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ORIGINAL RESEARCH

Proportion of Hyperlactatemia during Cardiopulmonary Bypass and its Impact on Post-operative Outcomes in Coronary Artery Bypass in a Tertiary Care Centre

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Abstract

Background: In this study, we wanted to identify the proportion of patients with high blood lactate levels during cardiopulmonary bypass (CPB) in coronary artery bypass grafting and its association with post-operative morbidity and mortality. We also wanted to determine the proportion of hyperlactatemia during CPB in patients undergoing CABG and assess the association between hyperlactatemia during CPB in patients undergoing CABG and post-operative morbidity and mortality.

Methods: This was a hospital based single centre retrospective record study conducted among 130 patients who underwent coronary artery bypass surgery in the Department of Cardiovascular Thoracic Surgery, Government Medical College, Thiruvananthapuram, from January 2018 to January 2020 after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

Results: Preoperatively females had higher lactate levels as compared to males, and this was statistically significant. The correlation between CPB time and peak intra-operative lactate level and also correlation between aortic cross-clamp time and peak lactate level was also found to be statistically significant. In post-operative morbidity, the length of ICU stays (<5 days - 32 [57.1%] vs. 57[76.5%]; ≥5 days - 24 [42.9%] vs. 17 [23.5%]; P = 0.013) were found to be significantly higher in the HL group.

Conclusion: Hyperlactatemia during CPB in CABG points to perilous outcomes of cardiac surgery. It points to pathologies that need prompt correction to avert serious perioperative morbidity and mortality. It is an independent predictor of post-operative complications including all- cause mortality and severe morbidity after cardiac surgery in adult patients.

Keywords: Hyperlactatemia, Cardiopulmonary Bypass, Postoperative, Outcomes, Coronary Artery Bypass.

Introduction

Cardiopulmonary bypass (CPB) is widely preferred for cardiac surgery to maintain systemic perfusion and oxygenation.[1] It is well known that tissue hypoperfusion due to circulatory failure is associated with an increase in lactate levels secondary to anaerobic metabolism.[2,3,4] This situation is termed as Type A lactic acidosis, which results from an imbalance between tissue oxygen demand and supply.[5,6,7,8] Therefore, increase in lactate levels as seen in Type

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A lactic acidosis is closely associated with total oxygen deficit and tissue hypoperfusion.[5,6,7,8,9] Hyperlactatemia (HL) in patients who undergo cardiac surgery with CPB can be due to tissue hypoxia, non-hypoxic causes such as drug therapy, cardioplegia solution, hypothermia, and CPB itself.[10,11] In a recent study done by Demers et al., it was found that in adult patients undergoing cardiac surgery, HL is detected in 10–20% of patients[11,12] and was associated with significant post-operative morbidity and mortality.[11] In a study done by Broder and Weil, more than 88% of patients who had blood a lactate level of > 4.0 mmol/L had a high risk of mortality due to circulatory shock.[6] The same authors documented that the chances of survival from shock declines from 90 to 10% as blood lactate levels escalates from 2.0 to 8.0 mmol/L.[7,13]

The outcome after any cardiac surgery is determined by the pre-operative characteristics of the patient as well as intra-operative factors such as surgical technique, strategies of myocardial protection, hemodynamic management of the patient, and duration of CPB, which play a crucial role in determining the post-operative course of the patient.[14-20] Monitoring of such factors during the perioperative period may help in early recognition and treatment, which may improve the overall outcome of the patient. Serum lactate levels have been used frequently in critical care settings as a guide for clinicians to begin and optimize early treatment in patients with shock and thereby help to decrease morbidity and mortality.[11,13-15,20,21] Patients undergoing cardiac surgery under CPB, despite having normal arterial blood gases (ABGs), may still experience lactic acidosis secondary to tissue hypoperfusion. Therefore, monitoring blood lactate levels in cardiac surgery patients might be more sensitive than ABG analysis alone and will thereby help in early detection of an imbalance between oxygen supply and demand. The hypothesis of this study is that patients with high blood lactate levels in the period of CPB are at a higher risk for post-operative morbidity and mortality. The goal of this study was to proportionate hyperlactatemia in patients undergoing coronary bypass surgery under CPB and its effect on post-operative outcomes.

Aims and Objectives

- To identify the proportion of patients with high blood lactate levels during CPB in coronary artery bypass grafting and its association with post-operative morbidity and mortality.
- To determine the proportion of hyperlactatemia during CPB in patients undergoing CABG.
- To assess the association between hyperlactatemia during CPB in patients undergoing CABG and post-operative morbidity and mortality.

