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Comparison of Ringer Lactate and Plasmalyte-A As Cardiopulmonary Bypass Prime for Bypass Associated Acidosis in Valve Replacement Surgeries

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Abstract

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 to compare the metabolic effects of Ringer lactate and Plasmalyte-A as CPB prime in causing bypass associated acidosis in valve replacement surgeries. 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.. The results were analyzed in a quantitative manner. In Ringer Lactate group, during CPB, there was reduction in pH from 7.428 $\pm$ 0.029 at T_1 to 7.335 $\pm$ 0.06 (P<0.01) and 7.358 $\pm$ 0.06 (P<0.01) at T_2 and T_3 respectively. Mean bicarbonates decreased in Ringer Lactate group during CPB from 24.28 $\pm$ 1.65 mEq/L at T_1 to 20.98 $\pm$ 2.97 mEq/L at T_2 (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 $\pm$ 0.35 mmol/l at T_1 to 4.29 $\pm$ 1.78 mmol/L (P<0.01) and 4.17 $\pm$ 1.28 mmol/L (P<0.01) at T_2 and T_3, 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 T_1 to 35.66 mEq/L (P=0.033) at T_2 implying metabolic acidosis. Numbered patients having hypotension and arrhythmias were also higher in Ringer Lactate group again indicating higher acidosis.

Keywords: Metabolic acidosis, CPB, Ringer Lactate, Plasmalyte-A, bypass prime

Introduction

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

The CPB circuit is primed with the prime fluid, which generally is a balanced electrolyte solution containing normal plasma concentrations of many of the standard

ions.[2] Drugs like heparin, bicarbonate, albumin are added to attenuate its dilutional effect and 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, circulatory failure.[4]

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

Ringer 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 lactate is significantly different from that of plasma. The osmolarity of ringer lactate is 278 mOsmol/L. Excess lactate production reduces strong ion difference and causes metabolic acidosis. Plasmalyte-A (another intravenous fluid) has physiochemical properties similar to plasma. The osmolarity of plasmalyte-A is 294 mOsmol/L which is same as plasma osmolarity.[9,10] Therefore, it can safely be used as prime fluid without causing much side effects.

Hence, this study is designed to understand the role of Ringer Lactate as a pump prime fluid in causing lactic acidosis and compare it with Plasmalyte-A solution which is devoid of lactate in patients of 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 cardiopulmonary bypass for the valvular heart surgeries. Patients with deranged acid base metabolism pre-operatively, renal dysfunction or having complex congenital heart diseases were excluded from the study.

Patients were randomly allocated in 2 groups with 40 patients in each group according to randomization technique.

Group-I: received Ringer Lactate as CPB prime fluid. Cardioplegia solution and peripheral intra vascular crystalloid fluids were also Ringer Lactate.

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

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 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 Lactate. For group II, cardioplegia solution was prepared using 500 mL of Plasmalyte-A.

Demographic details, history, diagnosis including any co morbidities, routine biochemistry investigations including pre and post-operative renal function tests were documented. Arterial samples for ABG analysis were taken at the following time intervals : 5 minutes before initiating CPB ($\mathbf{T_1}$), 30 minutes after initiating CPB ($\mathbf{T_2}$), 60 minutes after initiating CPB ($\mathbf{T_3}$), 90 minutes after initiating CPB ($\mathbf{T_4}$), after termination of CPB ($\mathbf{T_5}$) and after half an hour stay in the ICU ($\mathbf{T_6}$). Strong ion difference was calculated. SID in mEq/l = ($Na^+ + K^+$) – (Cl^- + Lactate)[11] Any additives and its amount added to the pump fluid to correct acid base

balance during bypass and duration of bypass was also noted.

Ethics

The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional). The Institute Ethical 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. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then the non-parametric 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

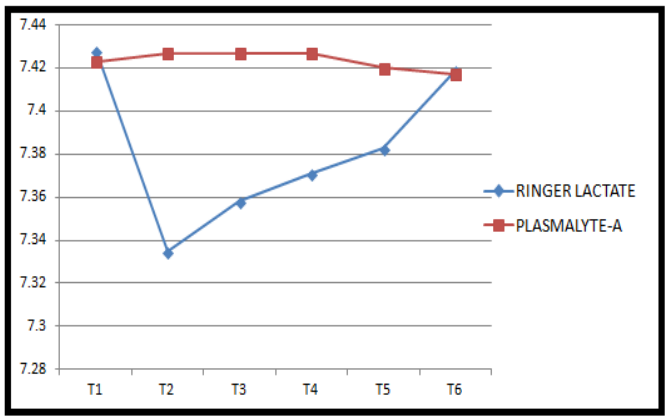
Demographic profile- age, gender; duration of the cardiopulmonary bypass and the type of the cardiac surgery were comparable in both the groups. The renal parameters (urea, creatinine and creatinine clearance) and serum electrolyte profile were comparable in both the groups.

