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Original Article

Anaesthesia Section

Comparison of Albumin, Hydroxyethyl Starch and Ringer Lactate Solution as Priming Fluid for Cardiopulmonary Bypass in Paediatric Cardiac Surgery

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ABSTRACT

Introduction: In paediatric cardiac surgery, there is still not any information with regard to the best choice of priming fluids for Cardiopulmonary Bypass (CPB). Albumin, Hydroxyethyl Starch (HES) & ringer lactate are equally used, but each has its advantages & disadvantages. Albumin & HES had better fluid balance which affect outcome in paediatric cardiac surgery significantly.

Aim: To compare priming solution containing albumin, hydroxyethyl starch and ringer lactate during elective open-heart surgery in paediatrics aged up to 3 years.

Materials and Methods: All patients were managed by standardized institution protocol and were randomly distributed into three groups based on the priming solution which is used in the CPB Circuit and having 35 patients in each group. Group A: Receive albumin 10 ml/kg in priming solution, Group B: Receive Hydroxyethyl starch (HES130/0.4) 6% 20ml/kg in priming solution, Group C: Receive ringer lactate priming solution. Primary outcome variable included perioperative haemoglobin, total protein, colloid osmotic pressure, platelets, fluid balance, urine output, post-operative blood loss, blood products usage, renal & liver function, extubation time, ICU stay & outcome.

Results: Patients receiving albumin had higher perioperative platelet count, total protein level & colloid osmotic pressure, lesser post-operative blood loss & blood products requirement. Patients receiving HES had lower level of platelets post-operatively than ringer lactate group but not associated with increase blood loss. HES did not affect renal function & haemostasis in this dose. Patients receiving ringer lactate had positive fluid balance intraoperatively. All three groups have similar effect on renal & liver function, urine output, time to extubation, ICU stay & outcome.

Conclusion: We conclude that albumin is expensive but better prime as maintain haemostasis, colloid oncotic pressure & reduced blood product requirement. HES will not hamper haemostasis & renal function in lower dose & better than crystalloid as maintain negative fluid balance. Patient outcome & ICU stay was similarly affected by priming solutions.

Keywords: Colloid, Crystalloid, Haemostasis, Renal function

INTRODUCTION

Priming solutions are solutions which are used to prepare the extracorporeal perfusion line in cardiopulmonary bypass applications. Paediatric cardiac procedures require extremes of temperature and haemodilution. Organ system in paediatric patient is not matured and they require high flow rate per body surface area 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]. Dilution of plasma protein produce fall in colloidal oncotic pressure and favours interstial fluid shifting, which leads to water lodging of vital organs and adverse outcome [3]. For these reasons priming volumes should be kept to minimum and transfusion should be avoided.

Crystalloid solutions are cheap, easily available and devoid of anaphylatic reaction but they reduce colloidal oncotic pressure significantly [4,5].

Albumin a natural colloid which is responsible for 75 to 80% plasma oncotic pressure, is very costly and not easily available and also contains risk of anaphylatic reaction. Albumin maintains plasma oncotic pressure and prevent capillary leak of fluid resulting in improved organ functions [5,6].

Hydroxyethyl starch (HES/130/0.4) 6% is synthetic colloid produced from amylopectin. It was introduced in 1975 as priming solution in cardiac surgery. It produces volume expansion with very less incident of anaphylatic reaction. HES may affect haemostasis by weakening thrombus formation and also associated with renal dysfunction [7,8].

AIM

Aim of this study was to compare efficacy of priming solution containing albumin, hydroxyethyl starch and ringer lactate during elective open-heart surgery, in paediatrics aged up to 3 years.

