ORIGINAL ARTICLE

Balanced Salt Solution in Type-2 Diabetes Mellitus undergoing Off-pump Coronary Artery Bypass Grafting: Ringer Lactate vs Plasmalyte®

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Abstract

Background: Coronary artery bypass grafting (CABG) is a surgical option for patients with significant coronary artery disease (CAD) who are not suitable candidates for percutaneous interventions. Cardiopulmonary bypass (CPB) with cardiac arrest (on-pump) provides a surgical field free of motion and blood, allowing safe anastomosis construction. Off-pump CABG (OPCABG) avoids serious complications associated with CPB such as stroke, renal dysfunction, and systemic inflammatory response syndrome. Intravenous fluids are administered to maintain the circulation blood volume and cardiac output during surgical manipulation of the heart during OPCABG. This study was performed to compare the effects of Ringer's lactate (RL) and Plasmalyte® (PL) on the acid base status and electrolyte balance in patients suffering from type-2 diabetes mellitus (T2-DM) undergoing elective OPCABG surgery.

Methods: After obtaining ethical approval and informed consent, this study was performed on patients with type-2 DM undergoing elective OPCABG. Patients undergoing CABG on CPB, concomitant procedures, emergency, renal dysfunction, conversion to CPB were excluded. OPCABG was performed as per the standard institutional protocol. Intraoperative management of DM was done using recommended guidelines namely maintenance of blood sugar between 140 and 180 mg% and insulin infusion titrated to achieve the blood glucose in the desired range. Serum potassium was maintained between 4 and 5 mmol/L. Arterial blood gases and lactate levels were determined at two hourly intervals throughout the perioperative period. Comparison of serum lactate levels, base deficit levels, potassium levels, and pH values was done by paired *t*-test. Outcome measures included low-output state, renal dysfunction, bleeding, tracheotomy, ICU stay, hospital stay, and mortality.

Results: There were 50 patients in the group with 25 in each group. None of the patients was converted to on-pump and complete data were available to all patients. At 12th postoperative hour, lactate was significantly lower ($p < 0.014$) and serum potassium levels were significantly higher ($p < 0.018$) in PL group. When compared to the PL group, the base excess levels were significantly higher ($p < 0.035$) in ringer lactate group at 24th postoperative hour. Excepting for this, there were no significant differences in any of the measured parameters, outcomes, length of ICU stay, and hospital stay in the two groups.

Conclusion: In well-controlled patients of type-2 DM with precise perioperative monitoring and management of blood glucose and serum potassium, there were no significant differences in outcomes between RL and PL in diabetic patients undergoing OPCABG.

Keywords: Blood sugar, Electrolyte balance, Insulin, Potassium, Renal dysfunction, Systemic inflammatory response syndrome, Tracheotomy.

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Introduction

Cardiovascular disease (CVD) is a leading cause of all deaths and disability worldwide. As per the report of Global Burden of Disease in 2017, CVD caused an estimated 17.8 million deaths worldwide, corresponding to 330 million years of life lost and another 35.6 million years lived with disability.[1,2] CABG is a surgical option available for patients with significant CAD who are not suitable candidates for percutaneous interventions. CPB with cardiac arrest (on pump) provides a surgical field free of motion and blood, allowing safe anastomosis construction. Yet, the use of CPB is associated with complications peculiar to extracorporeal circulation that may be a major determinant of perioperative morbidity, hospital stay, and costs. CABG surgery on the beating heart without extracorporeal circulation (off-pump) has been successfully introduced in clinical practice. Off-pump coronary artery bypass (OPCAB) may avoid serious complications associated with CPB such as stroke, renal dysfunction, and systemic inflammatory response syndrome.

