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"IMPACT OF MEAN ARTERIAL PRESSURES MAINTAINED DURING CARDIOPULMONARY BYPASS ON POST-OPERATIVE LACTATE LEVELS IN CORONARY ARTERY BYPASS GRAFTING PATIENTS".

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ABSTRACT

Lactate, a byproduct of anaerobic metabolism is produced when the body breaks down glucose for energy. The problem with this is that it can build up in the blood stream more quickly than it is eliminated. Lactate is noted to be a marker for cellular hypoxia and tissue hypoperfusion. By monitoring lactate, patients who have an increased risk of post-operative morbidity and mortality can be identified and they may benefit from early aggressive intervention. Hyperlactatemia during cardio pulmonary bypass (CPB) appears to be related mainly to insufficient oxygen delivery and blood flow. This study was aimed to show the impact of mean arterial pressure (MAP) during CPB on the patient's blood lactate level and post-operative outcomes. 40 patients undergoing coronary artery bypass grafting (CABG) surgery were enrolled for the study. The patients were blindly divided into 2 groups based on the target mean arterial pressure set, as Group-1 [40-60mm Hg] and Group-2 [61-80mm Hg]. All patients underwent CABG surgery on CPB. Perfusion flow rates are well maintained throughout the surgery. Lactate levels, Hemodynamic parameters and Post-operative outcomes of the patients were noted. Results revealed that the Lactate level in Group-2 was low as compared to the Group-1 after surgery. Early extubation and speedy recovery of the patients are also seen in Group-2 patients. This study shows high MAP of 61-80mm Hg during CPB could decrease the blood lactate level and tissue hypoxia.

KEYWORDS: MAP, CPB, CABG, Lactate

INTRODUCTION

Coronary artery disease (CAD) affects the quality of life of a patient. The surgical treatment for severe CAD is Coronary Artery Bypass Grafting (CABG) surgery with or without using Cardiopulmonary Bypass (CPB). Traditional approach for CABG is ON-PUMP CABG, which is still practiced in many centers. In this surgery, the heart is arrested in diastole, providing a bloodless and motionless field for the surgeon to do anastomosis of the graft to the coronaries. Even though the survival rate of the CAD patients is increased with the help of surgery, there are some complications that might rise during or after the surgery causing morbidity or mortality.

Tissue hypoxia is caused by an imbalance between the oxygen consumption and delivery. If tissue hypoxia is not treated it can result not only in organ damage and dysfunction but also post-operative problems, which can be avoided by promptly identifying and treating tissue hypoxia. To detect tissue hypoxia, a number of hypoxia biomarkers have been proposed. The most extensively used indicator of tissue hypoxia is lactate (3) . Lactate is the conjugate base of Lactic acid. Lactate can exist as two optical isomeric forms - Levo (L) and Dextro (D). While some bacteria, especially those in the gastrointestinal system, can synthesize D-lactate, mammalian cells cannot. Only L-lactate is taken into account because it causes peri-operative Hyperlactatemia (12).

It has been long understood that a reduction in tissue oxygen supply leads to an increase in blood lactate levels (4) . Since lactate is a natural byproduct of glucose metabolism, factors other than hypoxia may also contribute to its rise. Both early and late onset hyperlactatemia have been identified in patients who have undergone cardiac surgery. Early onset hyperlactatemia refers to hyperlactatemia that manifest in the operating room or very soon after ICU admission (5). As opposed to this, Late onset hyperlactatemia is a benign, self-limiting illness that normally develops 6-12 hours after ICU admission and resolves on its own within 24 hours (12) . Early-onset Hyperlactatemia is closely linked to unfavourable outcomes and is likely the result of both hypoxic causes (such as microcirculatory shock) and non-hypoxic causes (such as faster aerobic metabolism). There is no indication of localized or global tissue hypoxia when late-onset hyperlactatemia occurs (12) .

Treatment with β2-agonists, such as epinephrine, frequently causes hyperlactatemia. It is believed that epinephrine induced hyperlactatemia results from faster aerobic metabolism and doesn't require any special treatment (12) .

Our objective was to evaluate the association between intra-operative mean arterial pressure (MAP) and early post-operative lactate levels.

