Original Article

Comparison of plasma-lyte A and trometamol-balanced priming solutions for cardiopulmonary bypass in a swine model: a pilot study

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Abstract

Currently, the optimal priming solution for cardiopulmonary bypass (CPB) remains debatable. However, plasma-lyte A solution (PLAS) has been widely used in the United States and is considered to be the standard priming solution worldwide. Therefore, we designed a trometamol-balanced solution (Resculyte® solution, RS) to evaluate the safety and feasibility for its use as a priming solution during CPB compared to PLAS. In total, 8 white pigs that underwent CPB were assigned 1:1 to PLAS and RS groups. Hemodynamic parameters were recorded using an Abbott i-STAT analyzer with CG4+ (for pH, pressure of carbon dioxide, pressure of oxygen , total carbon dioxide, bicarbonate, base excess, oxygen saturation, and lactate), CG6+ (for sodium, potassium, chloride, blood glucose, blood urea nitrogen, hematocrit, and hemoglobin), and cardiac troponin I (cTnI) cartridges during and after CPB. The parameters of chemistries, electrolytes, and blood gas exhibited similar trends and revealed no considerable changes during and after CPB. However, the pH values of the RS group remained stable compared with the PLAS group. Moreover, the cTnI levels of the RS group were lower than those of the PLAS group, particularly on day 2. In conclusion, RS was a safe and feasible priming solution in this pilot study during CPB. Future study will increase the data of swine models with CPB to assess the clinical practice of RS compared to PLAS.

Keywords: cardiopulmonary bypass, plasma-lyte A solution, priming solution, swine model, trometamol-balanced solution

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Introduction

A priming solution is used to fill the extracorporeal circuit in cardiopulmonary bypass (CPB) applications during cardiac surgery. Basically, priming solutions can have crystalloids, colloids or blood as primary constituents (Gu and Boonstra, 2005). Crystalloid solutions are cheap and have a low risk of infection and anaphylactic reactions, compared with blood and colloid solutions. Nevertheless, determining the ideal priming solution is based on personal experience, religious beliefs and institute preferences, and it therefore remains debatable (Liskaser *et al.*, 2000; Lilley, 2002; Himpe, 2003[a]; Russell *et al.*, 2004). Although CPB offers cardiopulmonary support during cardiac surgery, it engenders a systemic inflammatory response syndrome, and various inflammatory mediators and vasoactive substances may deteriorate organ perfusion during CPB. Furthermore, changes in colloid osmotic pressure are related to postpump organ dysfunction, which results from hemodilution caused by priming solutions (Goto *et al.*, 1991).

Metabolic acidosis is also a potential complication of CPB and is associated with the types of priming solutions in the CPB circuit line (Liskaser *et al.*, 2000; Osthaus *et al.*, 2008). To alleviate or prevent metabolic acidosis, some strategies have been applied, including alterations to the priming fluid using additives of L-lactate, acetate, gluconate, and bicarbonate (Takkunen *et al.*, 1985; Himpe *et al.*, 2003[b]; Morgan *et al.*, 2008). Acetate and gluconate in plasma-lyte A solution (PLAS) are metabolized to bicarbonate, which possesses approximately 53% of the buffering capacity to regulate the pH through hydrogen cation consumption. Nevertheless, a trometamol-balanced solution (Resculyte® solution, RS) uses trometamol, a biologically inert amino alcohol that has a higher alkalizing capacity than bicarbonate for alleviating acidosis (Nahas *et al.*, 1998).

The present study investigated the influence of RS on chemistries and electrolytes as well as hematology, blood gas and cardiac biomarkers in a CPB circuit. Moreover, the study compared the effects of RS and PLAS on pigs that underwent thoracic surgery with cardiopulmonary support and evaluated the safety and feasibility of RS in clinical practice.

Materials and Methods

Animals: In the experiment, 8 white female pigs (aged 6-8 months; weight approximately 55-65 kg) were used and randomly assigned 1:1 to PLAS and RS groups. All pigs underwent CPB with different priming solutions at the National Taiwan University (NTU) Laboratory Animal Center (AAALAC-accredited facility) and were supervised by the Animal Care and Use Committee of the National Taiwan University (IACUC number: 20140366).

Priming solutions: The total volume of the priming solutions ranged from 2 to 3 liters according to the body weight of the pigs. The compositions of the two priming solutions were as follows:
1) PLAS: pH, 7.4; osmolality, 294 mOsml/kg; Na+, 140 mmol/L; K^+, 5 mmol/L; Cl^-, 98 mmol/L; Mg^{2+}, 3 mmol/L; acetate, 27 mmol/L; and gluconate, 23 mmol/L (Baxter Healthcare Corporation, Deerfield, IL, USA).
2) RS: pH, 7.4; osmolality, 282 mOsml/kg; Na+, 135 mmol/L; K^+, 4 mmol/L; Cl^-, 100 mmol/L; Mg^{2+}, 2 mmol/L; acetate, 24.5 mmol/L; gluconate, 25 mmol/L; and trometamol, 10 mmol/L (Resculyte® solution, Taiwan Biotech Co. Ltd., Taoyuan, Taiwan).