MATERIALS AND METHODS

This prospective, randomized study was approved by institutional ethics committee and informed and written consent was obtained from all the patients' guardian. Inclusion criteria were all paediatric cardiac surgery patients age up to 3 years & weight up to 15 kg. Both genders were accepted. Exclusion criteria were preoperative renal & liver dysfunction, coagulopathy, complex surgery, repeat surgery, septicemia, on ventilator, emergency surgery. Study was done in the period of January 2014 to December 2014 at U.N. Mehta Institute of Cardiology and Research Center, Ahmedabad. This is pilot study & after employing inclusion & exclusion criteria total 105 patients were selected for this study. Participants, theatre staff, ICU staff, data collector & data processor were kept blind to this study. Operating surgeon, anaesthetist & paediatric intensivist were similar during study period. A computerized randomization table was used to assign patients to three groups with respect

to the priming solution used. Group A: Receive albumin 10 ml/kg in priming solution, Group B: Receive Hydroxyethyl starch (HES130/0.4)6% 20 ml/kg in priming solution, Group C: Receive ringer lactate priming solution. Patients were induced with Fentanyl 2µg/kg, Midazolam 0.2 mg/kg and Vecuronium 0.2mg/kg. Anaesthesia was maintained until the end of operation with continuous infusions of Fentanyl, Midazolam and Sevoflurane 1.5 MAC. Intraoperative standard monitoring was done. The CPB circuit was primed with 350 ml to 550 ml of predetermined solution according to weight of patient. Heparin was added in priming solution in dose of 5 IU/ml of priming solution. Blood was added to maintain haematocrit more than 28% in all groups. After anticoagulation with heparin in dose of (400 U/kg) activated clotting time was kept over 450 sec. CPB was established using roller pump with membrane oxygenator. The average flow rate varied from 0.5 to 1.5 lt/min according to body surface area. The mean arterial pressure was kept between 35-50mm of Hg. Cold blood cardioplegia of 10°C temp in dose of 20 ml/kg was administered after aortic cross clamp and repeat dose was 10ml/kg every 15-20 min. After aortic cross clamp blood sample was taken for total Protein, haemoglobin and platelet count. All patients were rewarmed to 36°C (nasopharyngeal temp) before weaning from CPB. Heparin was neutralized with 1:1 protamine sulfate. A 5 minute after complete weaning from bypass & before giving any blood & blood products, blood sample was taken from patient for total protein, platelet level & haemoglobin level. In postoperative period, rate of fluid infusion were adjusted according to haemodynamic measurement.

A packed red blood cell was given if haematocrit fall below 28%. If the platelet count was decreased below 1lac, 1unit of platelets were transfused. If the activated partial thromboplastin time or prothrombin time was prolonged 1.5 times the preoperative values fresh frozen plasma were transfused. The decision of re-exploration was done if chest tube drainage 20 ml/kg/hr for first 2 hours. Blood loss through the chest tubes was measured from the time of sternal closure until 72 hours after surgery. The amount of blood products, albumin and ringer lactate transfused were recorded. Level of haemoglobin, platelets, urea & creatinine, SGPT, bilirubin, & total protein, urine output, fluid balance were recorded during the postoperative period for 3 day. Landis and Pappenheimer developed an empirical model to predict Colloid Osmotic Pressure (COP) in human plasma in term of Total Protien (TP) concentration [9]. This model is given as: COP = 2.1 (TP) (TP^2) (TP^3). We calculated COP through this equation.

Primary outcome variable included incidence of renal and liver dysfunction, perioperative fluid balance, urine output, haemoglobin level, total protein, colloid osmotic pressure, platelets and post-op blood loss, re-exploration for haemorrhage, no of used blood products, time to extubation, ICU stay, anaphylatic reaction, in hospital mortality.

STATISTICAL ANALYSIS

The statistical analysis was performed using SPSS version 20.0. The values were expressed as Mean±SD. To compare the data between two groups, one sample t-test were used. Independent-sample t-test was used to compare the categorical variables. 'p' <0.05 was considered statistically significant.