METHODOLOGY

This study was performed in the Cardiothoracic and Vascular surgery department at Sree Balaji Medical College and Hospital from Feburary 2022 to October 2022. The study was approved by the research committee of Sree Balaji Medical College and Hospital. 40 patients, who met the inclusion criteria, undergoing coronary artery bypass grafting surgery on CPB were enrolled in the study. Informed consent for the study was obtained from the patients. The data collection was based on routine measurements performed during the operation. The pre-operative data like demographics, ejection fraction, arterial blood gas analysis (ABG), LFT, RFT were also collected and analyzed.

INCLUSION CRITERIA

- Patients of either gender above 30 years and below 80 years of age.
- Patients undergoing on-pump CABG surgery.
- Patients with pre-operative Serum Creatinine level <1.3mg/dl, Serum Alanine Transaminase (ALT) <50U/L, blood lactate level <2mmol/L.

EXCLUSION CRITERIA

- Patients who underwent re-exploration within 24 hours after the initial operation due to surgical factors.
- Emergency cases (eg: ventricular septal rupture, tear in coronary artery due to iatrogenic causes).

- Patients undergoing CABG + Valvular replacement surgery

The enrolled patients were divided into 2 groups as Group-1with MAP of 40-60mmHg and Group-2 with 61-80mmHg of MAP, each group consisting of 20 patients. Their pre-operative blood lactate level, serum creatinine and serum alanine transferase (ALT) are noted.
Anesthesia was started with the placement of ECG leads, pulse oximetry, arterial line catheter to monitor MAP and right internal jugular vein is cannulated for central venous pressure monitoring under general anesthesia. After tracheal intubation, the lungs were ventilated. Vasoactive drugs were administered to maintain stable hemodynamics. Surgical technique was standardized in all patients. Approach is through midline sternotomy. CPB is assembled and deaired with crystalloid priming fluids. Heparin coated circuit is used in all patients.
ACT was maintained greater than 480sec with intermittent intravenous heparin administration during CPB. The AV loop is divided and connected to the cannulas. Perfusion flow rates on bypass are well maintained throughout the surgery. The MAP in patients belonging to Group-1 was maintained between 40-60mmHg and in Group-2 between 61-80mmHg. Appropriate drugs were given to maintain the MAP on CPB if necessary. The blood lactate level of the patient was measured by noting the values from ABG when the patient is on bypass. MAP, tissue perfusion, blood lactate, electrolytes and the urine output of the patient are monitored continuously throughout the peri-operative period.
After completion of the procedure, patient is weaned off bypass protamine administered and the patient is shifted to ICU for continuous monitoring after skin closure. Post-operatively the patient's blood lactate levels and urine output was monitored for 24hours, serum creatinine and serum ALT levels are checked on 1st POD. Duration of post-operative hospital stay was also noted. The outcomes in both the groups were analyzed and compared.

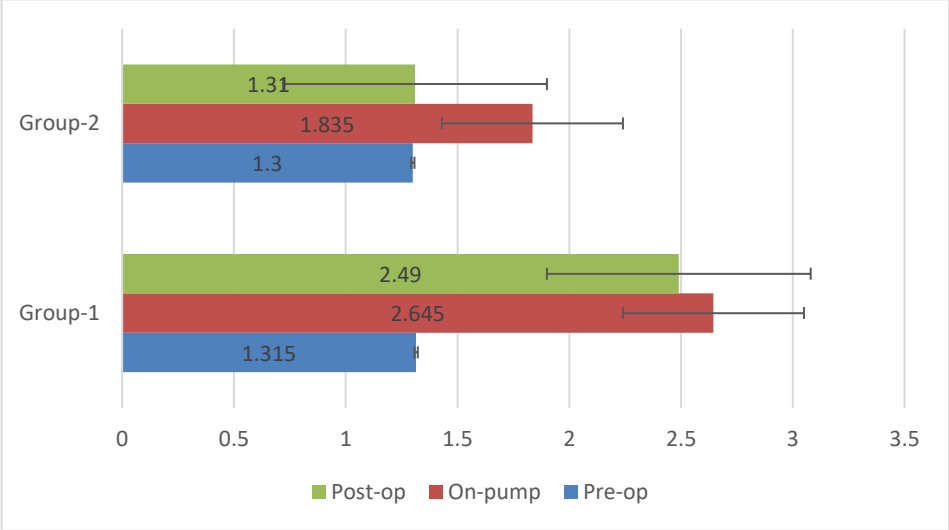
RESULTS

Descriptive analysis for all the data were reported in terms of mean values and standard deviation. Data was also represented using appropriate diagrams like bar diagram. P value <0.05 is considered as statistically significant.
Group-1 mean arterial pressure was maintained within a range of 40-60mm Hg on CPB
Group-2 mean arterial pressure was maintained within a range of 61-80mm Hg on CPB
Demographic data is represented in Table:1, The age of the patients ranged from 20-80years. Mean age was 57.95±9.640 in group 1 and 54.2±10.614 in group 2 with p value of 0.2439, which shows no significant differences in age categorization between the groups. Similarly, male and female patients were equally distributed among the two groups.

