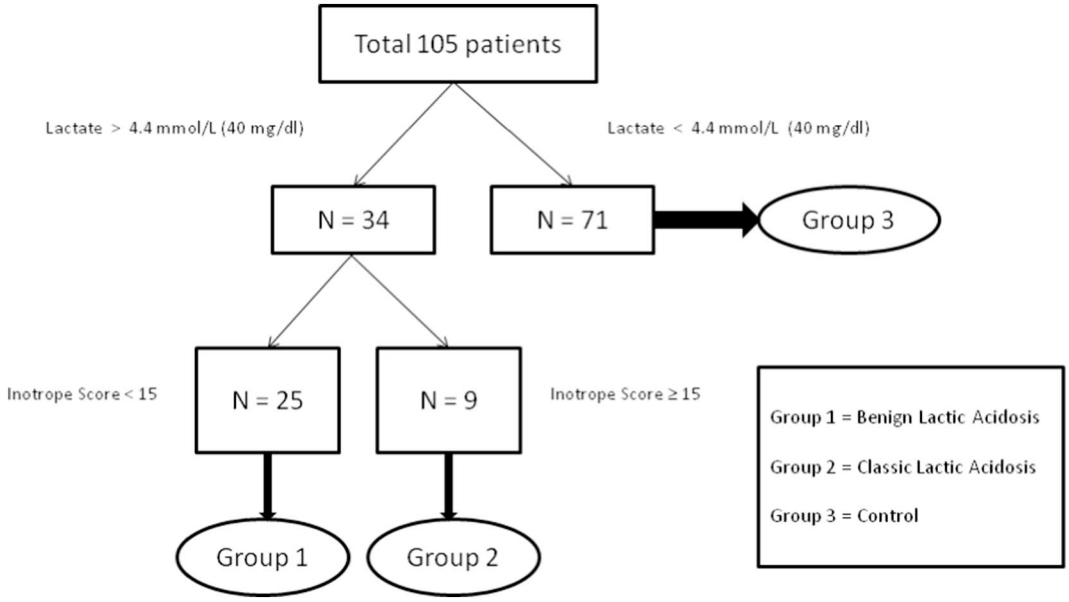

Fig. 1. Flow chart for patient selection based on the postoperative lactate and inotrope score. *Lactic acid unit conversion: 10 mg/dL = 1.11 mmol/L.

Table 1
Surgical diagnosis in ALL patients.

Surgical diagnosis	n	%
RV-PA conduit placement	31	29.5
Pulmonary valve repair/replacement	21	20
Aortic valve repair/replacement	13	12.4
Repair of anomalous origin of a coronary artery	8	7.6
Mitral valve repair/replacement	6	5.7
AVSD repair	4	3.8
Other[a]	22	21

AVSD: atrioventricular septal defect.
RV-PA: right ventricle-pulmonary artery.
[a] Includes the following procedures: ventricular septal defect closure with aortic valve repair, atrial septal defect closure, sub-aortic membrane resection, tricuspid valve repair, Cone procedure, Ross procedure, Glenn procedure, and right ventricular outflow tract resection.

3.3. Clear vs. blood cardiopulmonary bypass prime

In the benign group, patients who received clear vs. blood prime had higher mean serum lactate during the first 10 postoperative hours (5.02 mmol/L or 45.2 mg/dl versus 4.30 mmol/L or 38.7 mg/dl), but this difference was not statistically significant ($p = 0.34$).

3.4. Propofol infusion

Most of our patients (92.4%) received Propofol infusion as part of their postoperative sedation with a mean duration of administration of 6 (1 − 30) hours. Propofol administration was not associated with significantly different lactate levels, when compared to the group of patients who did not receive propofol (4.65 mmol/L or 41.89 (+/− 25.7) mg/dl versus 4.2 mmol/L or 37.8 (+/− 31.7) mg/dl, $p = 0.382$).