Anesthesia and CPB: Anesthesia, surgery and CPB were performed by the same team and in the same manner in all pigs. Atropine sulphate (Taiwan Biotech Co. Ltd., Taoyuan, Taiwan; 0.05 mg/kg intramuscular injection [IM]), cefazolin sodium (Taiwan Biotech Co. Ltd., Taiwan; 25 mg/kg, IM), and zoletil (Zoletil 50, Virbac, France; 5 mg/kg, IM) were administered as premedication. Each pig was then oxygenated with 100% oxygen, which was followed by induction with propofol (Fresenius Kabi, Austria; 0.5 mg/kg intravenous injection [IV]) and orally intubated with a cuffed endotracheal tube. Anesthesia was maintained with volume-controlled ventilators with oxygen (1.5 L/min), air (1.5 L/min), and isoflurane (Aesica Queenborough Ltd., UK; 1.5%–2%). The surgical sites (ventral chest and right and left groins) were shaved and treated with iodine. The arterial and central venous lines were placed percutaneously in the left femoral artery and vein for arterial and central venous pressure monitoring, respectively. Electrocardiography and temperature monitoring were conducted using electrode patches and rectal probes, respectively.

After the administration of succinylcholine chloride (Shinlin Sinseng Pharmaceutical Co. Ltd., Taoyuan, Taiwan; 2 mg/kg IV), a median sternotomy was performed: an incision was made from the suprasternal notch to the xiphoid process, and a reciprocating saw was subsequently used to divide the sternum along the previously created incision. After heparin sodium (Leo Pharma A/S, Ballerup, Denmark; 300 IU/kg IV) was administered to achieve an activated clotting time of >350s, an arterial cannula (HLS Cannula, 15-Fr, Maquet Cardiopulmonary GmbH, Rastatt, Germany) was inserted into the aorta; venous cannulation (DLP Single Stage Venous Cannula, 24-Fr, Medtronic, Minneapolis, MN, USA) was achieved through the right atrium. The CPB circuit was designed for the pigs using a centrifugal pump (Medtronic Biomedicus 560 centrifugal pump, Medtronic, Minneapolis, MN, USA), venous reservoir (Medtronic Cardiotomy reservoir, Medtronic, USA) and membrane oxygenator (Advanced Affinity Oxygenator, Medtronic, USA). CPB was initiated at a flow rate of 1.2–1.8 L/min/m^2.

CPB was initiated for 180 minutes and blood samples were collected every 30 mins. At the end of 180 minutes, CPB was weaned and an interval of 30 mins was waited to monitor the arterial and central venous blood pressure and oxygen saturation. Finally, protamine sulphate (Cannexi, Fontenay-sous-Bois, France; 50 mg/pig IV) and furosemide (Yung Shin Pharm. Ind. Co. Ltd., Taichung, Taiwan; 20 mg/pig IV) were used after decannulation. All the pigs were successfully weaned from CPB and kept alive for 8 days. Finally, the pigs were euthanised on day 9 by injecting them with an overdose of propofol (2 mg/kg

IV) and potassium chloride (Taiwan Biotech Co. Ltd., Taoyuan, Taiwan; 100 mg/kg IV). The heart, liver, kidney, spleen, and lung tissues were excised and stored until for examination.

Blood sampling: Blood samples were collected at the following time points: preoperatively (baseline); 5 mins after heparin administration (heparin + 5 min); 30, 60, 90, 120, 150, and 180 mins after CPB (CPB + 30, + 60, + 90, + 120, + 150, and + 180 mins, respectively); 30 mins after the completion of CPB (end of bypass [EB] + 30 mins); day 2 (EB + 2 days); day 4 (EB + 4 days); day 7 (EB + 7 days); and day 9 (EB + 9 days). The blood samples were obtained from an arterial catheter placed in the femoral artery from the baseline to EB + 30 mins and from the jugular vein at EB + 2, + 4, + 7, and + 9 days.

Hemodynamic parameter measurement: The collected blood samples were analyzed using an Abbott i-STAT (Abbott Point of Care, Princeton, NJ, USA) analyzer. Blood samples for the i-STAT CG4+ cartridge (for pH, pressure of carbon dioxide [PCO_2], pressure of oxygen [PO_2], total carbon dioxide [TCO_2], bicarbonate [HCO_3], base excess [BE], oxygen saturation [sO_2], and lactate) and CG6+ cartridge (for sodium [Na], potassium [K], chloride [Cl], blood glucose, blood urea nitrogen [BUN], hematocrit [Hct] and hemoglobin [Hgb]) were obtained at the baseline; heparin + 5 mins; CPB + 60, + 120, and + 180 mins; EB + 30 mins; and EB + 2, + 4, + 7, and + 9 days. Blood samples for the cardiac troponin I (cTnI) cartridge (Abbott Point of Care, USA) were obtained at the baseline; CPB + 180 mins; and EB + 2, + 4, + 7, and + 9 days.

Statistical analysis: Statistical analysis was performed using R (version 3.3.2; The R Foundation) for Mac. All data is presented as means ± standard deviations. The two-sample *t* test was used to determine the differences in parameters between the PLAS and RS groups from the baseline to selected time points, and $p < 0.05$ was considered statistically significant.

