Influences on Lactate Levels in Children Early After Cardiac Surgery: Prime Solution and Age

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ABSTRACT

Objective: *Hyperlactataemia is often seen after cardiac surgery in children and is associated with an increased risk of adverse outcome, especially in infants and young children. However, we noticed that many older children after cardiac surgery had elevated lactate levels in the absence of other markers of oxygen debt or cardiovascular instability and had an uncomplicated postoperative course. Many older children undergo surgery without blood products being used in the cardiopulmonary bypass (CPB) circuit prime. The aim of this study was to determine whether lactate levels in children after CBP are influenced by age and/or pump prime solutions.*

Methods: *We studied 100 children undergoing open heart surgery in a tertiary paediatric cardiac surgical unit. Fifty children were aged 2 months to 4 years (Group 1) and 50 were aged 4 years or older (Group 2). Blood samples were obtained from an arterial catheter and serum lactate levels were collected at the time of admission to the paediatric intensive care unit (PICU) and 4 hours later. The following data were collected from the medical records or laboratory databases: weight, age, lowest haemoglobin during CPB, total bypass time, aortic cross clamp time, priming solution used, length of postoperative ventilation and PICU stay, type of surgery and occurrence of adverse perioperative events, including cardiac arrest, need for extracorporeal support or death.*

Results: *All children in Group 1 had a blood prime. All children in Group 2 had a bloodless prime. Although there were differences in the types of anomalies and surgical procedures performed, there were no significant differences between the two groups in terms of surgical complexity, CBP time, aortic cross clamp time and haemoglobin during CPB. Lactate levels in children in Group 2 were higher than in Group 1. Sixteen children (32%) in Group 2 had a lactate level of ≥ 4 mmol/L, whereas only 3 children (6%) in Group 1 had a lactate level of ≥ 4 mmol/L (Fisher's exact test p = 0.0002). Using multivariate analysis the pump prime solution was independently associated with high lactate levels after CPB.*

Conclusions: *Lactate levels after cardiac surgery in older children who have a bloodless prime may not have the same physiological or prognostic implications as in infants who have a blood prime.* (**Critical Care and Resuscitation 2005; 7: 87-91**)

Key words: lactate, children, cardiac surgery, pump prime, age, outcome

Hyperlactataemia results from anaerobic metabolism, in response to inadequate cellular oxygen delivery.[1] It is often used as a marker of oxygen delivery and circulatory status and as a predictor of the post-operative course after cardiac surgery.[2-7] However, after cardiac surgery in older children we frequently observed an elevated blood lactate without any other evidence of oxygen debt or cardiovascular compromise. We investigated the serum lactate levels after cardiac surgery in children of different ages undergoing cardiac surgery with cardiopulmonary bypass (CPB).

PATIENTS and METHODS

One hundred consecutive children undergoing

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elective cardiac surgery with CPB between March and October 2002 were studied. Fifty children were aged between 2 months to 4 years (Group 1) and 50 children were over 4 years old (Group 2).

One child who underwent surgery during that period and who was mechanically ventilated, receiving inotropic support and had an elevated lactate level prior to surgery was excluded from the analysis. All data were retrospectively collected from medical and laboratory records. Surgical complexity was determined by the operative classification reported by Gallivan and colleagues.[8]

Anaesthesia was induced and maintained with fentanyl (50 - 70 µg/kg) with isoflurane inhalation or a ketamine/midazolam infusion. Pancuronium was given to facilitate tracheal intubation. All patients were given 20 mL/kg of Hartmann's solution (Baxter, Sydney, Australia) before CPB. In order to minimise their exposure to blood products, many children in our unit underwent cardiac surgery without blood primed CPB circuits. Cardiopulmonary bypass was initiated with the use of heparin, and the circuits were primed with Plasmalyte 148 (Baxter, Sydney, Australia), 5% glucose and blood (for blood prime), and with Plasmalyte 148, Haemaccel (Hoechst, Sydney, Australia) and 5% glucose (for bloodless prime). No prime solutions contained lactate.

Following the operation, patients were transferred to the paediatric intensive care unit (PICU). Blood samples were obtained from an arterial catheter and serum lactate levels were collected at the time of admission to the PICU and 4 hours later. The following data were collected from the medical records or laboratory databases: weight, age, lowest haemoglobin during CPB, total bypass time, aortic cross clamp time, priming solution used, length of post-operative ventilation and PICU stay, type of surgery and occurrence of adverse perioperative events, including cardiac arrest, need for extracorporeal support or death.

