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COMPARISON OF THE EFFECT OF LACTATE LEVELS DURING CARDIOPULMONARY BYPASS ON PATIENT OUTCOME

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ABSTRACT

Objective: To compare the effect of high and normal lactate levels during cardiopulmonary bypass (CPB) on post-operative outcome.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Army Cardiac Center, Lahore from 1st Nov 2015 to 30th Jun 2016.

Material and Methods: Ninety eight consecutive patients undergoing coronary artery bypass grafting (CABG) on CPB were divided in two groups according to lactate levels at the time of re-warming on CPB, group A with lactate <4mmol/L and group B with lactate >4mmo/L. Outcome was measured in the post-operative intensive care unit (ICU) in terms of duration of ventilation; need for re-ventilation, increase in inotropic support and / or IABP; and ICU length of stay (LOS).

Results: About 59.18% patients had hyperlactatemia during CPB. There was no statistically significant difference in the pre-operative characteristics of the patients in two groups. Mean duration of ventilation in group A was longer (3.54 ± 2.76 hours) compared to group B (4.09 ± 2.96 hours) with a higher frequency of need of re-ventilation in group B (*p*<0.01); need of increase in inotropic support (*p*=0.01); and need of intra-aortic balloon pump in the post-operative ICU (p<0.01). There was no statistically significant difference in the duration of post-operative inotropic support (*p*=0.14) and ICU length of stay (*p*=0.08). The mortality was significantly higher in the group with high lactate during CPB (3.45% vs Nil).

Conclusion: High lactate levels during CPB can lead to post-operative complications including hemodynamic compromise and longer duration of ventilation.

Keywords: Cardiopulmonary bypass, Intensive care units, Lactate, Ventilation.

INTRODUCTION

Since its inception more than 5 decades ago, cardiopulmonary bypass (CPB) remains an important component of cardiac surgery. Despite large number of coronary revascularization surgeries being performed "off pump", CPB is still required in valvular repair and replacement surgeries and repairs of congenital heart disease. There is almost always some degree of hypoperfusion of the tissues during CPB resulting in lactic acidosis. The hypoperfusion is caused by constriction of pre-capillary arteriolar sphincters, edema, decreased lymphatic drainage, loss of pulsatile flow, "sludging" in the capillaries due to hypothermia, altered deformability of red blood cells (RBCs) and microaggregation and adhesion of white cells, platelets, and fibrin onto the endothelium[1].

A rising trend in serum lactate level is seen from baseline to the time of institution of CPB and 30-45 minutes into the CPB[2]. The lactate levels tend to progressively decline at the time of rewarming and after termination of CPB, however, persistent higher lactate levels are sometimes observed in some patients, that lead to post-operative complications including increased ventilation time and ionotropic support requirement[3]. Post-CPB serum lactate levels >4mmol/L at the time of ICU admission has been labeled as a biomarker to identify early postoperative morbidity and mortality in cardiac transplant patients[4]. Similarly, lactate levels of 4 mmol/L or higher during adult cardiac surgery

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has been associated with higher morbidity & mortality[5]. No studies have so far documented correlation between blood lactate level elevations during CPB, and use of inotropic support during weaning from CPB. There has been no study for such correlation in our population.

This study was conducted to compare the effect of different levels of serum lactate during CPB on patient's outcome; determine the causative factors of high lactate levels and to suggest the measures to keep lactate levels within acceptable limits during CPB.

MATERIAL AND METHODS

This comparative cross-sectional study was conducted in the department of cardiac anesthesia and intensive care at the Army Cardiac Center, Lahore from 1st November 2015 to 30th June 2016. After approval from the hospital ethics committee, 98 consecutive patients coming for coronary artery bypass grafting (CABG) on CPB were selected. Patients of either genders; between the age of 25 and 65 years; presenting with 2 or 3 vessels disease; and undergoing on-pump CABG were included in the study. Emergency surgeries; CABG with valve surgeries; patients with left ventricular ejection fraction (LVEF) <35%; patients with pre-existing renal disease (creatinine clearance <40ml/min); or patients with pre-operative intra-aortic balloon pump (IABP) were excluded from the study. All patients received induction and maintenance of anesthesia as per standard protocol and ventilation was turned off on commencement of CPB. Anesthesia was maintained during CPB with propofol infusion at 25mcg/Kg/min. The target mean arterial pressure (MAP) was set to 65-75mmHg and achieved with intermittent boluses of phenylephrine where necessary.

