Original Article

Comparison of ringer's lactate and plasmalyte-a as cardiopulmonary bypass prime for bypass associated acidosis in valve replacement surgeries

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ABSTRACT

Introduction: A wide range of acid base fluctuations are seen during Cardiopulmonary bypass (CPB) and the development of metabolic acidosis is well recognized. We conducted a study tocompare the metabolic effects of Ringer lactate and Plasmalyte-A as CPB prime in causing bypass associated acidosis in valve replacement surgeries.

Methods: We performed a prospective, randomized controlled study on a total of 80 adult patients undergoing CPB for valvular heart surgeries. The patients were randomized into two groups: Group I (Ringer Lactate) and Group II (Plasmalyte-A). Arterial blood samples were taken before initiating CPB, 30 minutes after starting CPB, then every half hourly till termination of CPB and after half an hour stay in the ICU post operatively to analyze primarily H+ ions, bicarbonates, lactate and strong ion difference.

Results and Discussion: The results were analyzed in a quantitative manner. In Ringer Lactate group, during CPB, there was reduction in pH from 7.428 ± 0.029 at T1 to 7.335 ± 0.06 ($P < 0.01$) and 7.358 ± 0.06 ($P < 0.01$) at T2 and T3 respectively. Mean bicarbonates decreased in Ringer Lactate group during CPB from 24.28 ± 1.65 mEq/L at T1 to 20.98 ± 2.97 mEq/L at T2 ($P < 0.01$). In Plasmalyte-A group, mean pH, bicarbonate, strong ion difference (SID) were comparable at all time intervals ($P > 0.05$). In Ringer Lactate group, maximum surge in mean blood lactate levels was seen from 0.85 ± 0.35 mmol/l at T1 to 4.29 ± 1.78 mmol/L ($P < 0.01$) and 4.17 ± 1.28 mmol/L ($P < 0.01$) at T2 and T3, respectively. Such surge was not seen in Plasmalyte-A group. The mean SID decreased during the CPB in Ringer Lactate group from 41.102 mEq/L at T1 to 35.66 mEq/L ($P = 0.033$) at T2 implying metabolic acidosis. Numbered patients having hypotension and arrhythmias were also higher in Ringer Lactate group again indicating higher acidosis.

Conclusion: The different composition of Plasmalyte-A and Ringer Lactate have different metabolic implications for patients undergoing cardiac surgery. Patients who received Plasmalyte-A as cardiopulmonary bypass prime developed less metabolic acidosis. Hence we conclude that Plasmalyte-A is the preferred cardiopulmonary bypass prime in adult patients undergoing valve replacement surgeries.

Keywords: Bypass prime, cardiopulmonary bypass, metabolic acidosis, Plasmalyte-A, ringer lactate

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INTRODUCTION

Cardiopulmonary bypass (CPB) is widely used to maintain systemic perfusion and oxygenation during open-heart surgery.[1]

The CPB circuit is primed with the prime fluid, a balanced electrolyte solution containing normal plasma concentrations of many of the standard ions.[2] Drugs such as heparin, bicarbonate, and albumin are added to

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attenuate its dilutional effect while mannitol is added to encourage diuresis.[3]

Several causes have been suggested to explain CPB associated acidosis including an increase in serum lactate, chloride levels, tissue ischemia, hypoperfusion, hypoxemia, and circulatory failure.[4]

Metabolic acidosis is frequently encountered in CPB. Acidosis causes arrhythmias and decreased responsiveness to catecholamines. Both of these factors lead to hypotension which further affects the contractility of the heart muscle. Similarly, a fall in pH in the intracellular fluid also reduces the contractility of the heart muscle.[5,6]