RESULTS

The patients were distributed into three groups based on the priming solution which is used in the CPB circuit, and having 35 patients in each group. The mean age of the patients in Group A was 15.80±13.11 months, in Group B 16.20±14.24 months and in Group C 16.40±16.31 months. There were M=21 & F=14 in Group A, M=24 & F=11 in Group B and M=20 & F=15 in Group C. Preoperative demographic findings and intraoperative characteristics of the patients are given in [Table/Fig-1].

No statistical difference between the groups was detected in terms CPB time (p= 0.166) in terms of cross clamp time (p=0.886) lowest temp (p= 0.760) and in lowest haematocrit (p=0.989). Median data and statistical analysis of the parameters which were comparable in postoperative day 1, day 2 and day 3 are documented in [Table/Fig-2].

In group A (albumin) level of platelets on pump & postoperatively was higher compared to other two groups which was statistically significant (p<0.05), this indicate that platelet level was better preserved by adding albumin in priming. Patients receiving HES had lower level of platelets postoperatively first day than ringer lactate group but not associated with increase blood loss.

The level of total protein & colloid osmotic pressure was higher in group A as compared to other two (p<0.05), which indicate that albumin is beneficial in maintaining on pump as well as postoperative total protein level & colloid osmotic pressure.

Serum urea, serum creatinine level, urine output was similar in all three groups, which indicate renal function is not affected by these priming fluids especially HES will not cause renal dysfunction in this dose. Serum bilirubin & SGPT level were similar in all three groups postoperatively which indicate that liver function is not affected by any priming solution.

Postoperative drainage was minimal in albumin group as 29 patients out of 35 had less than 30 ml drainage over 72 hours, while in group B&C had 25 & 26 patients out of 35 had less than 30 ml drainage over 72 hours which indicates albumin better preserve haemostasis leads to lesser postoperative drainage, while HES & crystalloid had similar effect on it. Blood & blood products requirement was less in albumin group but similar in HES & crystalloid group which indicates albumin has beneficial effect on haemostasis while HES will not hamper haemostasis in this dose in paediatric age group.

Fluid balance was well maintained (Group A mean -30.8, Group B mean -4.11 and in Group C mean 81.71) which indicates colloid better preserve haemodynamic with their plasma expanding property & decrease fluid overload & tissue oedema. Peri operative urine output was similar in all three groups. There was no difference in time to extubation, ICU stay, and discharge time in all three groups. We did not observe any allergic reaction, any re-exploration for blood loss & any in hospital mortality in all groups.

	Group A Mean ± SD	Group B Mean ± SD	Group C Mean ± SD	p-value
Age (Months)	15.80 ± 13.11	16.20 ± 14.24	16.40 ± 16.31	0.985
Sex	M=21, F=14	M=24, F=11	M=20, F=15	
Weight (kg)	5.83 ± 2.34	6.75 ± 5.06	6.88 ± 4.53	0.516
CPB time (min)	51.0 ± 29.34	63.80 ± 30.34	57.42 ± 23.94	0.166
Cross Clamp Time (min)	36.85 ± 23.71	39.19 ± 18.32	38.94 ± 21.26	0.886
Lowest Temp	32.30± 1.83	32.22 ± 2.28	32.56 ± 1.78	0.760
Lowest HCT	29.57 ± 2.66	29.45 ± 4.52	29.45 ± 3.51	0.989
Ventilator stay (hr.)	11.031 ± 10.938	16.4 ± 11.80	15.714 ± 11.890	0.128
ICU Stay (days)	3.264 ± 0.863	3.531 ± 1.26	3.48 ± 1.32	0.610
Postoperative Drainage < 30 ml (no.of patients out of 35 patients)	29	25	26	0.5054
Postoperative Fresh frozen plasma requirement (no. of patients out of 35 patients)	6	16	14	0.0287
Postoperative Platelet Requirement (no. of patients out of 35 patients)	4	12	10	0.0701