4. Discussion

Transient elevation of lactate is commonly observed in children after open heart surgery. This hyperlactemia by itself is not a hallmark of worsening cardiac output and patients with lactic acidosis but without compromised cardiac output have similar clinical outcomes to those of the patients who had no elevation in their lactate levels postoperatively [5]. In the literature, this benign lactic acidosis is differentiated from the classic or type A lactic acidosis [3,6], which is characterized by a low redox potential state in the milieu of impaired tissue perfusion secondary to low cardiac output. While the lactate:-pyruvate ratio is elevated in classic lactic acidosis, in benign or type B lactic acidosis the lactate:pyruvate ratio is normal [4,6] indicating there is no cellular hypoxia at the mitochondrial level.

In the pediatric literature, there are multiple case reports addressing this phenomenon. According to Meert et al. [11] 45% of children admitted to the pediatric intensive care unit for severe asthma and who received beta adrenergic stimulants for treatment, had lactate levels of > 5 mmol/L due to adrenergic overstimulation. They found normal lactate:pyruvate ratios in these patients, corresponding to type B lactic acidosis. Another well documented presentation of type B lactic acidosis is in metformin intoxication [12]. In sepsis, lactic acidosis can be due to a low oxygen delivery state, as well as a consequence of a pyruvate overproduction from adrenergic overstimulation. In early stages of sepsis type B lactic acidosis is common, with preserved oxygen delivery [13].

Because we did not have pyruvate levels available in this retrospective study, we used inotrope scores as a surrogate marker to identify benign and classic lactic acidosis in patients with significant lactic acidosis (peak lactate ≥ 4.44 mmol/L or 40 mg/dl). We selected a lactate value cutoff of 4.4 mmol/L (40 mg/dl). Based on the current pediatric literature, lactate levels above 4 mmol/L are associated with significantly worse postoperative clinical outcomes [8,14]. Since type B lactic acidosis is not associated with low cardiac output, we hypothesized that the benign group would be the clinically identifiable correlate of type B lactic acidosis and the classic group would correlate with type A lactic acidosis (Fig. 1). In this cohort, the overall incidence of benign lactic acidosis was 23.8% and classic lactic acidosis 8.6%. The classic group had significantly elevated heart rate and central venous pressure, decreased systolic blood pressure and urine output in the first 6 postoperative hours, compared to the control group (Fig. 2). Despite having the same RACHS category throughout all groups, the classic group had longer length of cardiopulmonary bypass time, postoperative chest tube output, length of intubation and length of hospital stay (Table 2). The benign group had similar postoperative mean vital signs and clinical outcomes as the control group in every aspect (Table 2), except the presence of hyperglycemia and lactic acidosis.

When comparing the characteristics of lactic acidosis in the classic to the benign group (Fig. 3), we found that the duration of the lactic

Table 2
Patient clinical variables in the three separate groups.