Results

During the study period, 8 white female pigs (aged 6-8 months; weight approximately 55-65 kg) were randomly assigned 1:1 to the PLAS and RS groups. All pigs underwent CPB with different priming solutions at the NTU Laboratory Animal Center. In total, eight pigs were included in the present study and the results are shown in Table 1.

Chemistries and electrolytes: The sodium levels of the PLAS group were stable and increased until EB + 2 days. The RS group also exhibited a similar trend to the PLAS group in that the sodium levels were slightly below the normal range and increased until EB + 2 days, but did not differ significantly between the two groups (Fig. 1A). The chloride levels of the PLAS group decreased gradually until EB + 9 days. The chloride levels of the RS group also declined slowly until CPB + 180 mins and slightly increased further until EB + 4 days (Fig. 1B). However, there were no significant differences between the two groups. By contrast, the potassium levels of both groups remained stable during the study period and the potassium levels of the RS group at EB + 9 days was significantly higher than the PLAS group ($p < 0.05$) (Fig. 1C).

Blood glucose levels increased gradually and peaked at the end of surgery, after which they decreased slightly (Fig. 2A). Neither group showed significant differences in blood glucose levels. Except for at EB + 2 days, the blood glucose levels in the PLAS group were significantly higher than those in the RS group ($p < 0.05$). Furthermore, the BUN levels in both groups were within the normal range and showed similar trends and peaked at EB + 2 days (Fig. 2B). Both groups revealed no significant differences during the study except EB + 9 days ($p < 0.05$). The lactate levels of both groups fluctuated in abnormal ranges from the baseline to EB + 2 days, declined to the lowest points at EB + 4 days ($p < 0.05$), and increased gradually at EB + 4 days until the end of the study period (Fig. 2C).

Hematology: Hct and Hgb levels were slightly reduced at heparin + 5 mins. Subsequently, these levels remained stable until EB + 9 days (Figs. 3A-B). The PLAS and RS groups did not exhibit significant differences.

Blood gases: The pH values of both groups increased from the baseline to EB + 30 mins and then decreased sharply to the lowest value at EB + 2 days. Subsequently, the pH values returned to the normal range and remained stable until the end of the study period (Fig. 4A). The pH values of the PLAS group at EB + 4 days was significantly higher than the RS group ($p < 0.05$).

The PCO_2 levels of both groups remained stable from the baseline to EB + 30 mins and then increased until the end of the study period (Fig. 4B). However, there were no significant differences among all time points. Specifically, the PO_2 levels of both groups exhibited similar trends; high PO_2 levels were observed until EB + 30 mins, followed by a decrease below 40 mmHg until the end of the study period (Fig. 4C). But no significant differences were noted. Furthermore, the TCO_2 and HCO_3 levels of both groups exhibited similar trends and fluctuated slightly in abnormal ranges during the study period (Figs. 4D-E). There were no significant differences between the two groups.

The base excess levels of both groups increased from heparin + 5 mins to EB +7 days and then decreased at EB + 9 days (Fig. 4F). The SO_2 levels of both groups remained stable before EB + 180 mins and then declined below 80% until the end of the study period (Fig. 4G). The PLAS and RS groups did not reveal significant differences.

cTnI: The cTnI levels of both groups increased gradually from the baseline to EB + 2 days (Fig. 5). Subsequently, the cTnI levels decreased to the normal range until EB + 9 days. At EB + 2 days, the cTnI levels in the PLAS group were significantly higher than those in the RS group ($p < 0.05$).

Table 1 Chemistries, electrolytes, hematology, blood gas and cTnI in PLAS and RS groups