Ringer's lactate is commonly used in pump prime but many studies have proved its role in causing lactic acidosis.[7,8] The electrolyte composition of Ringer's lactate is significantly different from that of plasma. Ringer's lactate contains 131 mEq/L sodium ions, 111 mEq/L chloride ions, potassium content is 5 mEq/L, calcium content is 2 mEq/L, and lactate content of 28 mEq/L. Also, the pH of Ringer's lactate is 6.5 and the osmolarity is 278 mOsmol/L. Excess lactate production reduces strong ion difference (SID) and causes metabolic acidosis. Plasmalyte-A (another intravenous fluid) has physicochemical properties similar to plasma. Plasmalyte-A contains 140 mEq/L sodium ions, 111 mEq/L chloride ions, potassium content is 5 mEq/L, magnesium content is 3 mEq/L, acetate content of 27 mEq/L, and gluconate content of 23 mEq/L.The pH of Plasmalyte-A is 7.4 and the osmolarity is 294 mOsmol/L which is same as plasma osmolarity.[9,10] Therefore, it can safely be used as prime fluid without causing many side effects.

Hence, this study is designed to understand the role of Ringer's lactate as a pump-prime fluid in causing lactic acidosis and compare it with Plasmalyte-A solution which is devoid of lactate in patients undergoing valve replacement surgeries.

MATERIALS AND METHODS

A prospective comparative randomized controlled study was conducted on a total of 80 adult patients (18–50 years of age group) undergoing CPB for valvular heart surgeries. Patients with deranged acid-base metabolism preoperatively, renal dysfunction, or having complex CHD were excluded from the study.

A randomized blinded study on 50 adult patients, undergoing elective CABG and heart valve replacement surgeries, was conducted to study the acid-base effects of priming fluid during CPB.[11] Taking this study as a reference study, the required sample (taking power of study as 90% and 5% level of significance) constituted 40 patients in each study group. Thus, the total sample size taken is 80.

According to the computer-generated randomization technique (using the software link http://www.randomizer.org.), 80 adult patients were randomly allocated in two groups with 40 patients in each group.

Group-I received Ringer's lactate as CPB prime fluid. Cardioplegia solution and peripheral intravascular crystalloid fluids were also Ringer's lactate.

Group-II received Plasmalyte-A as CPB prime fluid. Cardioplegia solution and peripheral intravascular crystalloid fluids were also Plasmalyte-A.

Written informed consent was obtained from all enrolled patients.

PRIME FLUID: The CPB circuit was de-aired with the prime fluid. The prime fluid was prepared by the perfusionist using mannitol, heparin, sodium bicarbonate, normal saline, and Ringer's lactate (for group I)/ Plasmalyte-A (for group II). Approximately 1500–1700 mL of fluid was used for an average adult patient weighing about 60 kg.

CARDIOPLEGIA: For group I, cardioplegia solution was prepared using 500 mL of Ringer's lactate. For group II, cardioplegia solution was prepared using 500 mL of Plasmalyte-A.

Demographic details, history, diagnosis including any comorbidities, routine biochemistry investigations including pre and postoperative renal function tests were documented. Arterial samples for ABG analysis were taken at the following time intervals: 5 min before initiating CPB (T_1), 30 min after initiating CPB (T_2), 60 min after initiating CPB (T_3), 90 min after initiating CPB (T_4), after termination of CPB (T_5) and after half an hour stay in the ICU (T_6). SID was calculated. SID in mEq/L = $(Na^+ + K^+) – (Cl^- + \text{lactate})$.[12]

Any additives and its amount added to the pump fluid to correct acid-base balance during bypass and duration of bypass were also noted.

To exclude confounding factors such as the stress of anesthesia and surgery which can cause metabolic acidosis, maximum duration of CPB taken was 120 min.

Table 1: Demographic profile

	Ringer's lactate	Plasmalyte-a
Mean age (years)	34.975	33.05
Gender: male	19	23
Gender: female	21	17
Duration of CPB (min)	78.3	87.075
Duration of aortic cross clamp time (min)	74.5	80.12

Ethics

The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 2000 (available at http://www.wma.net/e/policy/17-c_e.html). The Institutional Ethics Committee approval was taken and the approval reference number was 2017-059.

Statistical analysis

Data Analysis: Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± standard deviation. The normality of data was tested by the Kolmogorov-Smirnov test. If the normality was rejected then the nonparametric test was used.