Statistical analysis

Normally distributed data are presented as mean $\pm$ SD, while non-normally distributed data are presented as median $\pm$ interquartile range (IQR). Student t test for normally distributed data or Wilcoxon test for non-normally distributed data were used to compare the differences between groups. Univariate and multivariate regression analysis were used to assess the relationship between lactate levels and other variables. Statistical analyses were carried out with the use of SAS (SAS Institute Inc, Cary, NC, USA) software and Stata Intercooled 7 (Stata Corp, Texas). A p-value of less than 0.05 was considered statistically significant.

RESULTS

Although there were major differences in the nature of operations performed between the two groups, there was no significant difference in level of procedural complexity. The patient characteristics are displayed in Tables 1 and 2. All younger patients (Group 1) had blood-primed CPB circuits, whereas none of the older patients (Group 2) did. Lactate levels for children in Group 2 were significantly higher than in Group 1 (Table 2 and Figure 1). Sixteen children (32%) in Group 2 had a lactate level of $\geq$ 4 mmol/L, whereas only 3 children (6%) in Group 1 had a lactate level of $\geq$ 4 mmol/L (Fisher's exact test p = 0.0002).

Table 1. Patient characteristics

	Group 1	*Group 2*
Patient number	50	50
Age (months)	6 (3-13.3)	120 (73.5-168)
BW (kg)	6.2 (4.2-8.9)	30.0 (19.9-49.7)
VSD closure	17	2
ASD closure	2	2
AVSD repair	9	3
BCPC	6	1
TOF repair	3	
Aortic valve		11
Conduit replacement		5
Fontan		4
Mitral valve		11
Other	13	10

Values are presented as median (interquartile range), BW = body weight, VSD = ventricular septal defect, ASD = atrial septal defect, AVSD = atrioventricular septal defect, BCPC = bidirectional cavo-pulmonary connection, TOF = tetralogy of Fallot.

In univariate analysis there was no association between lactate levels at PICU admission and bypass time, cross clamp time, or lowest haemoglobin recorded during CPB. On univariate analysis there were minor correlations between lactate at PICU admission and age (R^2 = 0.06, p = 0.015) and between lactate levels and prime solution (blood or bloodless) used (R^2 = 0.1, p = 0.001). Table 3 shows the multivariate analysis. The type of prime (blood or bloodless) had the strongest independent correlation (R^2 = 0.11, p = 0.036) with post-operative lactate levels.

DISCUSSION

In our study, lactate levels after CPB were higher in older children who had a bloodless prime than in younger children who had a blood prime, with the bloodless prime being a stronger independent risk factor for

Table 2. Measurements in each group

	Group 1	*Group 2*	*p*
Lactate at PICU admission (mmol/L)	2.10 (1.80 - 2.75)	3.05 (2.05 - 4.45)	0.006
Lactate at 4 hr (mmol/L)	1.85 (1.48 - 2.43)	2.60 (1.80 - 4.13)	0.001
Haemoglobin during bypass (g/L)	73.1 ± 10.9	76.4 ± 18.2	0.262
Haemoglobin at PICU admission (g/L)	104.2 ± 17.4	102.7 ± 20.7	0.700
Bypass time (min)	126.3 ± 55.8	128.7 ± 55.5	0.834
Aortic cross-clamp time (min)	68.8 ± 42.6	73.3 ± 57.2	0.655
Duration of ventilation (hr)	23.3 (9.0 - 61.0)	10.1 (6.5 - 16.5)	0.0001
Duration of PICU stay (days)	1.9 (0.9 - 3.7)	0.9 (0.8 - 1.1)	0.0001
No of adverse events (no of deaths)	6 (2)	0 (0)	0.027

Data for haemoglobin, bypass time, and cross clamp time are presented as mean ± standard deviation and data for lactate, ventilation time, and length of PICU stay as median (IQR). PICU = paediatric intensive care unit

Table 3. Multivariate modelling of effect of haemoglobin, age, cardiopulmonary bypass and aortic cross-clamp times and type of prime on blood lactate levels

	Coefficient	*Standard error*	*P value*
Haemoglobin	-0.0073	0.914	0.507
Age	-0.0012	0.0011	0.765
Cardiopulmonary bypass time	-0.0013	0.004	0.752
Cross clamp time	0.0019	0.004	0.665
Type of prime	0.5796	0.272	0.036

PICU = paediatric intensive care unit

hyperlactataemia than older age. However, there were several other differences between the two groups: particularly the type of cardiac anomaly and type of procedures performed. As the study was retrospective and non-randomised it was difficult to distinguish the effects of any one of these, or other unknown potentially confounding factors, from the effects of the type of prime and age on lactate levels. For example, the two populations may have differed in terms of severity of illness pre-operatively, proportion of children with cyanosis, presence of hypotension on induction of anaesthesia etc. While on multivariate analysis the type of prime had a stronger influence on lactate levels than the patient's age, neither factor explained a large proportion of the variability of the lactate levels.