Diabetes is an important cardiovascular risk factor for CAD. The prevalence of T2-DM in patients undergoing CABG surgery is nearly 30–40%.[3] This proportion is greater in India where studies have reported that almost 40–50% have T2-DM. It is expected that patients undergoing OPCAB may suffer from acidosis intraoperatively as a consequence of decrease in cardiac output owing to displacement/verticalization of the heart. Uncontrolled diabetes mellitus may cause numerous physiochemical changes in the blood glucose, volume status, acid-base balance, and plasma electrolytes. Excess blood sugar

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increases blood osmolarity resulting in the efflux of intracellular water in extracellular compartment and dilution of serum sodium leading to hyponatremia. There is also a redistribution of potassium from intracellular to extracellular space.[4,5] Serum lactate levels may also increase due to metformin (regularly prescribed in T2-DM) in patients with reduced glomerular filtration rate (GFR) as metformin is cleared by the kidneys.[6] It is known that in cardiac surgery, increased serum lactate levels during surgery and after transferring the patient to the ICU are associated with poor prognosis.[7–9]

In a survey of fluid and vasopressor practices among clinicians involved in the care of patients after cardiac surgery, it was demonstrated that balanced crystalloid solutions are the most preferred first choice for fluid resuscitation overall. Intravascular fluid administration is necessary to maintaining volume status, especially during displacement and verticalization of heart on OPCAB with a view to maintain hemodynamic stability and cardiac output. RL is more acidotic than plasma (pH 6.5 of RL vs 7.4 of plasma), has dissimilar physiochemical contents compared to plasma and may result in increased serum lactate levels.[10] In contrast, PL has similar sodium, potassium and chloride concentration as the plasma and doesn't contain lactate. The pH of PL is 7.4 and osmolality is 294 mOsm/L.[11] PL is considered to be a safe priming solution for extracorporeal circulation.[12] We are not aware of any study which highlights the choice of intravenous fluid in OPCABG in diabetic patients. The selection of intravenous fluid in patients with T2-DM undergoing OPCAB is neither well understood nor established. This study was conducted to determine the influence of infusion of two different types of balanced solutions namely RL and PL in patients with preexisting T2-DM undergoing OPCAB.

Methods

This study was conducted at a tertiary care heart hospital in a prospective randomized single-blinded study design. The ethical clearance was obtained and informed consent was obtained from the patients prior to the study. Patients with T2-DM undergoing elective OPCABG surgery (CABG) were randomly allocated to either of the two groups: RL and PL. Exclusion criteria were CABG requiring CPB, emergency CABG, congestive heart failure, patients with renal disease and those undergoing combined procedures. Diagnosis of diabetes was made based on the published criteria,[13] namely (1) a glucose level equal to or greater than 126 mg/dL after fasting for 8 hours, (2) random venous plasma glucose equal to or greater than 200 mg/dL in a patient with classic symptoms of hyperglycemia (3) plasma glucose equal to or greater than 200 mg/dL measured 2 hours after a glucose load of 75 gm in an oral glucose tolerance test (4) hemoglobin A1C equal to or greater than 6.5%. Diabetes mellitus was well-controlled with oral antidiabetic medications prior to surgery. Acute kidney injury (AKI) was defined based on the Kidney Disease Improving Global Outcomes criteria as follows: occurrence of AKI was defined as (1) an increase in the serum creatinine levels of >0.3 mg/dL within 48 hours, (2) an increase of >1.5 times the baseline known or presumed to have occurred within the previous 7 days, and (3) urine output <0.5 mL/kg/h for 6 hours.