All variables studied were quantitative in nature and ANOVA was used to compare the variable values at different time intervals between two groups. A *t*-test was used to test the difference in values at individual time intervals between two groups. A paired *t*-test was used to test the difference in values between two-time intervals within each group. A *P* value of <0.05 will be considered statistically significant. The data was entered in MS Excel spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) latest version.

RESULTS

A demographic profile like age, gender; duration of the CPB, duration of aortic cross-clamp time, and the type of the cardiac surgery was comparable in both the groups [Table 1]. The renal parameters (urea, creatinine, and creatinine clearance) and serum electrolyte profile were comparable in both the groups as depicted in [Table 2 and 3].

Table 2: Comparison of Blood Urea (mg/dl) between Ringer Lactate and Plasmalyte Group

Time of sample collection	Plasmalyte group (mg/dl) Mean+sd	Ringer Lactate group (mg/dl) Mean+sd	P value (<0.05)
Prior to induction	14.5+3.2	15.4+2.9	0.227
1 hour after induction	14.3+3.3	14.7+2.7	0.566
Immediate post-operative period	13.9+3.3	14.5+2.9	0.431
24 hrs post-operative period	13.7+3.4	14.4+3.0	0.336
48 hrs post-operative period	14+3.3	14.2+3.0	0.777

Blood urea (mg/dl) was comparable between the two groups RL and PL throughout the period of study and was not statistically significant ($P > 0.05$)

Table 3: Comparison of Serum Creatinine between Ringer Lactate and Plasmalyte Group

Time of sample collection	Plasmalyte group (mg/dl) Mean+sd	Ringer Lactate group (mg/dl) Mean+sd	P value (<0.05)
Prior to induction	0.3+0.1	0.3+0.1	0.978
1 hour after induction	0.3+0.2	0.3+0.1	0.455
Immediate post-operative period	0.3+0.1	0.3+0.1	0.511
24 hrs post-operative period	0.3+0.2	0.3+0.1	0.421
48 hrs post-operative period	0.3+0.2	0.4+0.3	0.4+0.3

Serum creatinine (mg/dl) was comparable between the two groups RL and PL throughout the period of study and was not statistically significant ($P > 0.05$)

DISCUSSION

The acid-base effects and renal parameters were compared between the two prime solutions during the perioperative period. We proposed that Plasmalyte-A causes less metabolic acidosis in comparison to Ringer's lactate when used as the pump prime during the CPB in the valve replacement surgeries.

Our results showed that the adults receiving Ringer's lactate had a different acid-base profile as compared to Plasmalyte-A. Patients showed more severe metabolic acidosis 30 min after initiating the CPB ($P < 0.05$ at T_2) in the Ringer's lactate group as depicted by the fall in pH, decrease in bicarbonate, decrease in base excess, and increase in blood lactate levels.

In Ringer's lactate group, there was a reduction in pH from 7.428 ± 0.029 at T_1 to 7.335 ± 0.06 ($P = 2.46E-10$) at T_2 as shown in Figure 1. The mean bicarbonates decreased in Ringer's lactate group during CPB from 24.28 ± 1.65 mEq/L at T_1 to 20.98 ± 2.97 mEq/L at T_2 ($P = 4.14E-08$) as shown in Figure 2. The mean base excess values reduced from -0.36 at T_1 to -3.67 ($P = 0.0002$) and -3.16 ($P = 0.0006$) at T_2 and T_3, respectively as depicted in Figure 3. Consequently, in the Plasmalyte-A group, mean pH and bicarbonate values were more or less similar at all the time intervals ($P > 0.05$).