	Baseline	Heparin +5 mins	Bypass +60 mins	Bypass +120 mins	Bypass +180 mins	EB +30 mins	EB +2 days	EB +4 days	EB +7 days	EB +9 days
Na (mmol/L)										
PLAS	140.50 ± 1.29	139.50 ± 0.58	138.75 ± 0.96	138.00 ± 0.82	138.25 ± 0.96	138.50 ± 1.29	145.25 ± 1.71	141.75 ± 1.26	141.00 ± 1.83	143.00 ± 5.35
RS	133.38 ± 9.30	134.25 ± 6.85	134.25 ± 6.29	133.50 ± 5.69	133.50 ± 6.35	134.25 ± 5.56	142.50 ± 4.65	140.50 ± 3.87	140.75 ± 1.26	139.00 ± 1.15
K (mmol/L)										
PLAS	3.98 ± 0.25	3.80 ± 0.14	3.78 ± 0.10	3.85 ± 0.13	3.93 ± 0.17	4.13 ± 0.25	4.08 ± 0.43	4.10 ± 0.22	4.60 ± 0.54	3.98 ± 0.40*
RS	3.98 ± 0.15	4.03 ± 0.39	3.75 ± 0.42	4.03 ± 0.35	3.95 ± 0.53	4.03 ± 0.54	4.43 ± 0.21	4.25 ± 0.62	5.00 ± 0.96	5.00 ± 0.27*
Cl (mmol/L)										
PLAS	102.5 ± 2.52	100.25 ± 2.75	99.75 ± 2.50	99.00 ± 2.16	99.50 ± 2.52	98.75 ± 3.59	98.25 ± 1.89	97.75 ± 2.06	97.00 ± 1.63	95.75 ± 1.71
RS	100.00 ± 6.98	97.50 ± 6.61	96.25 ± 4.99	96.50 ± 4.43	95.00 ± 3.83	96.50 ± 4.36	97.25 ± 3.77	99.00 ± 0.82	96.50 ± 1.29	97.50 ± 1.00
BUN (mg/dL)										
PLAS	5.50 ± 3.00	5.00 ± 2.31	5.25 ± 2.63	6.00 ± 2.94	6.75 ± 3.30	7.25 ± 3.40	20.25 ± 4.11	6.25 ± 3.59	6.00 ± 2.58	4.50 ± 1.73*
RS	5.87 ± 1.02	5.20 ± 2.20	5.72 ± 1.70	6.12 ± 1.44	7.07 ± 1.42	7.50 ± 1.00	19.50 ± 3.87	7.00 ± 1.83	9.00 ± 1.83	7.00 ± 1.41*
Glucose (mg/dL)										
PLAS	105.00 ± 34.61	109.00 ± 34.34	151.75 ± 44.40	160.75 ± 45.33	174.50 ± 54.98	163.50 ± 41.22	128.25 ± 15.13*	91.75 ± 13.12	92.50 ± 10.08	105.75 ± 30.41
RS	99.13 ± 30.84	98.25 ± 22.04	136.00 ± 37.31	137.75 ± 31.97	145.25 ± 26.44	155.75 ± 26.40	108.25 ± 13.60*	83.25 ± 7.27	85.5 ± 8.58	115.5 ± 46.28
Lactate (mmol/L)										
PLAS	2.76 ± 1.41	2.19 ± 0.75	3.82 ± 2.01	3.45 ± 2.08	4.09 ± 2.69	4.11 ± 2.33	3.46 ± 0.87	0.96 ± 0.12*	1.86 ± 1.10	2.68 ± 2.45
RS	3.64 ± 3.01	2.65 ± 1.00	3.37 ± 1.19	3.26 ± 1.72	2.93 ± 0.50	3.55 ± 1.17	4.52 ± 1.78	1.79 ± 0.25*	2.11 ± 0.71	3.58 ± 2.20
Hct (%)										
PLAS	28.00 ± 2.94	21.75 ± 6.85	28.00 ± 3.37	27.75 ± 3.20	28.25 ± 2.50	26.75 ± 4.03	24.25 ± 0.96	22.75 ± 4.42	23.75 ± 2.87	23.75 ± 2.87
RS	30.38 ± 3.40	26.75 ± 4.57	26.00 ± 2.16	26.50 ± 2.24	26.50 ± 2.52	26.25 ± 1.71	27.25 ± 6.02	25.00 ± 4.24	26.00 ± 0.82	25.50 ± 4.20
Hgb (g/dL)										
PLAS	9.53 ± 0.97	7.43 ± 2.31	9.55 ± 1.14	9.45 ± 1.11	9.60 ± 0.84	9.10 ± 1.36	8.25 ± 0.33	7.73 ± 1.51	8.05 ± 0.96	8.10 ± 0.98
RS	10.35 ± 1.14	9.08 ± 1.54	8.85 ± 0.74	9.03 ± 0.99	9.03 ± 0.88	8.93 ± 0.57	9.28 ± 2.02	8.50 ± 1.45	8.83 ± 0.28	8.65 ± 1.44
pH										
PLAS	7.47 ± 0.09	7.48 ± 0.07	7.46 ± 0.12	7.50 ± 0.16	7.54 ± 0.12	7.45 ± 0.09	7.30 ± 0.13	7.43 ± 0.03*	7.40 ± 0.04	7.44 ± 0.12
RS	7.45 ± 0.12	7.50 ± 0.04	7.52 ± 0.06	7.50 ± 0.07	7.49 ± 0.09	7.50 ± 0.10	7.39 ± 0.03	7.38 ± 0.04*	7.45 ± 0.04	7.40 ± 0.08
***P*CO_2 (mmHg)**										
PLAS	39.35 ± 7.60	35.25 ± 7.86	39.78 ± 13.20	38.18 ± 12.63	34.00 ± 4.84	41.68 ± 4.86	63.80 ± 16.87	50.15 ± 3.97	54.28 ± 6.09	46.43 ± 10.89
RS	40.29 ± 10.07	31.48 ± 5.05	34.88 ± 5.26	36.83 ± 6.03	39.25 ± 5.32	36.40 ± 2.58	52.18 ± 3.86	55.13 ± 4.83	49.85 ± 4.10	46.50 ± 8.33
***P*O_2 (mmHg)**										
PLAS	313.33 ± 199.52	342.25 ± 101.98	227.00 ± 51.79	292.00 ± 64.94	316.50 ± 123.01	234.00 ± 247.29	26.00 ± 3.27	24.5 ± 4.12	25.75 ± 8.06	52.25 ± 31.53
RS	432.63 ± 106.48	327.50 ± 93.28	290.00 ± 55.53	278.25 ± 95.14	283.00 ± 77. 05	253.75 ± 217.22	25.50 ± 1.29	29.25 ± 8.66	27.75 ± 4.11	38.50 ± 15.76
BE (mmol/L)										
PLAS	4.75 ± 2.75	2.25 ± 3.50	3.75 ± 5.32	6.50 ± 6.45	6.50 ± 7.59	5.00 ± 6.27	4.50 ± 4.04	8.75 ± 1.50	8.25 ± 1.71	6.25 ± 2.50
RS	3.75 ± 4.79	1.25 ± 2.88	5.50 ± 1.29	6.00 ± 2.31	6.50 ± 4.65	5.25 ± 7.27	6.75 ± 3.77	7.50 ± 1.29	10.25 ± 2.87	4.25 ± 2.87
HCO_3 (mmol/L)										
PLAS	28.48 ± 1.60	25.80 ± 3.74	27.33 ± 4.81	29.68 ± 5.06	29.23 ± 5.88	29.23 ± 5.01	31.05 ± 1.94	33.33 ± 1.49	33.15 ± 1.53	30.63 ± 1.30
RS	27.53 ± 3.40	24.32 ± 2.91	28.33 ± 1.24	28.95 ± 1.78	29.88 ± 3.18	28.53 ± 5.35	31.80 ± 3.28	32.68 ± 0.93	34.38 ± 2.42	28.83 ± 2.47