Table-1: DISTRIBUTION OF DEMOGRAPHIC DATA

DEMOGRAPHICS			GROUP-1 N=20	GROUP-2 N=20	PVALUE
Age	Mean		57.95	54.2	P=0.2494
	SD		9.640	10.614	
Gender	male	N	10	12	
		%	50	60	
	female	N	10	8	
		%	50	40	
Weight	Mean		58.75	56.8	P=0.4659
	SD		7.50	9.162	

Figure-1: Comparison of blood lactate level



In Table-2, A significant difference in on-pump and post operative lactate levels can be noted in between the two groups with significant P value (<0.0001). Whereas there is no significant difference in the pre-operative lactate values between the groups. The same is depicted in Figure:1.

Table 2: DISTRIBUTION OF BLOOD LACTATE LEVELS

GROUPS	BLOOD LACTATE LEVEL					
	PRE-OPERATIVE		ON-PUMP		POST-OPERATIVE	
	MEAN	SD	MEAN	SD	MEAN	SD
Group-1 (N=20)	1.315	0.390	2.645	0.508	2.49	0.33
Group-2 (N=20)	1.3	0.4195	1.835	0.142	1.31	0.181
P value	P=0.9074		P<0.0001		P<0.0001	

The renal parameters like Serum Creatinine and Urine Output are compared in Table :3. Serum creatinine values show no significant difference in the preoperative values between the two groups, while postoperatively patients in Group 1 had a significant increase in the creatinine values compared to Group 2 (Figure: 2). On the contrary, urine output is significantly low in Group 1 both on pump and post operatively (Figure:3).

Table-3: DISTRIBUTION OF RENAL PARAMETER

GROUPS	SERUM CREATININE				URINE OUTPUT			
	PRE-OP		POST-OP		ON-PUMP		POST-OP	
	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD
Group-1 (N=20)	0.875	0.204	1.41	0.202	1376.25	106.07	2049.47	65.87
Group-2 (N=20)	0.86	0.255	0.87	0.19	1956.5	204.98	2529.75	216.278
P value	P=0.8383		P<0.0001		P<0.0001		P<0.0001	