Table 1 : Demographic Profile

	Ringer lactate	Plasmalyte-a
mean age (years)	34.975	33.05
no. of male patients	19	23
no. of female patients	21	17
mean duration of cpb (minutes)	78.3	87.075

Comparison of Ph Between Group I And Group II

Figure 1: Trend of pH between Ringer Lactate and Plasmalyte-A Group

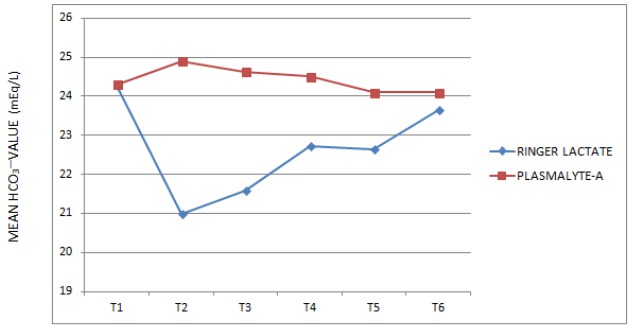


pH showed a significant fall in Group I from T_1 to T_2 from 7.428 to 7.335 (P=1.64E-12), stayed significantly low at all the time intervals but returned to T_1 as the patient stabilized in the ICU. Whereas in Group II, the pH values stayed stable throughout all the time intervals and were statistically insignificant as depicted in figure 1.

*Letter E in P value denotes standard scientific notation of powers of 10. It implies a highly significant result.

Comparison of Hco_3^- Between Group I and Group II

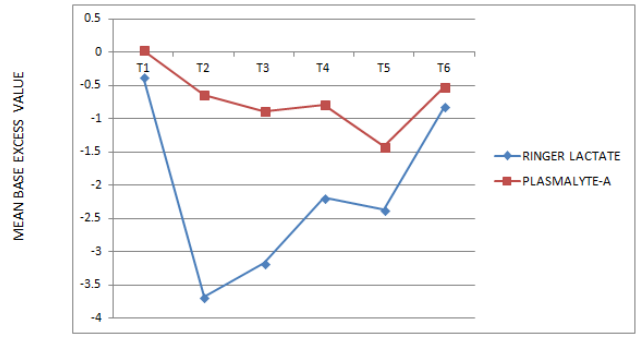
Figure 2: Trend Of Hco_3^- Between Ringer Lactate And Plasmalyte-A Group



Similarly, there was a decrease in the value of serum bicarbonate in the Ringer Lactate group in comparison to Plasmalyte-A group and was found to be statistically significant 30, 60, 90 minutes 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).

Comparison of Base Excess between Group I and Group II

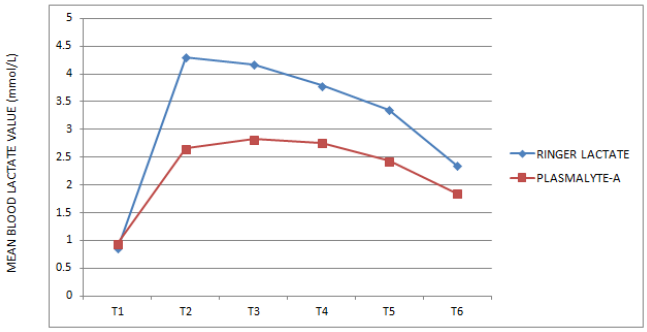
Figure 3: Trend of Base Excess between Ringer Lactate and Plasmalyte-A Group



- There is a decrease in base excess value in the Ringer Lactate group as compared to Plasmalyte-A group after 30, 60, and 90 minutes 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).

Comparison of Blood Lactate between Group I and Group II

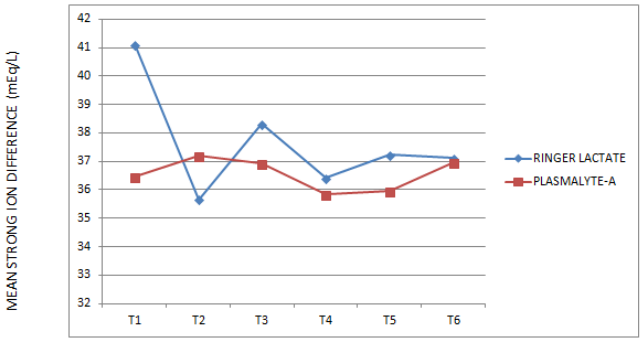
Figure 4: Trend of Blood Lactate between Ringer Lactate and Plasmalyte-A Group



- There was more increase in value of mean lactate levels in the Ringer Lactate group in comparison to Plasmalyte-A group. It was found to be statistically significant 30 minutes
- (P=6.90E-06 at T_2), 60 minutes (P=1.01E-06 at T_3) and 90 minutes (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).