TCO_2 (mmol/L)										
PLAS	29.75 ± 1.71	26.75 ± 3.69	28.50 ± 4.73	30.50 ± 5.26	30.5 ± 5.74	30.25 ± 4.86	33.00 ± 1.83	34.75 ± 1.71	34.75 ± 1.71	32.00 ± 1.41
RS	28.63 ± 3.50	25.25 ± 2.99	29.25 ± 1.50	30.00 ± 1.63	31.00 ± 3.16	29.75 ± 5.56	33.25 ± 3.20	34.50 ± 1.00	36.00 ± 2.16*	30.25 ± 2.50
sO_2 (%)										
PLAS	100.00 ± 0.00	100.00 ± 0.00	99.75 ± 0.50	100.00 ± 0.00	100.00 ± 0.00	74.75 ± 30.39	40.00 ± 3.92	44.50 ± 9.98	44.00 ± 20.77	72.75 ± 27.93
RS	100.00 ± 0.00	100.00 ± 0.00	100.00 ± 0.00	99.75 ± 0.50	100.00 ± 0.00	94.00 ± 10.10	45.25 ± 4.99	51.25 ± 20.35	53.80 ± 9.85	66.00 ± 24.40
Troponin I (ng/mL)										
PLAS	0.00					0.60 ± 0.22	1.32 ± 0.31*	0.23 ± 0.04	0.04 ± 0.01	0.04 ± 0.02
RS	0.03 ± 0.03					0.53 ± 0.19	0.60 ± 0.15*	0.31 ± 0.07	0.08 ± 0.04	0.06 ± 0.03

The data is given as the mean ± SD. * $p < 0.05$ between the two groups.

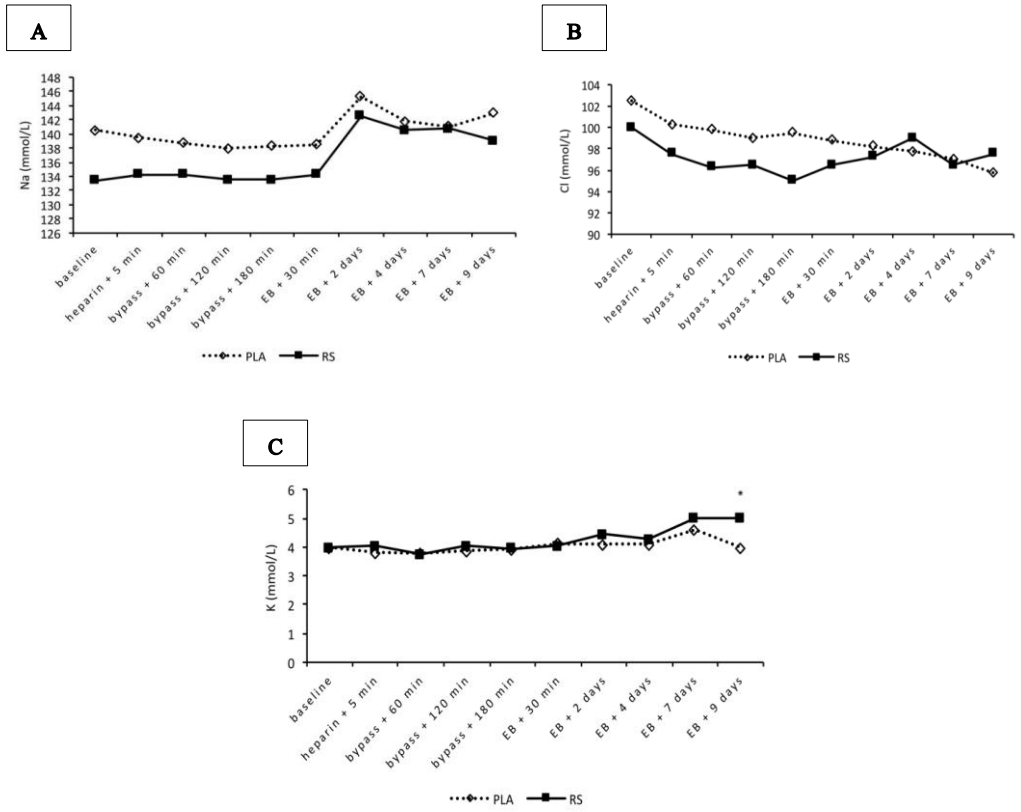

Figure 1 Sodium (A), chloride (B), and potassium (C) concentrations before, during, and after CPB. *$p < 0.05$ between the two groups.