Figure-2: Comparison of serum creatinine

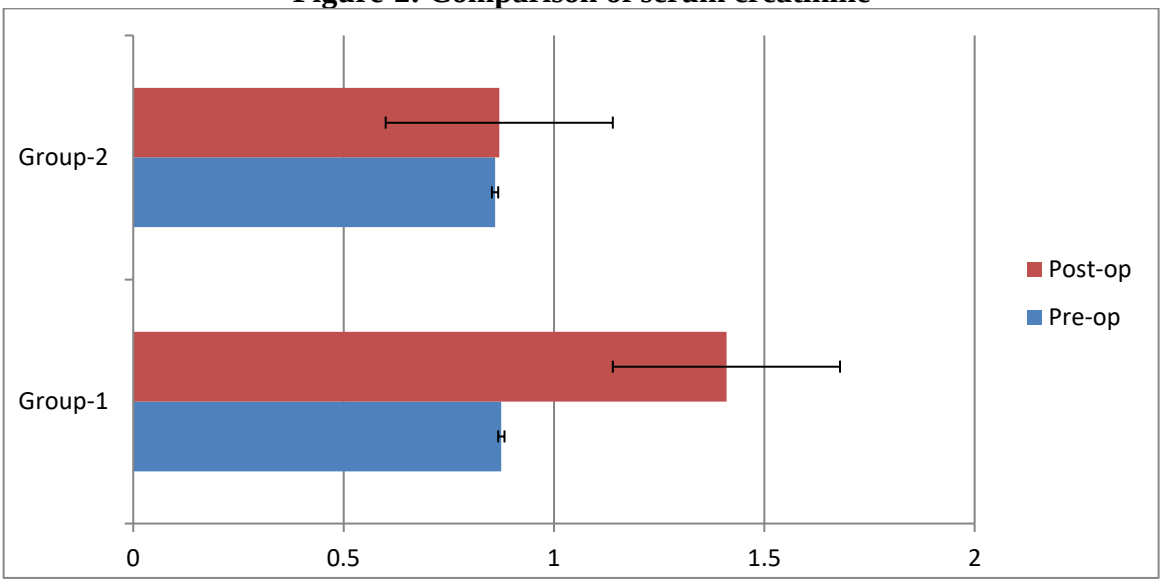
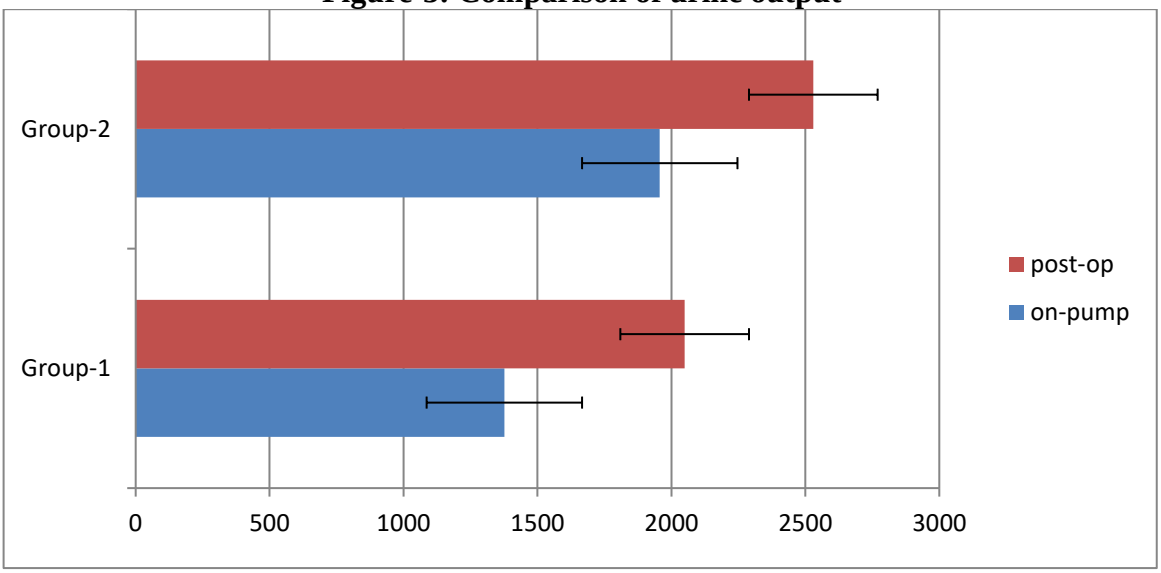


Figure-3: Comparison of urine output



Alanine Transferase (ALT) is taken as an indicator of Liver function. The results of which are shown in Table: 4 and same is depicted in Fig :4. There is no significant difference in the pre-operative values but the value of ALT in post-operative period shows a significant increase in Group 1, indicating altered Liver blood flow during CPB or metabolic changes postoperatively.

Table-4: DISTRIBUTION OF SERUM ALT

	SERUM ALT			
	PRE-OPERATIVE		POST-OPERATIVE	
GROUPS	MEAN	SD	MEAN	SD
Group-1 (N=20)	29.9	9.148	45.55	9.425
Group-2 (N=20)	29.65	9.931	26.9	7.368
P value	P=0.9344		P<0.0001	