Arterial blood gases (ABGs) were monitored throughout the surgery and serum lactate levels were measured at the time of rewarming, before coming off bypass. Patients were divided into two groups; lactate <4 mmol/L in Group A and lactate >4 mmol/L in Group B. Patient's outcome was measured in the post-operative intensive care unit (ICU) in terms of duration of ventilation (in hours); need for re-ventilation, increase in inotropic support and / or IABP; and ICU length of stay (LOS) in hours.

Independent sample t-test was used to compare the numerical data in the two groups while chi square test was used to compare the categorical data. Patient's hemoglobin (Hb) during CPB; and total CPB time were also noted in both groups and Pearson's correlation of these variables was calculated with lactate levels.

RESULTS

Out of 98 patients 58 (59.18%) had lactate levels of 4 mmol/L or higher at the time of rewarming during CPB. There was no statistically significant difference between the patient's demographics including age (*p*-value 0.99); pre-operative left ventricular ejection fraction (*p*-value 0.80); pre-operative hemoglobin (*p*-value 0.48); or pre-operative serum creatinine (*p*-value 0.08) between the two groups. The mean CPB time was 127.98 ± 53.6 minutes in group A while 115.71 ± 29.3 minutes in group B (*p*-value 0.22) (table-I).

Table-I: Comparison of patient characteristics.

Parameters	Group A (n=40)	Group B (n=58)	*p*-value
Patient's Age (in years)	54.08 ± 9.8	54.05 ± 11.2	0.99
Pre-op LVEF (%)	54.00 ± 9.9	53.48 ± 9.8	0.80
Pre-op Haemoglobin (g/dL)	11.22 ± 1.8	11.495 ± 1.7	0.48
Pre-op Serum Creatinine (mg/dL)	0.99 ± 0.3	0.8997 ± 0.2	0.08
Total Bypass (CPB) Time (in mins)	115.7 ± 29.3	127.9 ± 53.6	0.22
Cross-Clamp Time (in mins)	70.5 ± 18.8	81.28 ± 44.5	0.18

There was a weak negative correlation between lactate level and hemoglobin (r=-0.120; *p*=0.36) and total CPB time (r=-0.12; *p*=0.22). In the post-operative outcome, there was a significant difference in the serum lactate levels on arrival in ICU in both groups (*p*=0.01). There was a statistically significance difference in the mean duration of ventilation between group A (3.54 ± 2.76 hours) compared to group B (4.09 ± 2.96 hours) (table-II). There was a higher incidence of need of re-ventilation in group B (*p*<0.01); need of increase in inotropic support (*p*=0.01); and need of intra-aortic balloon pump in the post-operative ICU (*p*<0.01) (table-III).

Table-II: Comparison of post-operative parameters.

Parameters	Group A (n=40)	Group B (n=58)	*p*-value
Mean Lactate on ICU arrival (mmol/L)	4.73 ± 2.9	6.07 ± 2.5	0.01
Mean Post-op Ventilation Duration (in hours)	3.54 ± 2.76	4.09 ± 2.96	0.03
Mean Post-op Inotropes Duration (in hours)	6.79 ±9.8	192.8± 958.8	0.14
Mean Post-op ICU Stay Duration (in hours)	41.3 ± 23.69	63.47 ± 91.9	0.08

Table-III: Comparison of post-operative course.

Parameters	Group A (n=40)	Group B (n=58)	*p*-value
Number of patients requiring re-ventilation	Nil	4	0.01
Number of patients requiring increase in inotropes	10	40	0.01
Number of patients requiring IABP in ICU	Nil	2	0.01

However, there was no statistically significant difference in the duration of post-operative inotropic support (*p*=0.14) and ICU length of stay (*p*=0.08) (table-II). The mortality was significantly higher in the group with high lactate during CPB (3.45% vs nil) (table-II).