Materials &methods

This was a hospital based single centre retrospective record study conducted among 130 patients who underwent coronary artery bypass surgery in the Department of Cardiovascular Thoracic Surgery, Government Medical College, Thiruvananthapuram, from January 2018 to January 2020 after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

Inclusion Criteria

All patients who are admitted and will be undergoing coronary artery bypass surgery in Department of Cardiovascular and Thoracic Surgery, Government Medical College, Thiruvananthapuram during the course of the study

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Exclusion Criteria

Patients who undergo OPCAB or those with combined procedures that include CABG are excluded from the study. Those patients who had an abnormal plasma lactate level (>3.0 mmol/l) before entering CPB were also excluded.

Sampling Size

$$n = \frac{Z_{\infty}^2\, p(1-p)}{d^2}$$

Where, n= Sample size
$Z\infty$ = Z statistics for a level of confidence
P = Estimated proportion of an attribute present in the population
d = Level of precision
Present study: -
P = 0.427 (Proportion of hyperlactatemia during CPB)
d = 20% of p = 0.0854
$Z\infty$ = 1.96 for ∞ = 0.05
= 129
Final sample size for the study is 129

Statistical Methods

Categorical and quantitative variables were expressed as frequency (percentage) and mean ± SD respectively. Incidence of hyperlactatemia (>4.0 mmol/l) during cardiopulmonary bypass will be expressed in percentage with 95 % CI. Association will be tested using chi-square test. p <0.05 will be considered as the threshold for statistical significance. Statistical analyses will be performed by using a statistical software package SPSS, version 20.0.

Results

Variable	Lactate, n(%)		P
	<4	≥4	
Age: <60	32(56.6)	25(43.4)	0.815
≥60	42(57.8)	31(42.2)	
Sex: Male	52(62.1)	32(37.9)	0.011
Female	22(48.5)	24(51.5)	
Diabetes mellitus	27	19	0.540
Hypertension	32	21	0.310
COPD	4	3	0.798
Preoperative Risk Factors for Hyperlactatemia			
Table 1			

On comparing the 2 groups, age distribution was almost the same with no statistical significance (P = 0.815). Females had higher lactate levels as compared to males, and this was statistically significant (P = 0.011). The other co-morbidities such as diabetes, hypertension, ischemic heart disease and chronic obstructive pulmonary disease did not have any statistical significance in relation to the peak intra-operative blood lactate levels.

Variable	Lactate, n(%)		P
	≥4(mmol/l)	<4(mmol/l)	
CPB time (min)	92.4 ± 26.0	83.96 ± 28.18	0.003
AOX time (min)	55.8 ± 18.2	48.4 ±19.8	0.007

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Lowest Hb (mg/dl) on CPB	7.03 ± 1.20	7.04 ± 1.47	0.510
Flow rate(L/min/m2)	3.5 ± 2.1	3.3 ± 1.9	0.540

Comparison of Intraoperative Variables between the Two Groups

Table 2

Patients with HL had significantly longer CPB time (92.40 ± 26.0 vs. 83.96 ± 28.18 min; P = 0.003) and aortic cross-clamp time (55.8 ± 18.2 vs. 48.4 ± 19.8 min; P = 0.007). There was no significant difference in the lowest haemoglobin on pump or flow rate between the two groups.

Variable		Lactate, n(%)		P
		≥4	<4	
Arrhythmia	+	11(19.4)	4(5.3)	0.004
	–	45(80.6)	70(94.7)	
Inotropic support	+	19(34)	9(11.8)	0.001
	–	37(66)	65(88.2)	
Mech. ventilation	+	5(7.1)	3(3.9)	0.447
	–	51(92.6)	71(96.1)	
ICU stay	<5	32(57.1)	57(76.5)	0.013
	≥5	24(42.9)	17(23.5)	
SSI	+	19(34)	3(3.9)	0.003
	–	37(66)	71(96.1)	
Renal dysfunction	+	5(7.5)	0()	0.029
	–	51(92.5)	74(100)	
CNS dysfunction	+	nil	nil	–
Mortality		2	1	

Post-operative Morbidity

Table 3

The incidence of cardiac arrhythmia was found to be more common in the HL group (19.4% vs. 5.3%; P = 0.004). Patients in the HL group required more inotropic support (34% vs. 11.8%; P = 0.001). However, on comparing mechanical ventilator support, renal dysfunction and post-operative infections, there was no statistically significant difference between the two groups.

The length of ICU stays (<5 days - 32 [57.1%] vs. 57[76.5%]; ≥5 days - 24 [42.9%] vs. 17 [23.5%]; P = 0.013) were found to be significantly higher in the HL group. There were no neurological complications.