Anesthesia and Surgical Technique

After a thorough preoperative evaluation and preanesthetic preparation, all antianginal and antihypertensive medications were continued till the morning of surgery with the exception of angiotensin converting enzyme inhibitors and angiotensin receptor blockers. Optimal control of diabetes mellitus was ensured. Sedative premedication consisted of oral alprazolam the night before. Monitoring of electrocardiogram (ECG) with five leads with simultaneous display of leads II and V5 was done and automated ST segment analysis, pulse oximetry, and direct arterial blood pressure measurement were established. After preoxygenation for 3–5 minutes, anesthesia was induced with intravenous fentanyl 3–5 μg/kg, midazolam 0.05–0.1 mg/kg, and propofol 0.5–1 mg/kg. Muscle paralysis was achieved with rocuronium or vecuronium at the discretion of the anesthesiologist and endotracheal intubation was performed. Anesthesia was maintained with O2 + air + end tidal isoflurane of 1%. Fentanyl was used in a total dose of 10–15 μg/kg for the entire procedure. The perioperative management was tailored to achieve early extubation and fast-tracking. Heparin in a dose of 300 units/kg was administered prior to the grafting to maintain an activated coagulation time of over 400 seconds. Heparin was repeated in doses of 100 units/kg every hour till grafting was completed. Reversal of heparinization was achieved with protamine 3 mg/kg at the end of grafting. Hemodynamic monitoring included ECG, arterial pressure using invasive arterial catheter, and central venous pressure. Pulmonary artery catheter was used in patients with poor left ventricular function, with ejection fraction <40%, and transesophageal echocardiography was used to assess the cardiac function with special reference to mitral valve function to exclude patients with moderate and severe mitral regurgitation, if any. Urine output was recorded hourly. OPCABG was done after midline sternotomy using myocardial stabilizer (Octopus) for the distal coronary anastomosis. Proximal anastomosis on aorta was performed with a systolic arterial pressure (SAP) of 80–90 mm Hg and the distal anastomosis performed with SAP of 110–120 mm Hg unless indicated otherwise. A mean arterial pressure of 65–70 mm Hg was maintained throughout the procedure at times other than indicated above. A target glucose level between 140 and 180 mg/dL was maintained during the perioperative period as recommended by the consensus statement on inpatient glycemic control (American Association of Clinical Endocrinologists and American Diabetes Association).[14] A continuous infusion of soluble insulin was initiated through one of the central venous catheter lumen ports at the beginning of surgery and the infusion rate was titrated to the blood glucose levels. Serum potassium was maintained between 4 and 5 mmol/L. Arterial blood gases, serum electrolytes, and lactate levels were determined at two hourly intervals throughout the perioperative period. Serum creatinine values on postoperative days 1, 2, 3, 4, 5 and on the day of discharge were recorded from both the categories. Patients were electively ventilated till fully conscious, warm, not bleeding, and then extubated after a short trial of spontaneous respiration (for 2–4 hours for those performed in the forenoon in the first round and overnight for those performed in the afternoon in the second round of cases). Primary outcome measures were pH, base deficit, lactate, and potassium levels and the secondary outcome measures were intensive care (ICU) stay, hospital stay, and death. Statistical analysis was performed with SPSS software. Numerical variables were expressed as mean ± standard deviation (SD). Comparison of serum lactate levels, base deficit levels, potassium levels, and pH values was done by paired *t*-test. A p value of <0.05 was considered to be significant. Graphs were plotted using mean and SD values of serum lactate levels, base deficit levels, potassium levels, and pH values from intraoperative and first 24 hours postoperative period.

Results

There were 50 patients in the group 25 in each group. Complete data were available from all patients. None of the patients was converted to on-pump and there was no hospital mortality. Demographic and clinical details are shown in Table 1. There were no significant differences in age, sex, weight, body surface area (BSA), preoperative serum creatinine, and EuroScore. There were no differences in the outcome measures except that the period of elective ventilation was significantly longer in the PL group and the hospital stay was longer in the RL group (Table 1). Intraoperatively, there were no significant differences in the measured parameters in both the groups (Table 2). Postoperatively, at 24 hours, the base deficit was higher in RL, lactate was higher in the RL group at 12 hours and the serum potassium was higher in the PL group at 12 hours (Table 3). But none of these differences was clinically significant.