Figure-4: Comparison of serum ALT

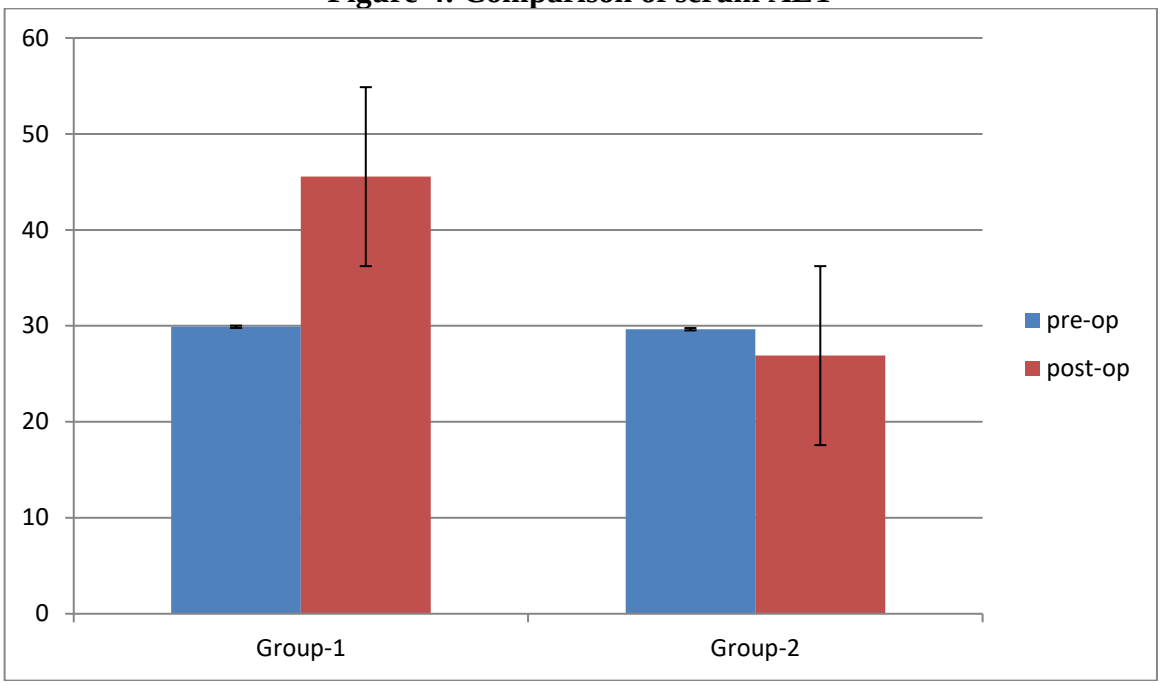
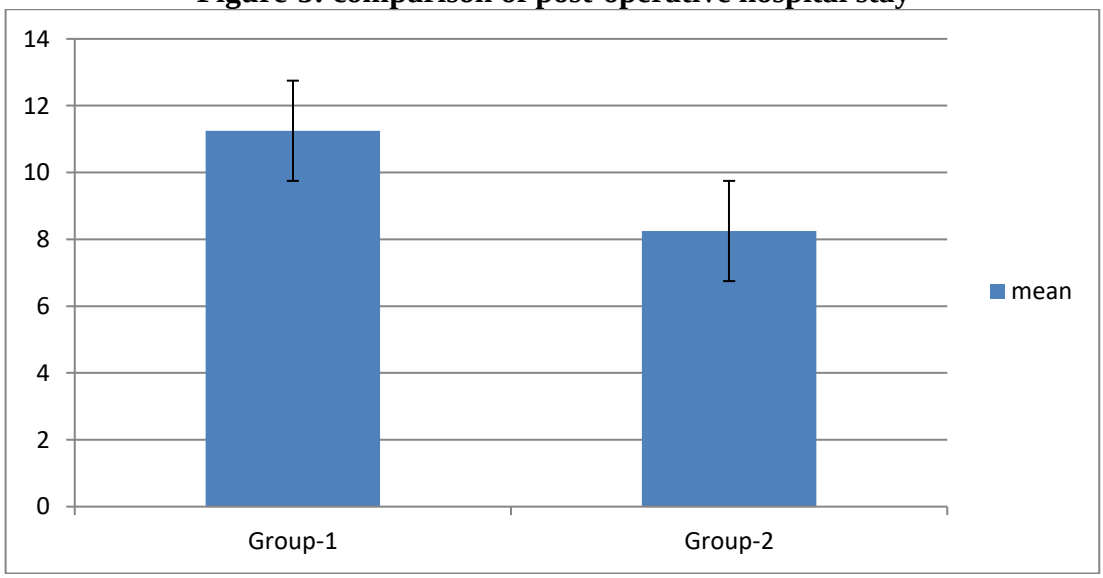


Table: 5 and Figure: 5 compares the outcome in the two groups in terms of 'Length of Hospital stay'. The mean number of days Group 1 patients stayed in hospital (11.25 ± 2.165) is significantly more than those in Group 2 (8.25 ± 0.829).