[Table/Fig-1]: Demographic data.
HCT: Haematocrit, ICU: Intensive Care Unit

	Group A (Mean ± SD)	Group B (Mean ± SD)	Group C (Mean ± SD)	p-value
HB				
Pre op HB	12.86 ± 2.92	13.691 ± 3.354	12.2 ± 1.99	0.09
Intraop HB	10.037 ± 1.199	9.614 ± 1.084	9.52 ± 1.111	NS
DAY 1	12.24 ± 2.028	12.26 ± 1.978	12.07 ± 1.746	NS
DAY 2	12.045 ± 1.989	11.86 ± 1.909	11.08 ± 1.380	NS
DAY 3	11.946 ± 1.908	11.769 ± 1.417	11.287 ± 1.549	NS
PLATELET				
Pre-op Platelet	2.995 ± 1.231	3.44 ± 1.688	3.027 ± 1.341	NS
Intra-op Platelet	1.710 ± 0.579	1.476 ± 0.841	1.243 ± 0.585	0.019
DAY 1	2.20 ± 0.669	1.967 ± 0.796	2.191 ± 1.014	NS
DAY 2	2.272 ± 0.803	1.636 ± 0.643	2.026 ± 0.799	0.003
DAY 3	2.356 ± 0.776	1.713 ± 0.713	2.128 ± 0.705	0.002
TOTAL PROTEIN				
Pre-op Total Protein	6.445 ± 0.540	6.674 ± 0.904	6.565 ± 0.799	NS
Intraop Total Protein	3.734 ± 0.485	2.805 ± 0.708	2.62 ± 0.699	<0.001
DAY 1	5.451 ± 0.804	5.074 ± 0.899	4.928 ± 0.567	0.016
DAY 2	5.551 ± 0.706	4.991 ± 0.920	5.154 ± 0.622	0.008
DAY 3	5.565 ± 0.771	4.977 ± 0.981	5.194 ± 0.615	0.01
COP				
Pre-op COP	22.67 ± 2.840	23.492 ± 5.465	23.339 ± 4.147	NS
Intra-op COP	11.274 ± 3.060	7.376 ± 2.322	6.856 ± 2.379	<0.001
DAY 1	17.810 ± 3.553	16.164 ± 3.908	15.638 ± 2.657	0.024
DAY 2	18.236 ± 3.258	15.816 ± 4.041	16.442 ± 2.771	0.01
DAY 3	18.338 ± 3.562	16.208 ± 4.076	16.642 ± 2.763	0.031
CREATININE				
Pre-op Serum creatinine	0.439 ± 0.094	0.460 ± 0.111	0.405 ± 0.104	NS
DAY 1	0.432 ± 0.135	0.492 ± 0.104	0.463 ± 0.106	NS
DAY 2	0.424 ± 0.079	0.474 ± 0.111	0.454 ± 0.0883	NS
DAY 3	0.405 ± 0.0765	0.440 ± 0.124	0.438 ± 0.090	NS
UREA				
Pre-op Urea	21.8 ± 6.874	20.626 ± 8.428	19.226 ± 5.761	NS
DAY 1	29.285 ± 6.635	24.88 ± 8.937	27.240 ± 8.526	NS
DAY 2	30.876 ± 12.116	25.264 ± 9.298	27.271 ± 10.073	NS
DAY 3	29.422 ± 9.184	26.80 ± 7.185	25.080 ± 7.944	NS
SGPT				
Pre-op SGPT	19.54 ± 7.034	23.217 ± 9.846	20.142 ± 9.777	NS
DAY 1	29.20 ± 12.06	24.83 ± 8.78	24.228 ± 7.795	NS
DAY 2	27.62 ± 7.57	25.36 ± 16.48	24.168 ± 7.284	NS
DAY 3	27.171 ± 7.261	24.44 ± 11.97	23.142 ± 7.515	NS
BILLIRUBIN				
Pre-op Bilirubin	0.581 ± 0.253	0.984 ± 1.287	0.733 ± 0.435	NS
DAY 1	1.044 ± 0.731	1.697 ± 2.025	1.279 ± 0.977	NS
DAY 2	1.040 ± 0.8170	1.560 ± 1.992	1.148 ± 0.761	NS
DAY 3	0.951 ± 0.566	1.394 ± 1.518	1.060 ± 0.583	NS
URINE OUTPUT				
DAY 1	443.74 ± 172.12	613.71 ± 347.68	555.45 ± 347.98	NS
DAY 2	495.28 ± 130.25	694.57 ± 425.22	631.85 ± 448.61	NS
DAY 3	455.94 ± 152.23	697.71 ± 316.28	604.02 ± 404.62	NS

