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## Comparative Analysis Between Ringer Lactate Versus Plasmalyte - A As Cardiopulmonary Bypass Priming Solutions & Its Outcomes In Paediatric Patients.

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### ABSTRACT

Paediatric heart surgery, particularly cyanotic congenital heart conditions, commonly requires the utilization of cardiopulmonary bypass to assist with surgical interventions. The choice of priming solution for the CPB circuit can influence postoperative outcomes. This study aimed to assess the impact of two different priming solutions, Ringer's lactate and plasmalyte -A, on postoperative outcomes, serum lactate level, blood biochemistry electrolytes (Sodium, Potassium, Calcium), mechanical ventilation time & intensive care unit (ICU) stay in children undergoing open cardiac surgery with CPB. The deairing of CPB circuit is done by priming solution, consisting of a Ringer Lactate or plasmalyte A. Priming causes hemodilution which improves flows during hypothermia. Adequate flow rates can be rapidly achieved on initiation of CPB without risk of air embolism.

**Keywords:** Cardiopulmonary bypass, Priming Solution, Ringer Lactate, Plasmalyte-A, Hemodilutions

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## INTRODUCTION

The cardiopulmonary bypass (CPB) circuit must be primed with a fluid solution, so that adequate flow rates can be rapidly achieved with initiation of cardiopulmonary bypass without risk of air embolism. Priming solutions are solutions which are used to prepare the extracorporeal perfusion line in cardiopulmonary bypass. Organ system in paediatric patient is not matured and they require high flow rate per body surface area (BSA) to meet metabolic demands. Significant haemodilution produced by priming solutions creates various problems like electrolyte imbalance, reduction in clotting factors and plasma protein, release of stress hormone and activation of complements [1, 2].

Disadvantage of the haemodilution is that it reduces the intravascular osmotic pressure and subsequently, interstitial edema develops. Consequently, malfunctioning of many organs, especially lungs decrease pulmonary compliance and cause hypoxia, peripheral edema, edema in muscles and gastrointestinal system and disturbance of the tissue oxygenation. Ringer lactate and plasmalyte-A solutions are among the most commonly used priming solutions [3, 4].

Plasmalyte -A is an isotonic, buffered intravenous crystalloid solution with a physiochemical composition that closely reflects human plasma.

Ringer lactate is an isotonic crystalloid solution considered more physiological than isotonic saline. However, it has certain disadvantages including high level of potassium and calcium and tendency of causing volume overload [5]. It may not be suitable for mixing with certain medications and some recommended against used in some infusion as blood transfusion [6].

The study aimed primarily to compare the postoperative lactate levels and secondarily to compare the clinical outcome of the paediatric patients receiving Plasmalyte-A and ringer lactate as priming solutions for undergoing cardiopulmonary bypass

## MATERIAL AND METHODS

Ours was a retrospective study was conducted at Pramukh Swami Medical College, Shree Krishna Teaching Hospital, Bhanubhai and Madhuben Patel Cardiac Centre, Karamsad, District: Anand, Gujarat, India. This hospital has an advanced central diagnostic laboratory that is well equipped and has been accredited by National Accreditation Board of Laboratories for Testing and Calibration of India. The study involved all children fulfilling inclusive criteria from January 2013 to January 2017.

### Inclusion criteria

All paediatric cardiac surgery patients having age up to 3 years and weight ranging from 2 to 15 kilogram were included for analysis. Patients having preoperative renal impairment (serum creatinine >1.5 mg %), liver dysfunction (serum bilirubin > 1.2mg/dl), sepsis or undergoing redo surgery, emergency, surgery or those requiring preoperative mechanical ventilator support were excluded from the study. Ethical approval was obtained from the Institutional Ethics Committee-2, H M Patel Centre for Medical Care and Education, Karamsad, Anand, Gujrat, India, IEC/HMPCMCE/91/Faculty/13/ 75/18 dated on 10/April/2018 review board prior to starting of the study.

### Primary outcome was serum lactate level (mmol/L)

Recorded at '0' post operative day (POD) , Immediate post operative , after postoperative 2 hours and then postoperative 4 hours, post operative day-1(POD-1<sup>st</sup>) .

### Secondary outcome were electrolytes Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>++</sup> (mmol/L)

Recorded at '0' post operative day (POD '0'), Immediate post operative, after postoperative 2 hours and then post operative 4 hours Post operative day-1(POD-1<sup>st</sup>) , Mechanical Ventilation Time "MVT" (hours) and Intensive Care Unit "ICU" stay (hours). The outcome variables were compared between the patient receiving Ringer's lactate and Plasmalyte- A as the priming solution for undergoing cardiopulmonary bypass.