Table-5: DISTRIBUTION OF POST-OPERATIVE HOSPITAL STAY

	HOSPITAL STAY	
GROUPS	MEAN	SD
Group-1 (N=20)	11.25	2.165
Group-2 (N=20)	8.25	0.829
P value	P<0.0001	

Figure-5: comparison of post-operative hospital stay



DISCUSSION

The normal blood lactate level is 0-2mmol/L. Hyperlactatemia is defined as a sustained, mild to moderate [2-4mmol/L] elevation in blood lactate concentration without metabolic acidosis. Hyperlactatemia differs from lactic acidosis, which is characterized by prolonged rise in blood lactate level (usually >5mmol/L) with metabolic acidosis. If there is a presence of excess of lactic acid in the blood, it is termed as Hyperlactatemia. It is classified as two types -

- Hyperlactatemia without tissue hypoperfusion- Primary (type B) is usually associated with an underlying disease like diabetes mellitus (DM), liver disease, sepsis etc.
- Hyperlactatemia with tissue hypoperfusion- Secondary (type A) is body buffering mechanism not able to compensate for the decreasing pH. Major causes can be cardiogenic shock, septic shock, mesenteric ischemia, severe anemia etc.(8)(13)

Hypoxic or non-hypoxic factors like medications, cardioplegic solutions, hypothermia and CPB itself with lower pump flow rates less than 1.6 l/m^2 are associated with higher lactate production. The liver's function is shown to be decreased by low temperature and reduced blood flow during surgery and the majority of patients had higher lactate levels during CPB(18). Type A Hyperlactatemia is seen during or immediately after the CPB initiation and Type B Hyperlactatemia can be seen 4-14 hours after surgery when the patient is in ICU(6). Hyperlactatemia may develop in patients undergoing cardiac surgery with CPB due to tissue hypoperfusion

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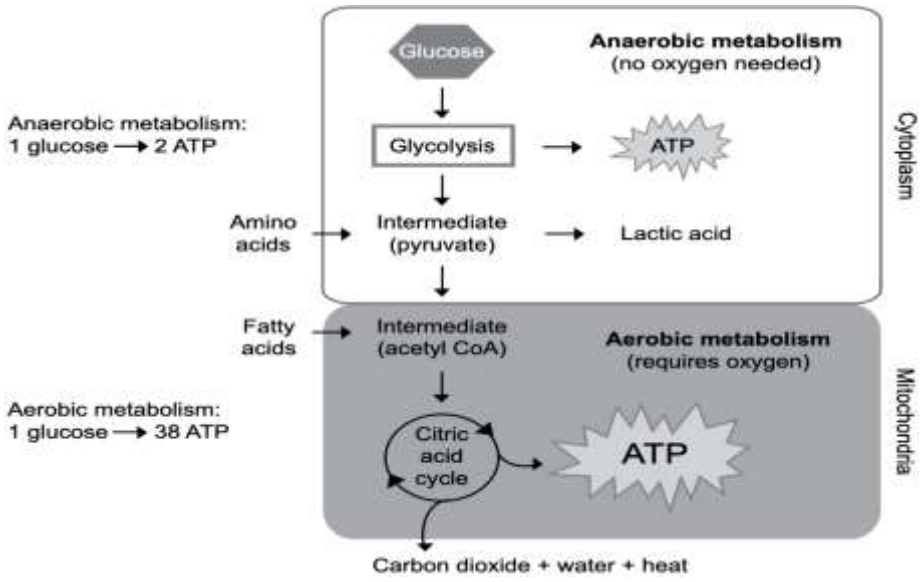
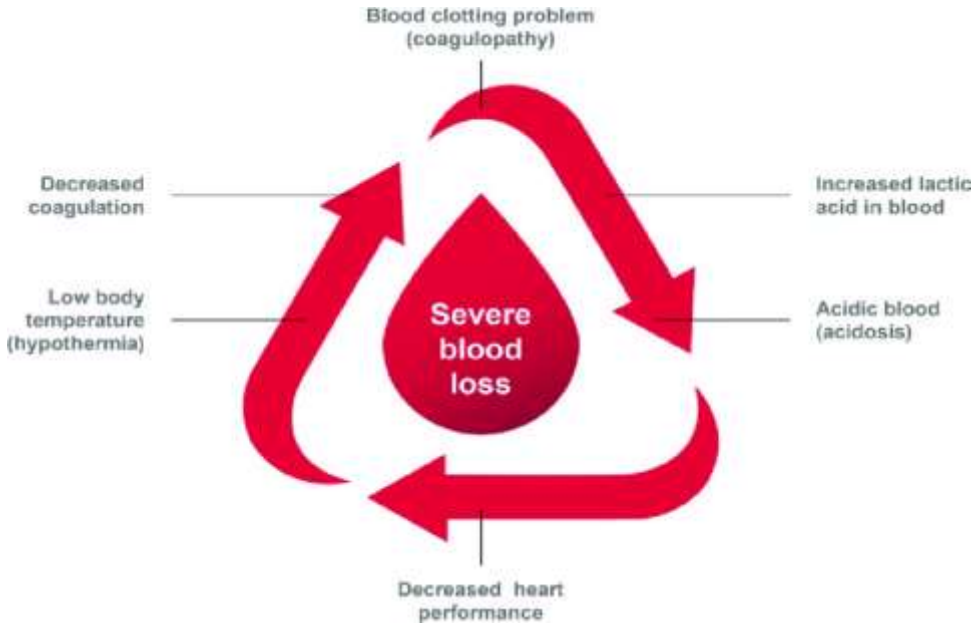