Discussion

This study was conducted on patients with T2-DM undergoing elective off-pump CABG, where the acid-base, electrolyte, metabolic parameters, and clinical outcomes were compared in two groups namely RL and PL. There were no significant differences in the acid-base, electrolyte levels and clinical outcomes between the two groups excepting the following, the lactate levels serially increased, while the base deficit, pH levels, and potassium levels were lower, in patients who received RL, although the difference was not statistically significant. At 12th postoperative hour, the lactate level was low and serum potassium level was high in patients who received PL. Compared to the PL group, the base excess levels were higher in patients receiving RL, at the 24th postoperative hour. Compared to the patients receiving RL, the duration of mechanical ventilation was longer in

Table 1: Demographic and clinical details of two groups of patients

Mean (SD)	*RL*	*PL*	*p-value*
Age (years)	56.81 (9.60)	69.82 (7.86)	0.062
Male/female	21/4	22/3	0.49
Weight (kg)	66.42 (8.10)	66.43 (10.25)	0.49
Height (cm)	161.7 (7.90)	164.91 (6.76)	0.0673
BSA (m^2)	1.72 (0.12)	1.7 (0.20)	0.38
Ejection fraction (%)	50.9 (6.33)	51.86 (3.2)	0.27
EUROScore II	1.20 (0.57)	1.29 (0.51)	0.33
Serum creatinine (mg/dL)	1.01 (0.30)	0.97 (0.28)	0.31
Hypertension	17	12	0.46
Creatinine clearance (mL/min)	82.8 (29.9)	82.9 (27.9)	0.49
Number of grafts	2.21 (0.77)	2.21 (0.59)	0.49
Duration of IPPV (hours)	10.76 (5.73)	13.93 (5.58)	0.03*
IABP	0	0	
AKI	0	0	
Tracheostomy	0	0	
ICU stay (days)	1.67 (0.6)	1.65 (0.47)	0.46
Hospital stay (days)	5.23 (1.28)	4.04 (1.12)	0.0015*
Mortality	0	0	

*Difference is statistically significant ($p < 0.05$); SD, standard deviation; RL, Ringer's lactate; PL, Plasmalyte®; M/F, male/female; BSA, body surface area; IPPV, intermittent positive pressure ventilation; ICU, intensive care unit; IABP, intra-aortic balloon pump; AKI, acute kidney injury

Table 2: Intraoperative parameters

		Mean (SD)		
Postoperative	*Time (hours)*	*RL*	*PL*	*p-value*
pH	0	7.38 (0.046)	7.4 (0.027)	0.11
	2	7.36 (0.066)	7.39 (0.06)	0.23
	4	7.34 (0.056)	7.34 (0.062)	0.99
Base deficit	0	−0.625 (2.66)	0.25 (1.7)	0.31
	2	−1.06 (3.92)	−0.61 (3.92)	0.73
	4	−2.37 (3.17)	−1.95 (2.75)	0.71
Potassium	0	4.01 (0.52)	3.78 (0.54)	0.21
	2	4.16 (0.51)	3.80 (0.80)	0.093
	4	3.59 (0.49)	3.83 (0.53)	0.21
Lactate	0	1.16 (0.48)	1.28 (0.64)	0.55
	2	2.05 (0.84)	1.81 (0.94)	0.49
	4	3.27 (1.1)	2.64 (1.22)	0.093