	All	Benign	Classic	Control	p-Value
N	105	25	9	71	–
Demographic data					
Gender, (male)	60(57.1)	17(68)	4(44.4)	39(54.9)	0.40
LOS (days)	5.16(3.2–17.3)	5.16(3.67–10.5)	9.25(4.13–15.2)	5.12(3.2–17.3)	0.004[b]
BMI (kg/m^2)	18.1(11.7–37.5)	17.5(13.7–25.1)	19.0(11.7–26.8)	18.2(11.9–37.5)	0.75
Cyanotic heart disease	5(4.8)	0	3(33.3)	2(2.8)	0.007[b]
Operative data					
Age at operation (years)	13(5–21)	12(5–19)	15(5–17)	13(5–21)	0.91
Weight at operation (kilograms)	41(10–116)	37.9(15.7–77)	50.7(12.5–78.8)	42(9.8–116)	0.92
RACHS scores	3(1–9)	3(2–3)	3(2–3)	3(1–3)	0.65
Aortic cross-clamp time (minutes)	39.5(0–172)	41(10–172)	87(30–172)	37(0–140)	0.06
Bypass time (minutes)	64(21–251)	61(21 − 223)	165(60–251)	60(25–192)	0.004[b]
Cardioplegia (doses)	1(0–5)	2(1–5)	3(1–5)	1(0–5)	0.06
Length of intubation (hours)	6(1–40)	6.4(1.2–39.3)	17(2.2–39.6)	5.3(1.1–27.8)	0.026[b]
Inotropes					
Inotrope score day 1	8(0–25)	8.2(3 − 13)	15(10.5–25)	8(0–15)	< 0.001[b]
Inotrope score day 2	5.1(0–24.5)	5.1(0 − 13)	15(10–24.5)	5(0–13)	< 0.001[b]
Insulin use (%)	3(2.9)	2(8)	1(11.1)	0(0)	0.05
Length of inotrope support (days)	3(0 − 10)	3(1–4)	5(3–9)	3(0–10)	< 0.001[b]
Changed IV fluids	12(11.4)	6(24)	2(22.2)	4(5.6)	0.019[b]
Post-operative data					
Pacemaker	12(11.4)	0(0)	3(33.3)	9(12.7)	0.022[b]
Received fluid bolus	34(32.4)	8(32)	8(88.9)	18(25.4)	0.001[b]
Chest tube output day 1 (ml/kg/day)	4.49(0.5–83.16)	5.83(0.16–14.08)	6.95(3.49–56.06)	4.17(0.5–83.16)	0.013[b]
Chest tube output day 2 (ml/kg/day)	3.19(0.17–39.51)	3.36(0.26–39.51)	8.69(1.23–38.46)	3.1(0.28–38.43)	0.05[b]
Received propofol	97(92.4)	23(92)	8(88.9)	66(93)	0.85
Survival	103(98.1)	23(92)[a]	9(100)	71(100)	0.10

BMI: body mass index.
IV: intravenous.
LOS: length of stay.
RACHS: risk adjustment for congenital heart surgery.
[a] 2 deaths in this group were post discharge, both for arrhythmia.
[b] Significant difference between three groups at α = 0.05 level. Data presented as median (range) or number (percentage).