Patients in the HL group had 3.5 times the risk of developing arrhythmia in the post-operative period as compared to those with lower lactate levels. Similarly, the requirement for inotropic supports was 5.66 times more in the HL group.

Discussion

HL and lactic acidosis are known to be associated with increased morbidity and mortality. Published literature shows a correlation between the post-operative peak lactate concentration and post-operative morbidity without considering intra-operative variables.[10,11,13,22,23] Early HL is defined as high lactate occurring during the first 4 h of surgery, and late HL is defined as increase. In lactate from 4 to 24 h post-surgery.[10] The study observed intra-operative hyperlactatemia, which could be used as a predictor for post-operative morbidity and mortality.

Normal lactate is defined as blood lactate level between 0.4 and 2.0 mmol/L. Lactate level between 2 mmol/L and 4.0 mmol/L is considered as mild to moderate HL and blood lactate

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>4.0 mmol/L is classified as severe HL.[11]Mirmohammad-Sadeghi et al. had defined HL as a lactate level more than 3 mmol/L.[24] This study used a lactate value of ≥4 mmol/L as HL. The percentage of severe HL was less in male patients compared to female patients. The results of the study support Demers et al. who identified female sex as a risk factor for post-operative HL.[11]

Patient co-morbidities such as hypertension, diabetes mellitus, or COPD did not have a statistically significant association with HL. Several investigators have identified hyperglycaemia as a risk factor for HL.[10,17] Contrary to published literature, the study did not find an association between preoperative anaemia and preoperative creatinine with HL.[10,12,13,16] This could be because of exclusion of patients with preoperative serum creatinine of more than 2 mg/dL. Furthermore, the mean preoperative haemoglobin of this study population was 12.68 ± 2.84. The number of severely anaemic patients was few to derive any statistical correlation.

Mirmohammad-Sadeghi et al. reported a 76% incidence of HL in his study with a definition of HL having a value of more than 3 mmol/L.[24] In this study with said criteria for HL (lactate value ≥4 mmol/L) when peak intra-operative lactate values were considered, there was an incidence of 42.7% (56 out of 130 patients). The reported incidence of HL is about 10–20%.[25]

Patients in the HL group had significantly longer CPB time (92.40 ± 26.0 vs. 83.96 ± 28.18 min) and aortic cross-clamping time (55.8 ± 18.2 vs. 48.4 ± 19.8 min). The correlation between CPB time and peak blood lactate level was found to be statistically significant (Pearson correlation coefficient r = 0.22; P = 0.003). There was also a strong correlation between aortic cross-clamp time and peak blood lactate level which was also found to be statistically significant (r = 0.281; P= 0.007). These similar findings were seen in the study on lactate and post-operative morbidity and mortality by Demers et al.[11]

Increased intra-operative peak blood lactate levels were both highly predictive of major cardiac morbidity such as arrhythmias and requirement for prolonged inotropic support. Serum lactate levels >4 mmol/L were associated with 3.5 times higher risk of developing arrhythmias and 5.66 times higher risk of prolonged inotropic support requirement compared to patients with serum lactate <4 mmol/L.

The study also observed a statistically significant difference in the duration of ICU stay in patients with HL. Peak serum lactate ≥4 mmol/L was associated with a significantly longer ICU stay (P = 0.013) compared to patients with lactate <4 mmol/L. However, the study failed to see any difference in the duration of mechanical ventilation days between the two groups. This could be due to our ICU protocol of electively ventilating most patients overnight.

Three patients died in the study population. One patient had graft thrombosis owing to poor coronary artery quality and the other two had sepsis. Observed lactate levels were not raised in two and thus did not predict mortality and a causal association could not be derived.

Conclusion

Hyperlactatemia during CPB in CABG points to perilous outcomes of cardiac surgery. It points to pathologies that need prompt correction to avert serious perioperative morbidity and mortality. It is an independent predictor of post-operative complications including all- cause mortality and severe morbidity after cardiac surgery in adult patients. Randomized controlled trails are needed to evaluate the potential benefit of a strategy aiming at normalizing lactate levels during cardiopulmonary bypass.