Many reports show increased lactate levels during and following CPB.[2-7] The causes of hyperlactataemia after CPB may be several: regional or global impairment of oxygen delivery, anaerobic metabolism and impaired lactate clearance may be important factors. In our study, there was no difference in haemoglobin between the two groups and pump flows were determined by patients' body surface area. Therefore, it is unlikely that global oxygen delivery during CPB differed between the two groups. Raper *et al*, described an increased lactate production despite normal oxygen delivery following CPB,[9] indicating that some cases of hyperlactataemia after CPB cannot be explained by a single phenomenon of anaerobic metabolism caused by hypoperfusion or inadequate tissue oxygen delivery. Chioléro *et al*, found no difference between lactate clearance in patients with cardiogenic shock early after heart surgery and in healthy volunteers.[10]

Some authors have investigated the role of the type of pump prime solution in the development of post-operative acidosis and hyperlactataemia,[11-13] or suggested beneficial effects of a bloodless prime for CPB.[14,15] However, there are currently no published comparisons of postoperative lactate between patients undergoing surgery using blood and bloodless primes. In addressing this question it is important to exclude possible confounding factors other than the use of blood, such as electrolyte and acid-base discrepancies between the two groups. In our study, electrolyte and acid-base homeostasis were managed in all patients using frequent intra-operative blood gas analysis. Bicarbonate, base-deficit, pH and electrolytes did not differ substantially between the two groups.

Age as an independent determinant of lactate levels after cardiac surgery has not been described. Pianosi *et al*, reported that exercise-induced increases in lactate concentration were greater with increasing age in healthy children,[16] suggesting that rates of lactate production and/or elimination may vary with age. However, these investigators only included children aged between 7 - 17 years, rather than younger children which were included by our study.

There are many reports that suggest that lactate levels predict outcome in patients who undergo cardiac surgery.[2-7] We previously reported that lactate levels 4 hours after ICU admission were a useful predictor of major adverse events in infants after CPB.[4] Other groups have reported similar findings in children,[2] and in adults.[7] The relatively small sample size of our current study and low incidence of adverse postoperative events do not allow us to measure any association between hyperlactataemia and outcome after CPB in older children. Despite considerably elevated lactate levels (Figure 1), the older children in our study experienced an uncomplicated postoperative course, but this does not prove a lack of association.

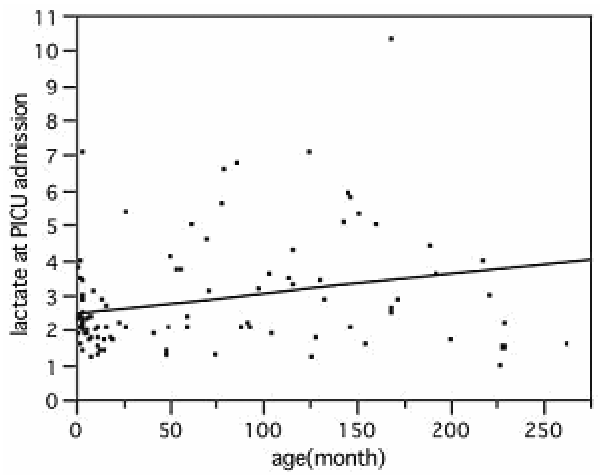

Figure 1. Relationship between the patients' age and lactate levels at PICU admission after cardiac surgery with CPB. The correlation was weak: $R^2 = 0.058$, $p = 0.015$.

There are several other problems with our study that require further scrutiny. Firstly, we recorded 'lowest' haemoglobin during CPB and not the duration of exposure to this nadir haemoglobin. It is likely that prolonged exposure to low a haemoglobin level may be a stronger stimulus to anaerobic metabolism and development of hyperlactataemia than a brief exposure. Secondly, others have reported that hyperlactataemia after CPB is associated with initial hypotension when CPB is commenced;[18] we did not investigate this in our study. Thirdly, although none of the patients in our series were critically ill before surgery, we do not have sufficiently detailed haemodynamic data to examine any possible contributions of preoperative status on the post-operative lactate. Finally, as epinephrine infusions increase lactate level,[19] we did not compare what catecholamines and how much were administered in each patient. However we believe none of our patients received epinephrine infusions in the operating room or before the lactate level was measured.

In conclusion, we found that early after surgery, older children with a bloodless primed CPB circuits have higher blood lactate levels than younger children with a blood primed circuit. This phenomenon seems more strongly related to pump prime differences than to age. Further research on the aetiology, prognostic significance and appropriate responses to hyperlactataemia in older children after cardiac surgery is required.

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