[Table/Fig-2]: Perioperative variables.
HB: Haemoglobin, SGPT: Serum Glutamic Pyruvic Transaminase,
NS: Not significant (p > 0.05).

DISCUSSION

Outcome in paediatric cardiac surgery is affected by intraoperative fluctuation in level of plasma protein and coagulation factors of blood. The normal reference range of colloid oncotic pressure is 25 to 30 mm of Hg. However, in paediatric patients undergoing CPB, a lower limit of 10 to 12 mmHg can be tolerated without leading to tissue oedema and organ dysfunction [2]. In paediatric cardiac surgery Haneda et al., reported that maintenance of COP on CPB with colloid and blood leads to reduce fluid accumulation in vital organs and made patient care easier postoperatively [3]. In our study we found similar results as albumin and HES maintain colloid oncotic pressure and prevent positive fluid balance peri-operatively while ringer lactate group had lower COP and positive fluid balance intraoperatively.

Russel et al., found that albumin prime as compared to crystalloid reduce on bypass drop of platelet counts and fall in oncotic pressure [5]. We also found similar results as albumin group has higher platelet count peri-operatively than HES and crystalloid group. Albumin can coat the fluid pathway surface, thereby diminishing contact between the blood and non-biological materials that could result in protein denaturation, platelet activation and consumption, release of inflammatory mediators. HES group had lower platelet count postoperatively but blood loss & product requirement is similar to ringer lactate group.

Kuitunen et al., compared HES solution and albumin as priming solution and reported that HES solution did not affect individual coagulation factors and platelet count or function but they weakens thrombus formation leads to increase blood loss [7]. Choi et al., studied that albumin and HES has similar effect in haemostasis and transfusion requirement [10]. In our study albumin group had lower postoperative blood loss and blood product requirement compared to HES and crystalloid groups. It indicates albumin preserve haemostasis but HES will not hamper haemostasis in dose of 20ml/kg as blood loss and product requirement are similar to ringer lactate group.

Akkucuk et al., & Hasan et al., found that HES did not have negative effect on renal function and it can be used as a priming solution as paediatric cardiac surgery [11,12]. Tiryakioglu et al., reported unfavourable effect of HES on renal function but the urea and creatinine levels where normal and ICU stays and discharge time are similar in both ringer lactate and HES group [8]. In our study we did not document any adverse effect on renal function and liver function in HES group. It indicates HES did not affect renal function in dose of 20ml/kg.

Liou et al., reported comparison between three different priming solutions; ringers lactate, human albumin and HES 10% [13]. Time to extubation, ICU stay and hospital stay did not differ among the groups. We found similar result in our study as time to extubation ICU stay and hospital stay are similar in all three groups.

LIMITATION

We measured colloid oncotic pressure by equation based on plasma protien level as we don't have colloid osmometer, so effect of HES on colloid oncotic pressure was not measured.

CONCLUSION

Albumin is expensive but better prime as to maintain haemostasis, colloid oncotic pressure & reduced blood product requirement. HES will not hamper haemostasis & renal function in lower dose and better than crystalloid as maintain negative fluid balance. Patient outcome & ICU stay was similarly affected by priming solutions.

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