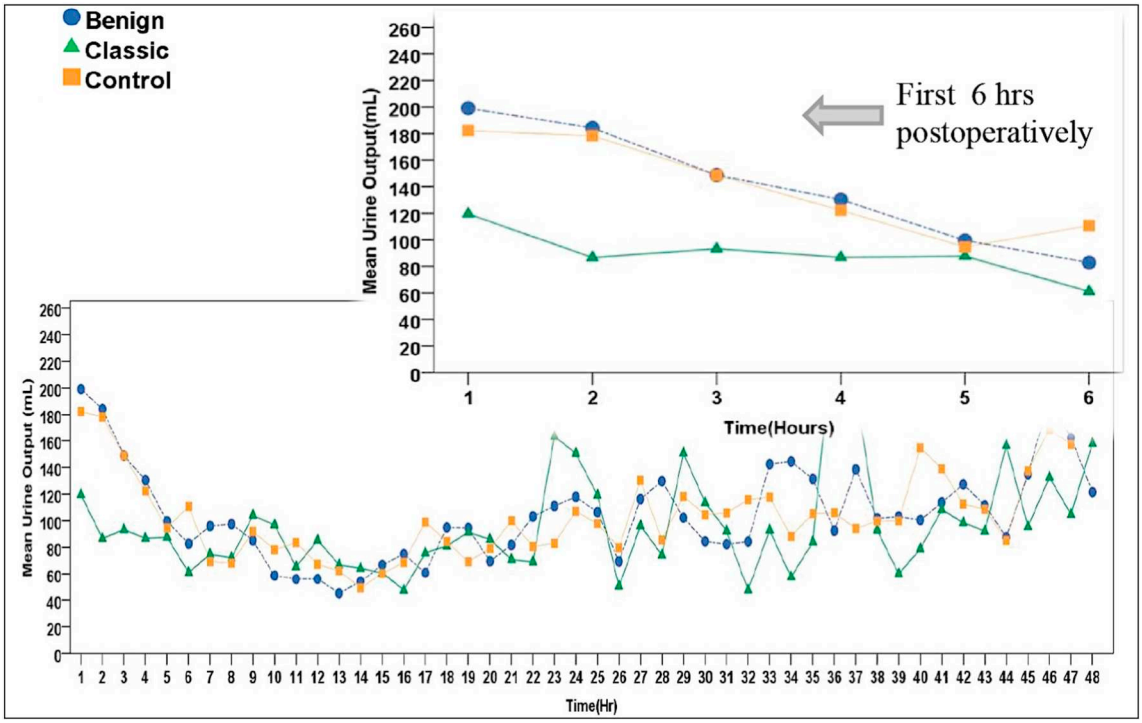

Fig. 2. Change in the mean postoperative urine output. Urine output was significantly decreased in the classic group during the first 6 postoperative hours (p = 0.041).

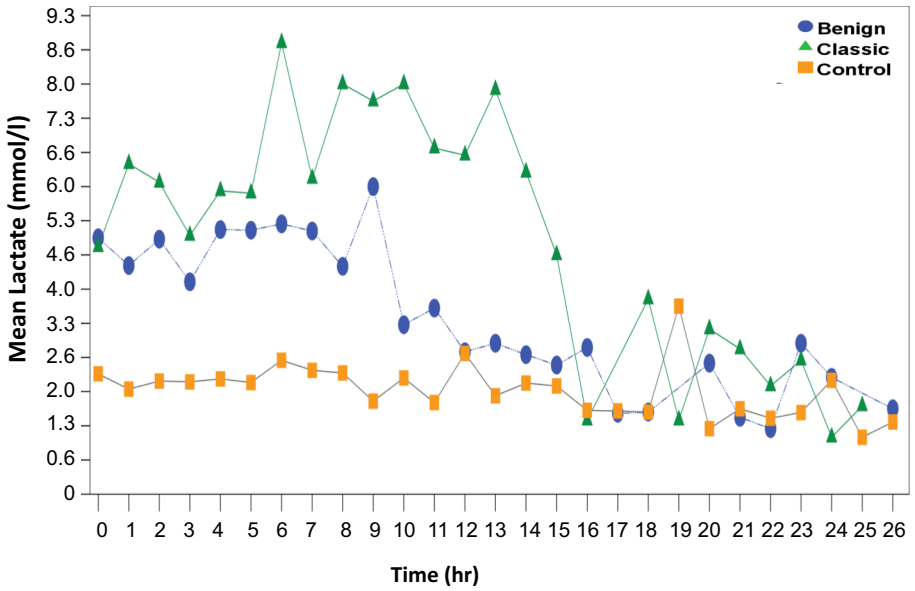

Fig. 3. Change in the mean postoperative lactate level.

acidosis was longer and more pronounced than in the benign group. Riad et al. used subcutaneous microdialysis probes to measure lactate:pyruvate levels in 10 postoperative Fontan patients [7]. They found normal lactate levels immediately postoperatively, with a gradual rise of the mean lactate levels and subsequent normalization within 12 h. Pyruvate levels and lactate levels correlated and the measured cardiac index and the oxygen delivery steadily increased, therefore defining the presence of type B lactic acidosis. In our benign group we observed that 8 out of 25 patients (32%) had normal lactate levels (below 2.44 mmol/L or 22 mg/dl) initially, with an increase above 4.4 mmol/L (40 mg/dl) at a later point.

We found hyperglycemia in all 3 groups, but the blood glucose levels were significantly elevated in the classic and the benign groups compared to the control group (Fig. 4). The resolution of the hyperglycemia paralleled the curve of the serum lactate levels, and resolution was faster in the benign group (the same duration as the control group) compared with the classic group. Similar parallel elevation and resolution of lactate and glucose in the first 24 postoperative hours was described by Parsapour et al. in a fourteen year old patient undergoing open heart surgery [15]. In 6 patients in the benign group, the attending critical care physician changed the intravenous fluid to glucose free fluid, which resulted in a trend toward earlier resolution of the hyperglycemia. This approach did not impact the duration of the lactic acidosis.