Table 3: Parameters during the postoperative 24 hours in the ICU

		Mean (SD)		
Postoperative	*Time (hours)*	*RL*	*PL*	*p-value*
pH	0	7.38 (0.06)	7.35 (0.07)	0.07
	6	7.37 (0.05)	7.32 (0.12)	0.09
	12	7.38 (0.06)	7.40 0.06)	0.22
	18	7.41 (0.053)	7.40 (0.025)	0.26
	24	7.42 (0.04)	7.42 (0.03)	0.14
Base deficit	0	−1.5 (2.68)	−2.26 (2.09)	0.18
	6	−2.52 (3.52)	−2.94 (3.43)	0.37
	12	−0.83 (3.91)	0.5 (3.10)	0.15
	18	1.58 (2.98)	1.76 (2.95)	0.44
	24	3.47 (3.55)	1.5 (2.1)	0.035*
Potassium	0	4.86 (5.15)	3.95 (0.57)	0.15
	6	3.84 (0.42)	4.09 (0.44)	0.16
	12	3.83 (0.33)	4.03 (0.18)	0.018*
	18	4.14 (0.42)	4.21 (0.32)	0.29
	24	3.7 (0.42)	3.97 (0.24)	0.13
Lactate	0	3.56 (1.75)	4.06 (2.44)	0.26
	6	4.69 (2.72)	4.97 (2.91)	0.4
	12	4.80 (3.07)	3.35 (1.22)	0.014*
	18	3.19 (2.67)	3.34 (1.05)	0.41
	24	2.36 (1.57)	3.08 (1.28)	0.16

*Difference is statistically significant ($p < 0.05$)

PL group, whereas the duration of hospital stay was significantly shorter in patients receiving PL®. However, the differences observed were of no clinical significance.

Published literature has shown a significant association between hyperchloremic acidosis and AKI with the use of chloride liberal intravenous fluids when compared to those with less or no sodium. Kim et al. have demonstrated benefits of balanced solutions in terms of significantly lower incidence of severe AKI and persistent AKI after OPCAB.[15] Similarly, Yunos et al. showed that liberal chloride therapy is associated with an increase of renal dysfunction[16] Meyer in their study found that chloride levels were lower and arterial pH was higher in the balanced group at all-time points except baseline. Indicating superiority of balanced solutions[17] and it is significant to note that McCluskey et al.,[18] Shaw et al.,[19] and Young et al.[20] demonstrated increased morbidity and mortality after noncardiac surgery was independently associated with hyperchloremia. Thus, the choice of intravenous fluids remains balanced salt solutions in preference to normal saline.

Patients with diabetes mellitus may be predisposed to hyperglycemia and associated acid-base disturbances due to the effects of sympathetic stimulation associated with surgery. This is compounded in patients undergoing OPCABG due to decrease in cardiac output associated with displacement and verticalization of heart during coronary anastomosis. Acidosis reduces calcium release from the sarcoplasmic reticulum, reduces the action potential duration, and has a negative effect on inotropy and excitation-contraction coupling.[21] Several studies have compared plasmalyte with other IV fluids (ringer lactate, ringer fundin, ringer acetate, Hartmann fluids). There are 12 such randomized controlled trials (RCT) comparing plasmalyte with other fluids. It was found in all of them that PL resulted in lower lactate levels, higher base excess levels, and no difference in potassium and pH levels.[22] Surabhi and Kumar,[11] and Vashisth et al.[23] have compared PL with other balanced solutions in cardiac surgery requiring CPB and have found that there was a fall in pH, strong ion difference and an increase in chloride and lactate levels during pre-bypass period and 30 minutes after initiating CPB. In one study, resuscitation of diabetic ketoacidotic patients with PL, was found to be beneficial in preventing hyperchloremia.[24] In patients undergoing liver resection, fluids devoid of lactate are beneficial, as lactate is completely dependent on liver for metabolism.[25] Plasmalyte lacks calcium and hence, it is compatible with blood products during transfusion. Hadimioglu and associates have concluded that plasmalyte maintains a better metabolic profile.[26]

The distinguishing feature of our study is that we have avoided the confounding effects due to effects of CPB. We have conducted our study on patients undergoing OPCABG and physiological and hemodynamic derangements due to surgical manipulations were precisely controlled.

The limitation of our study is the small sample size and we have not included those diabetes mellitus patients undergoing CABG as an emergency procedure.

Conclusion

Plasmalyte® (PL) may be a physiologically better intravenous fluid but in well-controlled diabetes, with precise intraoperative monitoring of blood glucose/electrolytes and continuous insulin administration there are no significant differences between RL and PL in the acid-base state, electrolyte levels, and overall outcome in diabetic patients undergoing elective OPCAB.

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