Comparison of Strong Ion Difference between Group I and Group II

Figure 5: Trend of Strong ion difference (SID) between Ringer Lactate and Plasmalyte-A Group



- A decrease in SID was observed during CPB in the Ringer Lactate group. The lowest strong ion difference was noted 30 minutes after initiating CPB (T_2) and was statistically significant (P=0.033).

Discussion

The acid base effects and renal parameters were compared between the two prime solution during peri-operative period. We proposed that Plasmalyte A causes less metabolic acidosis in comparison to Ringer Lactate when used as the pump prime during the cardiopulmonary bypass in the valve replacement surgeries.

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

In Ringer Lactate group, , there was a reduction in pH from 7.428 $\pm$ 0.029 at T_1 to 7.335 $\pm$ 0.06 (P=2.46E-10) at T_2.The mean bicarbonates decreasesd in Ringer Lactate group during CPB from 24.28 $\pm$ 1.65 mEq/L at T_1 to 20.98 $\pm$ 2.97 mEq/L at T_2 (P=4.14E-08). 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. Whereas in Plasmalyte-A group, mean pH and bicarbonate values were more or less similar at all the time intervals (P>0.05).

Both the groups devlepoed hyperlactemia during cardiopulmonary bypass. The increase in blood lactate levels was more in Ringer Lactate group as compared to the Plasmalyte-A group. In Ringer Lactate group, maximum surge in mean blood lactate levels was seen from 0.85 $\pm$ 0.35 mmol/l at T_1 to 4.29 $\pm$ 1.78 mmol/L (P=2.85E-15) and 4.17 $\pm$ 1.28 mmol/L (p=4.36E-15) at T_2 and T_3, respectively. In Plasmalyte-A, increase in mean blood lactate level was observed from 0.95 $\pm$ 0.74 mmol/L at T_1 to 2.66 $\pm$ 1.14 mmol/L, 2.82 $\pm$ 0.95 mmol/L, 2.76 $\pm$ 0.98 mmol/L and 2.43 $\pm$ 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 post operatively (1.849 mmol/L at T_6). However, lactate levels were still higher in the Ringer Lactate group post operatively (2.345 mmol/L at T_6).

This clearly indicates that Ringer 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 Plasmalyte-A group.

The mean strong ion difference decreased during the cardiopulmonary bypass in the Ringer Lactate group from 41.102 mEq/L at T_1 to 35.66 mEq/L (P=0.033) at T_2 implying metabolic acidosis. The mean SID were comparable at all the time intervals in the Plasmalyte-A group and were not statistically significant (P>0.05). The chloride levels were similar throughout CPB but the lactate level variation was continuous which showed that the cause of acidosis is related to the type of fluid used in the prime.

Liskaser FJ et al [8] conducted a study comparing Ringer's solution and Plasmalyte-A as bypass prime and concluded that the acidosis appeared to be iatrogenic in nature and derived from effect of the pump prime fluid 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 LD et al [12] on 50 adult patients undergoing cardiac surgeries comparing Plasma Lyte-A and Hartmann's solution. On delivery of pump prime both groups developed metabolic acidosis. Plasma Lyte-A, standard BE: 0.53mmol/L (BL) to -3.03mmol/L (T2), P<0.001; Hartmann's standard BE: 0.42mmol/L (BL) to -2.20mmol/L (T2),

P<0.001. There was significant hyperchloraemia with Hartmann's compared to Plasma Lyte-A. It was found that the mechanism of acidosis with Hartmann's solution was due to a combination of iatrogenic hyperlactemia and hyperchloremia. There was no hyperlactatemia in the Plasma Lyte-A group. The mechanism with plasmalyte-A was production of unmeasured anions (acetate and gluconate). Even in our study, both groups developed metabolic acidosis on delivery of pump prime. There was significant hyperlactemia with Ringer Lactate compared to Plasma Lyte-A. The strong ion difference decreased during the cardiopulmonary bypass in the Ringer 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 JK et al [13] on 25 patients undergoing elective isolated CABG with CPB revealed existence of transitional dilutional acidosis during CPB. Patients however did not show overt lactic acidosis.

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

Our study had many strengths 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 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. Strong ion difference could not be calculated in our study. Our study involved only valve replacement surgeries and findings cannot be generalized to congenital heart diseases and CABG.

Conclusion

We conclude that 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.

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 Lactate is hypoosmolar to plasma, but in contrast, Plasmalyte-A is a balanced salt solution having electrolyte constitution similar to that of plasma and is not associated with the disturbance of acid-base status caused by the hypotonic and lactate containing solution.

Hence we conclude that Plasmalyte-A is the preferred cardiopulmonary bypass prime in adult patients undergoing valve replacement surgeries.

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