**RESULTS**

During the study period, there were altogether 125 patients who fulfilled the criteria for analysis. Of them 72 patients had received Ringer’s lactate as the priming solution while 53 had received plasmalyte-A solution.

Patient’s demographic characteristics, cardiopulmonary bypass data comparing patients who received plasmalyte-A (PL-A group) and Ringers lactate (RL-group) is given table 1.

**Demographic Data**

Parameter	Group: A (RL) Ringer Lactate	Group: B (PL-A) Plasmalyte-A
Height (Centimetre)	67.62±16.58	65.08±18.44
Weight (Kilogram)	5.76±2.33	6.04±3.35
Gender (Male/Female)	52/20	36/16
Body Surface Area (Metre <sup>2</sup> )	0.31±0.094	0.35±0.16
Aortic Cross Clamp Time (Minute)	51.63±34.16	64.62±39.37
Cardiopulmonary bypass Time (Minute)	89.50±51.00	91.49±52.26
Lowest Temperature ° C ( Degree Celsius)	30.82±2.90	30.35±3.22
Lowest Hematocrit (%) (Percentage)	29.20±5.73	29.54±5.24

There was no statistical difference in patient characteristics (height, weight, gender, body surface area) as well as the Cardiopulmonary bypass data (aortic cross clamp time , cardiopulmonary bypass time, lowest temperature and lowest haematocrit) between the two groups.

**Serum Lactate Level**

**Table 1: Comparison of 'Lactate' level**

Variable	Ringer Lactate (n = 72)		Plasmalyte A (n=53)		p-Value
	Mean ± Standard Deviation	Median (Interquartile range)	Mean ± Standard Deviation	Median (Interquartile range)	
Post operative Day 'Zero'					
Immediate	3.48 ± 4.13	2.30 (1.73 – 3.31)	3.62 ±4.15	2.45 (1.85 – 4.03)	0.865
2 hours	2.72 ± 4.16	1.60 (1.30 – 2.60)	3.20 ± 3.27	1.86 (1.32-3.19)	0.589
4 hours	2.71 ± 4.82	1.60 (1.20 – 2.47)	3.39 ± 5.10	1.70 (1.23-2.28)	0.53
Post operative day '1'	1.82 ± 2.16	1.20 (0.89-2.03)	1.51 ± 0.56	1.55 (0.98 – 1.95)	0.488

**Table 2: Comparison of electrolytes (Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>++</sup>), Mechanical Ventilation Time (MVT) and ICU stay in hours**

Variable	Ringer Lactate (n = 72)		Plasmalyte A (n=53)		p-Value
	Mean ± Standard Deviation	Median(Interquartile range)	Mean ± Standard Deviation	Median(Interquartile range)	
<b>Sodium (Na<sup>+</sup>) Millimoles/Liter</b>					
<b>Post operative Day 'Zero'</b>					
Immediate	138.57 ± 5.05	139 (136 - 143)	135.83 ± 6.04	135.00 (132.50 - 139.00)	0.007
2 hours	140.44 ± 5.72	140.50 (138-145)	138.09 ± 5.06	138.00 (135.00 - 141.00)	0.019
4 hours	138.31 ± 17.40	141.00 (137-143.25)	137.48 ± 5.90	137.00 (134.00 - 141.00)	0.743
<b>Postoperative day '1'</b>	1.39.82 ± 7.13	140.00 (134.75-145.25)	137.67 ± 5.95	138.00 (133.00 - 142.00)	0.098
<b>Potassium (K<sup>+</sup>) Millimoles/Liter</b>					
<b>Post operative Day 'Zero'</b>					
Immediate	3.25 ± 0.47	3.20 (2.92 - 3.40)	3.28 ± 0.64	3.35(3.00 - 3.59)	0.776
2 hours	3.36 ± 0.57	3.30 (3.00-3.70)	3.45 ± 0.60	3.39(3.05-3.86)	0.357
4 hours	3.59±0.57	3.58 (3.26-3.89)	3.55 ± 0.48	3.50 (3.32 -3.83)	0.712
<b>Postoperative day '1'</b>	3.45 ± 0.57	3.41 (3.10- 3.70)	3.46 ± 0.45	3.52 (3.18 - 3.78)	0.885
<b>Calcium (Ca<sup>++</sup>) Millimoles/Liter</b>					
<b>Post operative Day 'Zero'</b>					
Immediate	0.97 ± 0.21	1.01 (0.84-1.10)	0.91 ± 0.26	0.90 (0.77-1.04)	0.171
2 hours	0.96 ± 0.24	0.99 (0.80-1.11)	0.98 ± 0.26	0.98 (0.79-1.14)	0.640
4 hours	0.97 ± 0.23	0.99 (0.87 -1.10)	0.96 ± 0.23	0.96 (0.83 - 1.10)	0.928
<b>Postoperative day '1'</b>	1.04±0.23	1.03 (0.95 - 1.11)	0.84 ± 0.23	0.84 (0.72-1.01)	<0.001
<b>Mechanical Ventilation Time (in hours)</b>	43.23 ± 57.36	16.00 (5.00 - 7.00)	60.07 ±86.48	18.00 (6.00 - 105.00)	0.197
<b>Intensive Care Unit(ICU) Stay in hours</b>	133.49 ± 90.59	140.00 (75.00 - 160.00)	134.17±211.83	48.00 (27.00-162.50)	0.981