Both the group developed hyperlactatemia during CPB as shown in Figure 4. The increase in blood lactate levels was more in Ringer's lactate group as compared to the Plasmalyte-A group. Similarly, in Ringer's lactate group, maximum surge in mean blood

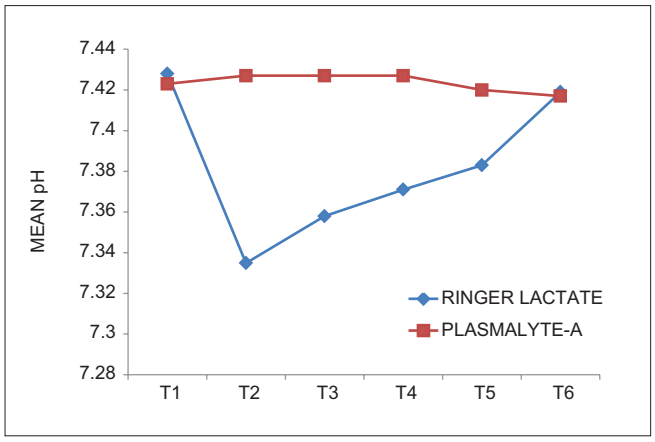

Figure 1: Trend of pH between Ringer's lactate and Plasmalyte-A group. pH showed a significant fall in Group I from T_1 to T_2 from 7.428 to 7.335 (P = 1.64E-12), stayed significantly low at all the time intervals but returned to T_1 as the patient stabilized in the ICU. Whereas in Group II, the pH values stayed stable throughout all the time intervals and were statistically insignificant. *Letter E in P value denotes standard scientific notation of powers of 10. It implies a highly significant result

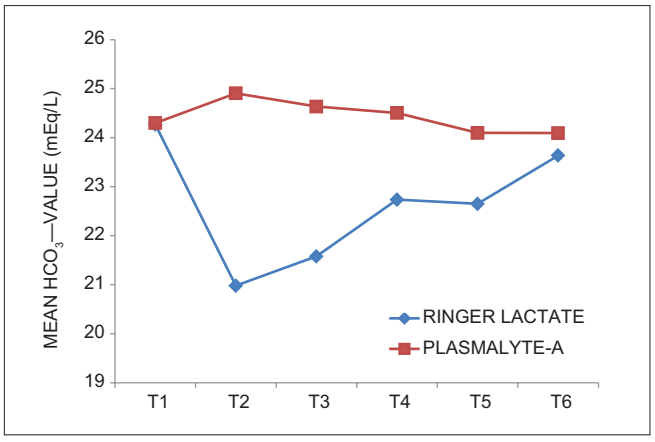

Figure 2: Trend of HCO_3^- between Ringer's lactate and Plasmalyte-A group. Similarly, there was a decrease in the value of serum bicarbonate in the Ringer's lactate group in comparison to Plasmalyte-A group and was found to be statistically significant 30, 60, and 90 min after initiating CPB and after termination of CPB (P = 4.14E-08 at T_2, P = 2.04E-06 at T_3, and P = 0.000131992 at T_4, respectively)

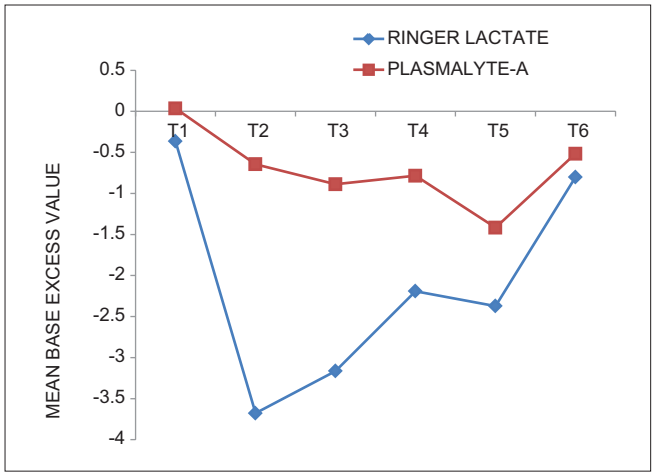

Figure 3: Trend of base excess between Ringer's lactate and Plasmalyte-A group. There is a decrease in base excess value in the Ringer's lactate group as compared to Plasmalyte-A group after 30, 60, and 90 min of initiation of CPB and was found to be statistically significant (P = 0.000254406 at T_2, P = 0.000671101 at T_3, and P = 0.007717731 at T_4, respectively)