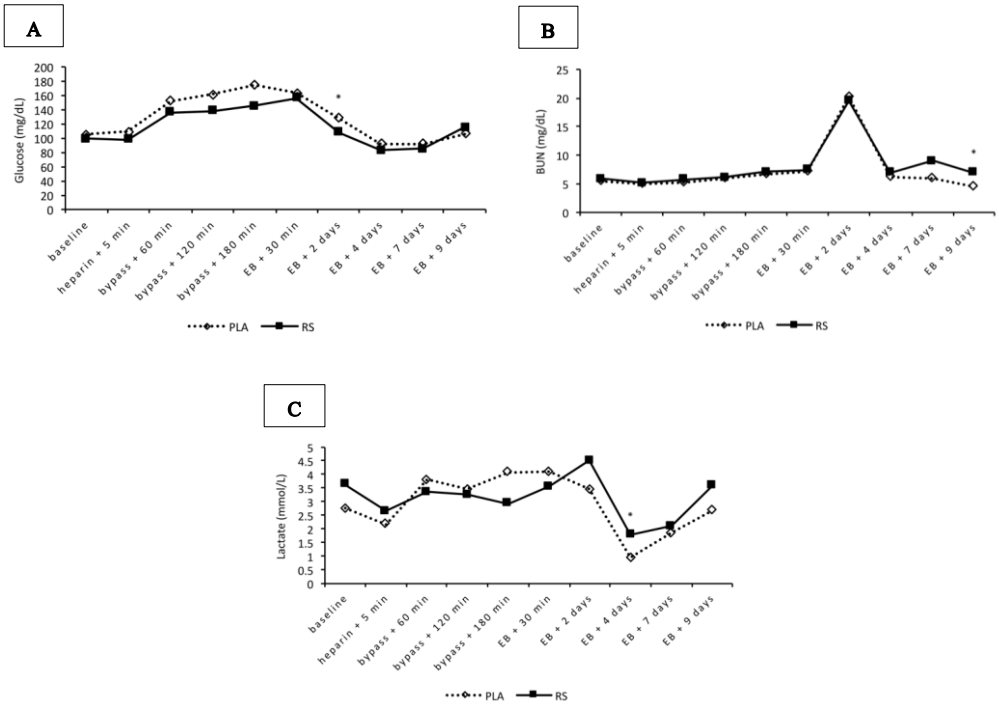

Figure 2 Blood glucose (A), BUN (B), and lactate (C) concentrations before, during, and after CPB. *$p < 0.05$ between the two groups.

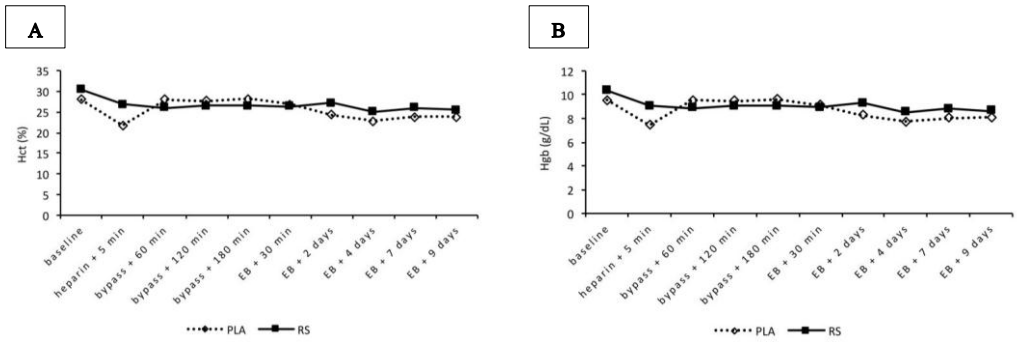

Figure 3 Hct (A) and Hgb (B) concentrations before, during, and after CPB.