**DISCUSSION**

All the patient’s preoperative demographic data showed no statistically significant and hence there were no major variations with respect to age, weight, height, body surface area, priming volume, Aortic cross clamp time, total CPB time, Lowest temperature and Lowest Haematocrit on CPB.

Metabolic acidosis is a frequent complication of cardiopulmonary bypass that is commonly believed to be the result of anaerobic metabolism and the accumulation of fixed acids, including lactate. There is increasing evidence that it is largely iatrogenic and results from the administration of intravascular fluids such as ringer's solution.

For group A immediate post operative mean lactate levels were 3.48 with standard deviation of ± 4.13 ,two hours postoperatively mean lactate level was 2.72 with standard deviation of ±4.16 ,Four hours Post operatively mean lactate level was 2.71 with standard deviation of ±4.82 and on post operative day one the mean lactate level was 1.82 with a standard deviation of ± 2.16 .For group

Immediate post operative mean lactate levels were 3.62 with standard deviation of  $\pm 4.15$ , two hours postoperatively mean lactate level was 3.20 with standard deviation of  $\pm 3.27$ , Four hours Postoperatively mean lactate level was 3.39 with standard deviation of  $\pm 5.10$ . and on postoperative day one the mean lactate level was 1.51 with a standard deviation of  $\pm 0.56$ . The P value for post operative Lactate level immediately was 0.865, post operatively after two hours was 0.589, post operatively after four hours was 0.0533 and post operatively on day one it was 0.488. The average cross clamp time in ringer lactate group plasmalyte A group is higher than that of "Ringer Lactate "group, plasmalyte A group which is an independent factor affecting cardiac output post operatively. In our study there was no significant difference in the serum lactate levels in between the two groups post operatively. The mean lactate level in group of patients receiving Plasmalyte-A was higher initially but slightly decreased on postoperative day one, when compared with group of patients receiving Ringer lactate. The use of Plasmalyte A which contains acetate as its organic anion may give some advantages over lactate containing crystalloids. Unlike lactate metabolism, acetate metabolism is not entirely dependent on hepatic function. Acetate metabolism is preserved in severe shock, in contrast to lactate metabolism, which can be significantly impaired [7-9]. Acetate is more rapidly metabolized than lactate, generating bicarbonate within 15 min after its administration [10-11]. Acetate is also more alkalizing than lactate, which may confer benefit in treating patients who are acidemic and who require fluid intervention. Unlike lactate metabolism, the metabolism of acetate does adversely affect insulin or glucose homeostasis [12-13]. Plasmalyte-A may therefore, confer clinical advantages in diabetic patients. In diabetic patients, intraoperative glycemic control may also be significantly impaired following the administration of lactate containing solutions [14].

For group A immediate post operative mean sodium levels were 138.57 with standard deviation of  $\pm 5.05$ , two hours postoperatively mean sodium level was 140.44 with standard deviation of  $\pm 5.72$ , Four hours Postoperatively mean sodium level was 138.31 with standard deviation of  $\pm 7.40$  and on postoperative day one the mean sodium level was 139.82 with a standard deviation of  $\pm 7.13$ . For group B immediate post operative mean sodium levels were 135.83 with standard deviation of  $\pm 6.04$ , two hours postoperatively mean sodium level was 138.09 with standard deviation of  $\pm 5.06$ , Four hours Postoperatively mean sodium level was 137.48 with standard deviation of  $\pm 5.90$ . and on post operative day one the mean sodium level was 137.67 with a standard deviation of  $\pm 5.95$ . The P value for post operative sodium level immediately was 0.007, post operatively after two hours was 0.019, post operatively after four hours was 0.743 and post operatively on day one it was 0.098. In our study difference in mean sodium levels immediate and two hours post operatively was statically significant but there was no significant difference in the serum lactate levels in between the two groups post operatively after four hours and on postoperative day one. The mean sodium levels in group of patients receiving Plasmalyte-A were lower when compared with group of patients receiving Ringer Lactate, but the sodium levels in both groups were in normal physiological range. Osmolarity of RL is 278mOsmol/L which is relatively hypotonic when compared with Plasmalyte-A. Plasmalyte-A is considered as balanced fluid and is isotonic with plasma, because it has a calculated normal physiological osmolarity of 294 mOsmol/L. Infused ringer lactate solution may lead to a small decrease in plasma osmolality which theoretically carries a risk of potential increase in brain water and effects on diuresis.