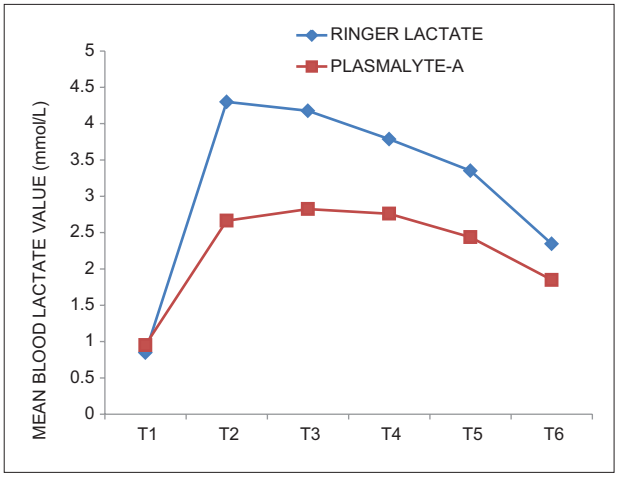

Figure 4: Trend of blood lactate between Ringer's lactate and Plasmalyte-A group. There was more increase in the value of mean lactate levels in the Ringer's lactate group in comparison to Plasmalyte-A group. It was found to be statistically significant 30 min. (P = 6.90E-06 at T_2), 60 min (P = 1.01E-06 at T_3), and 90 min (P = 0.04666554 at T_4) after initiating CPB, termination of CPB (P = 0.00147935 at T_5) and after half an hour stay in the ICU (P = 0.02549683 at T_6)

lactate levels was seen from 0.85 ± 0.35 mmol/L at T_1 to 4.29 ± 1.78 mmol/L (P = 2.85E-15) and 4.17 ± 1.28 mmol/L (P = 4.36E-15) at T_2 and T_3, respectively while in Plasmalyte-A, increase in mean blood lactate level was observed from 0.95 ± 0.74 mmol/L at T_1 to 2.66 ± 1.14 mmol/L, 2.82 ± 0.95 mmol/L, 2.76 ± 0.98 mmol/L and 2.43 ± 1.01 mmol/L at T_2, T_3, T_4, and T_5, respectively ($P < 0.05$). The blood lactate value reduced to less than 2 mmol/L in the Plasmalyte-A group postoperatively (1.849 mmol/L at T_6). However, lactate levels were still higher in the Ringer's lactate group postoperatively (2.345 mmol/L at T_6).

This clearly indicates that Ringer's lactate in prime solution is contributing to the rise in serum lactate levels leading to acidosis which stays for a longer duration of time when compared with the Plasmalyte-A group.

The mean SID decreased during the CPB in the Ringer's lactate group from 41.102 mEq/L at T_1 to 35.66 mEq/L (P = 0.033) at T_2 implying metabolic acidosis as depicted in Figure 5. The mean SID were comparable at all the time intervals in the Plasmalyte-A group. The differences in mean SID at different time intervals in this group were not statistically significant ($P > 0.05$). The chloride levels

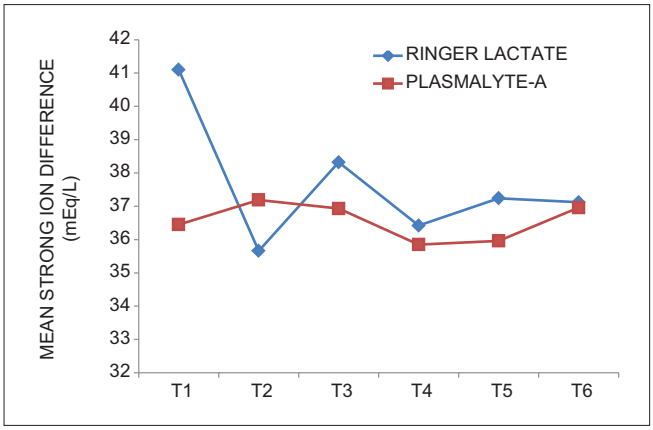

Figure 5: Trend of strong ion difference (SID) between Ringer's lactate and Plasmalyte-A group. A decrease in SID was observed during CPB in the Ringer's lactate group. The lowest SID was noted 30 min after initiating CPB (T_2) and was statistically significant ($P = 0.033$)

were similar throughout CPB but the lactate level variation was continuous which showed that the cause of acidosis was related to the type of fluid used in the prime.