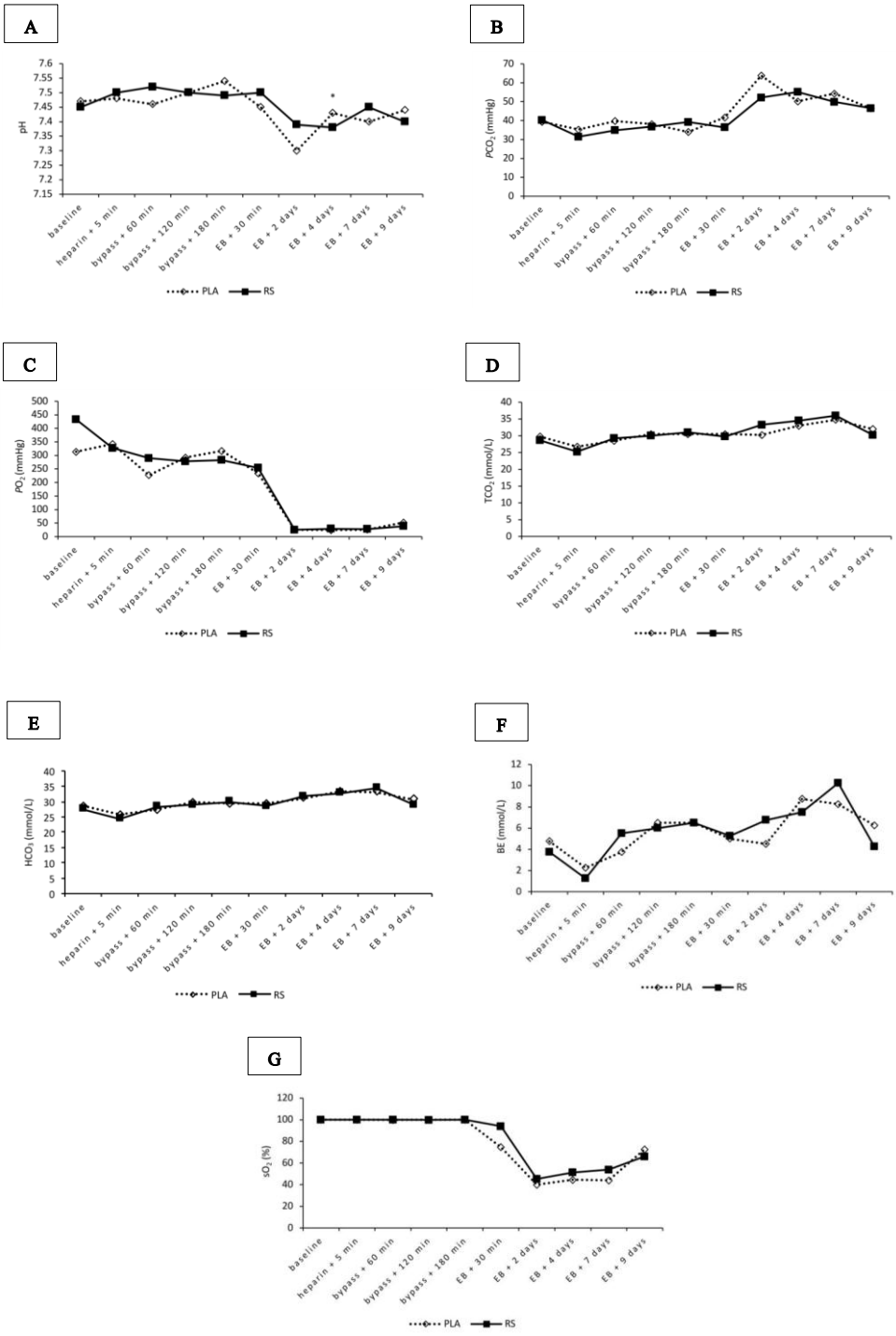

Figure 4 pH (A), PCO_2 (B), PO_2 (C), TCO_2 (D), HCO_3 (E), base excess (F), and sO_2 (G) levels before, during and after CPB. *$p < 0.05$ between the two groups.

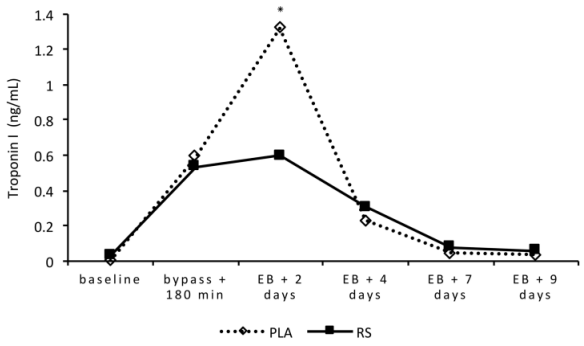

Figure 5 cTn I levels before, during and after CPB. *$p < 0.05$ between the two groups.

Discussion

Many different compositions of priming solutions for CPB have been developed using crystalloids, colloids or blood as primary constituents. However, the optimal priming solution for CPB remains debatable. Compared with blood and colloid solutions, crystalloid solutions are more advantageous because they are cheaper and have a lower risk of infection and anaphylactic reaction (Gu and Boonstra, 2005).

Currently, crystalloid solutions, including Lactated Ringer's solution, Ringer's solution, normal saline and PLAS, have been used. These solutions have similar sodium concentrations and may contain physiological potassium concentrations. PLAS has been widely used in the United States and is considered to be the standard priming solution worldwide. In this study, we designed a new priming solution, RS, and explored the differences between RS and PLAS in a swine model. Most components of these two solutions are almost the same. Both solutions comprise acetate and gluconate, which are metabolized to bicarbonate in the liver. The only difference is the use of trometamol in RS. The buffering capacity of trometamol is approximately three times that of bicarbonate; therefore, RS has a higher alkalizing capacity for alleviating acidosis, compared with PLAS (Nahas *et al.*, 1998).