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References

1. Clowes GH, Neville WE, Sabga G, Shibota Y. The relationship of oxygen consumption, perfusion rate, and temperature to the acidosis associated with cardiopulmonary circulatory bypass. Surgery 1958;44(1):220-39.
2. Ballinger WF, Vollenweider H, Pierucci L, Templeton JY. Anaerobic metabolism and metabolic acidosis during cardiopulmonary bypass. Ann Surg 1961;153(4):499-506.
3. Ballinger WF, Vollenweider H, Pierucci L, Templeton JY. The accumulation and removal of excess lactate in arterial blood during hypothermia and biventricular bypass. Surgery 1962;51(6):738-45.
4. Alston RP, Singh M, McLaren AD. Systemic oxygen uptake during hypothermic cardiopulmonary bypass. Effects of flow rate, flow character, and arterial pH. J ThoracCardiovascSurg 1989;98(5 Pt 1):757-68.
5. Mizock BA, Falk JL. Lactic acidosis in critical illness. Crit Care Med 1992;20(1):80-93.
6. Broder G, Weil MH. Excess lactate: an index of reversibility of shock in human patients. Science 1964;143(3613):1457-9.
7. Weil MH, Afifi AA. Experimental and clinical studies on lactate and pyruvate as indicators of the severity of acute circulatory failure (shock). Circulation 1970;41(6):989-1001.
8. Vitek V, Cowley RA. Blood lactate in the prognosis of various forms of shock. Ann Surg 1971;173(2):308-13.
9. Takala J, Uusaro A, Parviainen I, Ruokonen E. Lactate metabolism and regional lactate exchange after cardiac surgery. New Horiz 1996;4(4):483-92.
10. 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.
11. Demers P, Elkouri S, Martineau R, Couturier A, Cartier R. Outcome with high blood lactate levels during cardiopulmonary bypass in adult cardiac operation. Ann ThoracSurg 2000;70(6):2082-6.
12. Ranucci M, Isgrò G, Romitti F, Mele S, Biagioli B, Giomarelli P. Anaerobic metabolism during cardiopulmonary bypass: Predictive value of carbon dioxide derived parameters. Ann ThoracSurg 2006;81(6):2189-95.
13. Higgins TL, EstafanousFG, Loop FD, Beck GJ, Lee JC, Starr NJ, et al. ICU admission score for predicting morbidity and mortality risk after coronary artery bypass grafting. Ann ThoracSurg 1997;64(4):1050-8.
14. Toraman F, Evrenkaya S, Yuce M, Aksoy N, Karabulut H, Bozkulak Y, et al. Lactic acidosis after cardiac surgery is associated with adverse outcome. Heart Surg Forum 2004;7(2):E155-9.
15. Landow L, Phillips DA, Heard SO, Prevost D, VandersalmTJ, Fink MP. Gastric tonometry and venous oximetry in cardiac surgery patients. Crit Care Med 1991;19(10):1226-33.
16. Landow L. Splanchnic lactate production in cardiac surgery patients. Crit Care Med 1993;21(2 Suppl):S84-91.
17. RaperRF, Cameron G, Walker D, Bowey CJ. Type B lactic acidosis following cardiopulmonary bypass. Crit Care Med 1997;25(1):46-51.
18. McKnight CK, Elliott MJ, Pearson DT, Holden MP, Alberti KG. The effects of four different crystalloid bypass pump-priming fluids upon the metabolic response to cardiac operation. J ThoracCardiovascSurg 1985;90(1):97-111.
19. Himpe D, Van Cauwelaert P, Neels H, Stinkens D, Van den Fonteyne F, Theunissen W, et al. Priming solutions for cardiopulmonary bypass: Comparison of three colloids. J CardiothoracVascAnesth 1991;5(5):457-66.

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20. Higgins TL, EstafanousFG, Loop FD, Beck GJ, Blum JM, Paranandi L. Stratification of morbidity and mortality outcome by preoperative risk factors in coronary artery bypass patients. A clinical severity score. JAMA 1992;267(17):2344-8.
21. Hu BY, Laine GA, Wang S, Solis RT. Combined central venous oxygen saturation and lactate as markers of occult hypoperfusion and outcome following cardiac surgery. J CardiothoracVascAnesth 2012;26(1):52-7.
22. Stammers AH, Mejak BL. An update on perfusion safety: does the type of perfusion practice affect the rate of incidents related to cardiopulmonary bypass? Perfusion 2001;16(3):189-98.
23. Lassen NA. Cerebral blood flow and oxygen consumption in man. Physiol Rev 1959;39(2):183-238.
24. Mirmohammad-Sadeghi M, Etesampour A, Gharipour M, Saeidi M, Kiani A, Shamsolkotabi H, et al. Relationship between serum lactate levels and morbidity outcomes in cardiovascular patients after CABG. J Surg Pak (Int) 2008;13(2):88-91.
25. Totaro RJ, Raper RF. Epinephrine-induced lactic acidosis following cardiopulmonary bypass. Crit Care Med 1997;25(10):1693-9.