Liskaser *et al.*[8] conducted a study comparing Ringer's solution and Plasmalyte-A as a bypass prime and concluded that the acidosis appeared to be iatrogenic in nature and derived from the effect of the pump-prime fluid based on the acid-base balance. The extent of such acidosis and its duration varied depending on the type of pump prime.

In a study conducted by Weinberg *et al.*[11] on 50 adult patients undergoing cardiac surgeries comparing Plasmalyte-A and Hartmann's solution; upon delivery of pump-prime both groups developed metabolic acidosis. Plasmalyte-A, standard BE: 0.53 mmol/L (BL) to -3.03 mmol/L (T2), $P < 0.001$; Hartmann's standard BE: 0.42 mmol/L (BL) to -2.20 mmol/L (T2), $P < 0.001$. There was significant hyperchloremia with Hartmann's compared to Plasmalyte-A. In addition, it was found that the mechanism of acidosis with Hartmann's solution was due to a combination of iatrogenic hyperlactatemia and hyperchloremia. There was no hyperlactatemia in the Plasmalyte-A group. The mechanism with Plasmalyte-A was the production of unmeasured anions (acetate and gluconate). This result is in accordance with our study wherein both groups developed metabolic acidosis on the delivery of pump prime. There was significant hyperlactatemia with Ringer's lactate compared to Plasmalyte-A. The SID decreased during the CPB in the Ringer's lactate group (41.102 mEq/L at T_1 to 35.66 mEq/L [$P = 0.033$] at T_2) in comparison to Plasmalyte-A group. There was no hyperchloremia in our study.

In a study conducted by Teloh *et al.*,[13] 25 patients undergoing elective isolated CABG with CPB revealed the existence of transitional dilutional acidosis during CPB. Patients, however, did not show overt lactic acidosis.

Moreover, the findings from previous studies and our study are consistent with the identified advantages of Plasmalyte-A over Ringer's lactate in terms of improved acid-base status and the lactate level.

Our study had many strengths considering the fact that it was carried out in a major tertiary institution in a developing country with a high caseload of adult patients undergoing valve replacement surgeries. It involved the exclusive use of Plasmalyte-A or Ringer's lactate in either patient group, which reduced the confounding effects of having mixed fluids administered. The findings are logical, plausible, and consistent with expectations and previous literature.

There are also several limitations to our study. The observational nature of our study is susceptible to bias and confounding despite computer-based randomization. Our study involved only patients between 18–50 years of age and the findings cannot be generalized to the pediatric and geriatric population. SID could not be calculated in our study. Our study involved only valve replacement surgeries and findings cannot be generalized to CHD and CABG.

CONCLUSION

In conclusion, the different compositions of Plasmalyte-A and Ringer's lactate have different metabolic implications for patients undergoing cardiac surgery. Patients who received Plasmalyte-A as CPB prime developed less metabolic acidosis.

These findings provide the opportunity to understand the unique physiochemical properties of the different balanced crystalloid solution and to improve the practice of selecting optimal fluid for patients undergoing valve replacement surgeries.

An ideal crystalloid solution would resemble the electrolyte content of plasma. Ringer's lactate is hypoosmolar to plasma but in contrast, Plasmalyte-A is a balanced salt solution having electrolyte constitutions similar to that of plasma and is not associated with the disturbance of acid-base status caused by the hypotonic and lactate containing solution.

Therefore, we conclude that Plasmalyte-A is the preferred CPB prime in adult patients undergoing valve replacement surgeries.

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Conflicts of interest
There are no conflicts of interest.

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