DISCUSSION

High lactate levels have been recognized as a marker of circulatory insufficiency, due to any reason, and the severity of hyperlactatemia (HL) has been associated with increased morbidity and mortality in different clinical conditions. Metabolic acidosis due to HL is a considerable complication of the CPB occurring in 10% to 20% of cases and remains a source of worry for the cardiac anesthesiologists due to the associated morbidity and mortality. The frequency of HL was significantly high in our patients (59.1%) compared to the quoted studies. *Demers et al* found the incidence of HL (peak lactate levels 4 mmol/L or more) in 18% of the patients leading to higher post-operative hemodynamic instability (29.5% vs 10.9%) and higher mortality (11.0% vs 1.4%)[5,6,14].

This HL has been attributed to tissue hypoxia caused by haemodilution and impaired oxygen delivery. *Ranucci et al* have described preoperative serum creatinine value, the presence of active endocarditis, the cardiopulmonary bypass duration, the lowest oxygen delivery during cardiopulmonary bypass, and the peak blood glucose level as independent risk factors associated with HL[7]. However, unlike findings of *Demers et al*, it was not associated with higher mortality. Pre-operative clinical status of the patient according to New York Heart Association (NYHA) class has been shown to be correlated positively to higher lactate levels during CPB. Shinde et al compared the mean lactate levels in NYHA class I, II, III, and IV patients undergoing valvular heart surgery and found statistically significant high lactate levels in the intraoperative period and immediately post-CPB period ($p<0.01$) in patients with NYHA Class-IV. These values, however, were not significantly different in all classes at 24 and 48 hours after surgery[8]. Other significant predictors of HL identified by Svenmarker et al have been patients' age, complexity of surgery, need of blood transfusion during CPB, acid base level, emergency surgeries, pre-operative diabetes, vasoactive intervention, venous-blood-return to the heart-lung machine and renal function[9]. We found a weak negative correlation between lactate levels and haemoglobin during CPB as well as CPB duration, however, *Shinde et al*, we found significant difference in patient's pre-operative dyspnea symptoms (NYHA class) and incidence of HL (p-value <0.01).

There is a controversy whether or not using Lactated Ringer's solution for pump priming can contribute to development of metabolic acidosis. At one hand it has been shown that infusion of Ringer's lactate does not affect the accuracy of lactate measurement[10] and some studies show development of metabolic alkalosis due to metabolism of lactate to bicarbonate and the lactate act as a base and cannot cause acidosis[11-15]. *Himpe et al* compared the acid-base difference in two groups of patient who received lactated and non-lactated solution for CPB-prime. Hyperchloraemic metabolic acidosis was seen at the end of CPB in Group II (lactated prime), as evidenced by the negative base excess (median=2.90 mEq litre) and slightly increased chloride levels (median=108 mEq litre). We used only lactated Ringer's solution for pump priming in all our patients and hence could not find the correlation of prime solution with HL.

Shinde et al used lactate levels >4 mmol/ L as HL and they found these patients required prolonged inotropic and ventilatory support in the post-operative ICU[8]. Similarly, Svenmarker et al have described patients with HL requiring longer intensive care and postoperative ventilatory support, but the threshold for HL was set to equal 2 mmol/L[9]. In their study they found more complications like renal dysfunction, infections, respiratory and circulatory disorders in patients of HL during CPB with a higher hospital mortality (13.3% vs 2.2%)[9]. We used the threshold of 4 mmol/L of lactate level during rewarming period as marker of HL and we found that the patients who had higher lactate level during CPB had significantly longer duration of post-operative ventilation (median=3.00 vs ± 3.50 hours). Similarly, more patients required re-ventilation, increase in ionotropic support and intra-aortic balloon pump in the post-operative period. Likewise, the mortality in HL group was higher (3.45% vs nil). However, we found no significant difference in the duration of post-operative inotropic support or ICU length of stay.

CONCLUSION

High lactate levels during CPB can lead to post-operative complications including hemodynamic compromise and longer duration of ventilation. Short CPB duration and optimal hemoglobin can reduce incidence of hyperlactatemia.

Limitation of the Study

The study was conducted at single center with relatively small sample size. A multicenter study with larger sample size is needed.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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