Chemistries and electrolytes: Studies have suggested that CPB may result in electrolyte changes through intracellular shift and increased urination. However, the sodium, potassium and chloride levels in our study were within the normal range and did not exhibit significant changes (Polderman *et al.*, 2000). The sodium levels of both groups peaked at EB + 2 days, and this may have been due to dehydration caused by poor appetite because of surgical pain. Principally, a decline in sodium levels before the initiation of CPB and then an immediate increase in such levels after EB are common complications (Lee *et al.*, 2015; Bilal *et al.*, 2016). However, our data does not exhibit such significant changes during CPB, possibly because circulation was partially maintained by the heart rather than complete pumping through CPB. Furthermore, the RS group had lower sodium levels than the PLAS group. The gradual decrease in the chloride levels of both groups during CPB may be attributed to priming with large-volume solutions. In addition, the chloride levels of the RS group were relatively lower than those of the PLAS group, despite the higher chloride content of RS. The changes in chloride levels may have been caused by water balance alterations. Moreover, large volumes of priming solutions result in similar changes in sodium and chloride concentrations. However, the potassium levels remained stable and exhibited no significant differences between the groups.

Blood glucose levels increased from the initiation of CPB and peaked at EB. Slight hyperglycemia may be caused by the release of cytokines and catecholamines after inflammatory response during CPB (Anand *et al.*, 1990; Brix-Christensen, 2001; Yates *et al.*, 2006; Falcao *et al.*, 2008). In addition to inflammatory response, pain and anesthesia-induced stress response might engender increased blood glucose levels (Dawson *et al.*, 1997). However, the observed blood glucose levels remained constant during the 90-min period between the baseline and the initiation of CPB, suggesting that hyperglycemia may be caused by CPB. Furthermore, hyperglycemia during CPB was reported to be associated with poor prognosis, higher mortality and bloodstream infections (Gore *et al.*, 2001). The lower blood glucose levels in the RS group could have been related to trometamol, because trometamol has been known to increase insulin release and cause hypoglycemia. Therefore, the blood glucose curve for RS was slightly lower than that for PLAS, suggesting that RS may alleviate inflammatory response and have a lower risk of mortality and infection than PLAS.

Lactate levels are indicators of tissue perfusion and are influenced by hypothermia, CPB flow, hemodilution and neurohormonal activation (Munoz *et al.*, 2000; Shinde *et al.*, 2005). The RS and PLAS groups in this study exhibited moderate hyperlactatemia, which was caused by anesthesia and CPB until EB + 2 days. However, the lactate levels of both groups increased from EB + 4 days due to stress response to blood collection and wound pain. Basically, both groups exhibited similar trends regarding changes in lactate levels. BUN levels were examined to monitor renal function. The BUN levels of both groups were constant and peaked only at EB + 2 days because of poor kidney perfusion. Except at EB + 2 days, neither group exhibited obvious damage to renal function.

Hematology: The Hct and Hgb levels of both groups were slightly lower than those at the baseline due to hemodilution, blood loss during thoracic surgery and

the lack of blood transfusion after CPB. Furthermore, blood was collected from the surgical sites and pericardial cavity through suction and was infused back after CPB. Despite the decrease in Hct and Hgb levels caused by hemodilution, these levels remained stable in the RS group compared with the PLAS group.

Blood gases: Studies have revealed that CPB induces metabolic acidosis, which is associated with the acid-base balance in different priming solutions (Lilley, 2002; Himpe, 2003[a]) To prevent and alleviate acidosis, trometamol was used in RS. The present results reveal that pH values were higher than 7.35, $PaCO_2$ levels were within the normal range and HCO_3 levels were higher than 26 mmol/L during CPB, indicating uncompensated metabolic alkalosis. This phenomenon may be caused by the infusion of a large volume of HCO_3 that is metabolized from acetate and gluconate in both priming solutions. Notably, the pH values of the RS group were higher and more stable than those of the PLAS group. Despite metabolic alkalosis, the physiological parameters of neither group exhibited significant changes.

After surgery, the pH values were within the normal range and the $PaCO_2$ and HCO_3 levels were increased, signifying compensated respiratory acidosis. The major reason is abnormal CO_2 retention due to thoracic surgery. Theoretically, ventilators should be used to maintain gas exchange in the lungs. However, all pigs were weaned from ventilators and hypoventilation was observed due to low sO_2 after surgery. Notably, the pH values of the RS group were more stable than those of the PLAS group.

cTnI: cTnI is a biomarker released from cardiomyocytes; higher cTnI levels indicate myocardial injury. Therefore, higher cTnI levels in peripheral blood can result from CPB-induced hemodynamic changes (Thygesen *et al.*, 2010; Twerenbold *et al.*, 2012; Zymliński *et al.*, 2017). In clinical practice, cTnI levels increase at 3-12 hours after myocardial damage, peak at 24-48 hours, and finally return to normal levels at 5-14 days (Mohammed *et al.*, 2011). Our results indicate that RS causes less myocardial damage than PLAS. A possible explanation for this might be that RS has a higher alkalizing capacity for alleviating acidosis and contributes to improving organ micro-perfusion and reducing myocardial damage (Kimmoun *et al.*, 2015).

In conclusion, PLAS and RS priming solutions result in similar hemodynamic alterations. Both solutions alleviate metabolic acidosis during CPB. In addition, RS may cause less myocardium damage during CPB compared to PLAS. RS appears to be safe and feasible for use during CPB in pigs but further study of swine models is recommended for use in practice.

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