Picture depicting anaerobic and aerobic metabolism in a cell

The presence of active endocarditis, hemodilution, pre-operative increased serum creatinine value, peripheral circulatory failure, prolonged CPB duration and high blood glucose levels might all contribute to an increase in blood lactate during CPB(20).

Increased Hyperlactatemia in the post-operative period may also be caused by insufficient oxygen delivery during CPB. Post-operative cardiac dysfunction is closely related to higher myocardial lactate level. P. Kapoor and coworkers stated that the myocardial markers like lactate, pyruvate and their ratio may be effective in predicting the post-operative outcomes. Pre-CPB myocardial lactate value of 2.9mmol/L and myocardial pyruvate value of 0.07mmol/L can predict inotropic requirement post-CPB with good sensitivity and specificity(7).



Cyclic effects of severe blood loss

Hyperlactatemia following cardiac surgery with CPB can be a fatal complication with substantial morbidity, mortality and resource usage. When compared to individuals with lower MAPs, patients with higher MAPs during CPB had a lower incidence of cardiac and neurological problems as well as late neurocognitive impairments. Enhanced visceral perfusion during CPB is best achieved by increasing perfusion pressure via an increase in perfusion flow rates rather than by using peripheral vasoconstrictors alone. End-organ manifestations like ischemia and infarction may happen if MAP falls below 40mmHg to 60mmHg for an extended period of time. As a measure of tissue perfusion, lactate, a consequence of anaerobic metabolism, has been employed in our study. When performing CPB, a relatively high MAP may enhance microcirculation perfusion and help lower blood lactate levels.

The demographic data of the patients in both the groups doesn't show any significant difference. We observed that at rise of MAP above 60mm Hg (i.e., 61-80mm Hg) during CPB can significantly decrease the blood lactate levels in post-operative period showing that maintaining a high MAP during CPB improves tissue perfusion and reduce the lactate levels post-operatively. Even though maintaining safe range of MAP i.e., 40-60mm Hg, we could see a rise in lactate level post-operatively in some patients. The intra-operative and post-operative data showed significant differences between the groups and this can be noted well from - good urine output and short duration of hospital stay in Group 2.

There are no neurological complications observed in any of the patient in our study, indicating maintaining relatively higher mean arterial pressures on –pump is safe, as supported by few studies like –

1. Study done by Anne G Vedel, et.al showed that maintaining higher or lower MAP during CPB did not appear to impact the volume or number of new cerebral infarcts among the patients undergoing on-pump cardiac surgery (10).
2. JP Gold, et.al who believed that, the ideal way to obtain enhanced visceral perfusion during CPB is to use increased perfusion flow rates rather than just peripheral vasoconstriction. The brain and abdominal organs may be significantly protected by maintaining a high MAP during CPB, especially in the group of patients who are mostly at risk for embolization and end organ dysfunction(21).

Due to the maintenance of high mean arterial pressures in the group-2, an improvement in the post-operative serum creatinine, serum ALT, urine output were noted in our study. From our study, we consider a blood lactate level more than 3mmol/L to be an indicator for morbidity and mortality.

CONCLUSION

In conclusion, this study shows that maintenance of high MAP of 61-80mm Hg [Group-2] during CPB helps for the speedy recovery of the patients and shortens the length of post-operative hospital stay. An improvement in the post-operative blood lactate, serum creatinine, serum ALT and urine output is also noted in the group-2 patients as compared to the group-1.

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