The possible effect of the bloodless (clear) cardiopulmonary bypass prime solution on development of postoperative lactic acidosis was described by Toda et al. [16]. In their study they compared a younger group of patients, aged 2 months to 4 years, to an older group, aged 4 years and older. The former group received blood prime while the latter group received bloodless prime. Lactic acidosis of ≥ 4 mmol/L was independently associated with bloodless prime. When we compared patients who received bloodless versus blood prime in our benign group, we found a tendency toward higher lactate levels in the bloodless group, but statistically there was no significant difference between

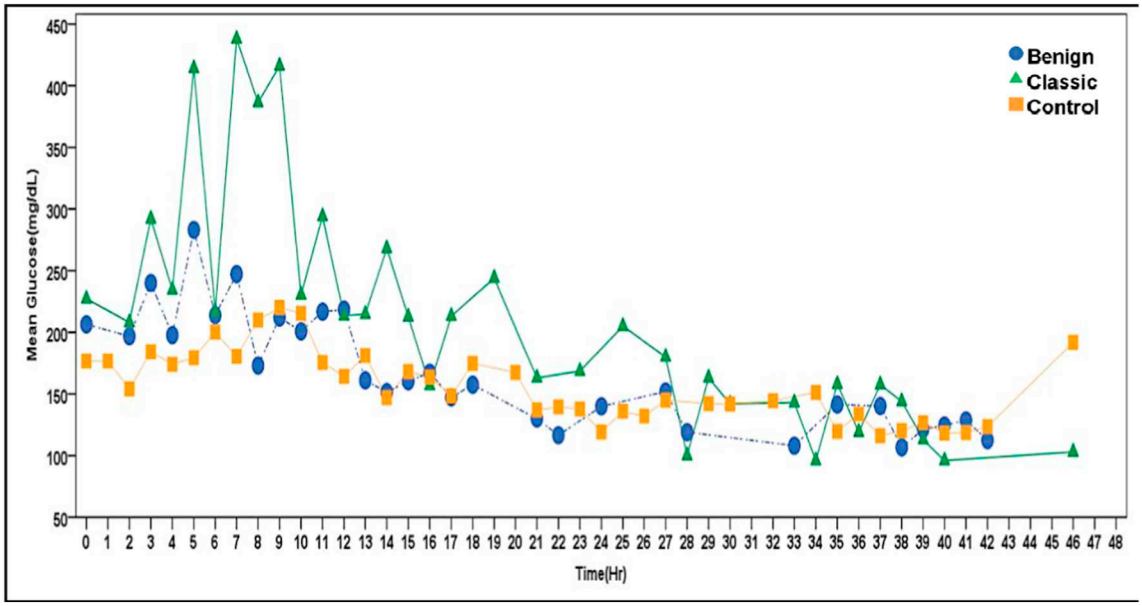

Fig. 4. Change in the mean postoperative glucose level.

the two.

Since the majority of our patients received propofol postoperatively for a brief period of time, we looked at patients' lactate levels, for those who had received propofol and who did not. We found no difference between the two groups. None of the patients were suspicious of developing any clinical signs of propofol related infusion syndrome [17].

5. Limitations

Our study has limitations from multiple perspectives: a retrospective design, the offset of timing of lactate measurements, lack of pyruvate measurements, and the large number of statistical comparisons, potentially contributing to increased type 1 error. Despite these limitations, our study is the largest study to date describing the postoperative benign lactate elevation in postoperative cardiac patients in the pediatric literature.

6. Conclusion

Benign lactic acidosis is clinically distinct from classic lactic acidosis. Despite presenting with elevated lactates and hyperglycemia, it has faster resolution, it is associated with low inotrope score and patients exhibit stable postoperative hemodynamics with similar postoperative clinical outcomes to the patients in the control group. Our study brings up an interesting question: if there is a “benign” form of lactic acidosis, what is causing it? To answer this question in depth, further prospective investigations are needed regarding the biochemical markers associated with postoperative lactic acidosis.