For group A immediate post operative mean potassium levels were 3.25 with standard deviation of  $\pm 0.47$ , two hours postoperatively mean potassium level was 3.36 with standard deviation of  $\pm 0.57$ , Four hours Postoperatively mean potassium level was 3.59 with standard deviation of  $\pm 0.57$  and on postoperative day one the mean potassium level was 3.45 with a standard deviation of  $\pm 0.57$ . For group B immediate post operative mean potassium levels were 3.28 with standard deviation of  $\pm 0.64$ , two hours postoperatively mean potassium level was 3.45 with standard deviation of  $\pm 0.60$ , Four hours Postoperatively mean potassium level was 3.55 with standard deviation of  $\pm 0.48$ . and on postoperative day one the mean potassium level was 3.46 with a standard deviation of  $\pm 0.45$ . The P value for post operative potassium level immediately was 0.776, post operatively after two hours was 0.357, post operatively after four hours was 0.712 and post operatively on day one it was 0.885. No significant difference in Potassium level was found in both the groups post operatively.

For group A immediate post operative mean calcium levels were 0.97 with standard deviation of  $\pm 0.21$ , two hours postoperatively mean calcium level was 0.96 with standard deviation of  $\pm 0.24$ , Four hours Postoperatively mean calcium level was 0.97 with standard deviation of  $\pm 0.23$  and on postoperative day one the mean calcium level was 1.04 with a standard deviation of  $\pm 0.23$ . For group B immediate post operative mean calcium levels were 0.91 with standard deviation of  $\pm 0.26$ , two hours postoperatively mean calcium level was 0.98 with standard deviation of  $\pm 0.26$ , Four hours

Postoperatively mean calcium level was 0.96 with standard deviation of  $\pm 0.23$ . and on postoperative day one the mean calcium level was 0.84 with a standard deviation of  $\pm 0.23$ . The P value for post operative calcium level immediately was 0.171, post operatively after two hours was 0.640, post operatively after four hours was 0.928 and post operatively on day one it was 0.001. The difference in calcium level on postoperative day one was found to be statically significant between both the groups. The mean calcium levels in Plasmalyte A group was significantly lower on postoperative day one Ringer Lactate solution contains calcium and should be used cautiously with blood or blood derivatives, due to the potential risks of precipitation and clot formation [10]. In contrast, Plasmalyte-A is calcium free and completely compatible with blood or blood components.

For group A mean mechanical ventilation time in hours was 43.23 with standard deviation of  $\pm 57.36$ . For group B mean mechanical ventilation time in hours was 60.07 with standard deviation of  $\pm 86.48$ . Intensive care unit stay in hours for group A was 133.49 with standard deviation of  $\pm 90.59$  and for group B it was 134.17 with standard deviation of  $\pm 211.83$ . There was no significant difference in the post operative mechanical ventilation time. and ICU stay in both the groups as p value for mechanical ventilation time is 0.197 and p value for Intensive care unit stay is 0.981. There is currently no completely physiological solution without any side effects that can be administered safely in all the patients. This study was conducted in patients without renal or hepatic dysfunction hence, there is a need to evaluate the effect of these priming solutions in patients with renal and hepatic impairment requiring cardiopulmonary bypass [15-17].

### CONCLUSION

When the two prime solutions that is Ringer lactate and Plasmalyte-A were compared, there was no significant difference in postoperative serum lactate levels, sodium levels, potassium levels, mechanical ventilation time and ICU stay. Calcium levels were lower in plasmalyte A group. Both the priming solutions were found to be safe to use in paediatric population and none were found superior, in terms of outcomes, than other. Further evaluation is needed for this study as patients having hepatic and renal dysfunction were excluded from the study.

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