Acknowledgements

We would like to acknowledge and thank Yi Lu, MS for her assistance with data management and statistical analysis. This study was presented as poster presentation at the 11th International Pediatric Cardiac Intensive Care Society meeting, on December 12th, 2014 in Miami, FL.

Compliance with ethical standards

The study has not received any funding. None of the authors have had any conflicts of interest, nor received any research grant for the purpose of the study. Ethical approval: This article does not contain any studies with human participants, performed by any of the authors. Informed consent was not required for a retrospective chart review.

Conflicts of interest and source of funding

None declared for all authors.

References

[1] Basaran M, Sever K, Kafali E, et al. Serum lactate level has prognostic significance after pediatric cardiac surgery. J Cardiothorac Vasc Anesth 2006;20:43–7.
[2] Duke T, Butt W, South M, et al. Early markers of major adverse events in children after cardiac operations. J Thorac Cardiovasc Surg 1997;114(6):1042–52.
[3] Baker S, Cadogan M. Varying clinical significance of hyperlactataemia. Crit Care Resusc 2005;7:57–9.
[4] Vernon C, Letourneau JL. Lactic acidosis: recognition, kinetics, and associated prognosis. Crit Care Clin 2010;26:255–83.
[5] Raper RF, Cameron G, Walker D, et al. Type B lactic acidosis following cardiopulmonary bypass. Crit Care Med 1997;25(1):46–51.
[6] Shinde S, Golam K, Kumar P, et al. Perioperative blood lactate levels, pyruvate levels, and lactate-pyruvate ratio in children undergoing cardiopulmonary bypass for congenital heart disease. Indian J Crit Care Med 2005;9(3):145–50.
[7] Hosein RB, Morris KP, Brawn WJ, et al. Use of tissue microdialysis to investigate hyperlactataemia following paediatric cardiac surgery. Interact Cardiovasc Thorac Surg 2008;7(3):384–8.
[8] Perfecto SM, Casas L, Balderas J, et al. Lactate level as an early prognostic marker of major adverse events in pediatric open heart surgery. Phil Heart Center J 2012;16(2):27–34.
[9] Gaies MG, Gurney JG, Yen AH, et al. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. Pediatr Crit Care Med 2010;11(2):234–8.
[10] Kumar, et al. Vasoactive Inotrope Score as a tool for clinical care in children post cardiac surgery. Indian J Crit Care 2014;18(10):653–8. oct.
[11] Meert KL, McCaulley L, Sarnaik AP. Mechanism of lactic acidosis in children with acute severe asthma. Pediatr Crit Care Med 2012;13(1):28–31.
[12] Gura M, Devrim S, Sagiroglu A, et al. Severe metformin intoxication with lactic acidosis in an adolescent: a case report. Internet J Anesthesiol 2009;27(2):1–5.
[13] Suetrong B, Walley KR. Lactic acidosis in sepsis: it's not all anaerobic implications for diagnosis and management. Chest 2016;149(1):252–61.
[14] Kalyanaraman M, DeCampli WM, Campbell AI, et al. Serial blood lactate levels as a predictor of mortality in children after cardiopulmonary bypass surgery. Pediatr Crit Care Med 2008;9(3):285–8.
[15] Parsapour K, Pullela R, Raff G, et al. Type B lactic acidosis and insulin resistant hyperglycemia in an adolescent following cardiac surgery. Pediatr Crit Care Med 2008;9(1):e6–9.
[16] Toda Y, Duke T, Shekerdemian LS. Influences on lactate levels in children early after cardiac surgery: prime solution and age. Crit Care Resusc 2005;7:87–91.
[17] Timpe EM, Eichner SF, Phelps SJ. Propofol-related infusion syndrome in critically ill pediatric patients: coincidence, association, or causation? J Pediatr Pharmacol Ther 2006;11(1):17–42.