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Inflammatory Response to Colloids Compared to Crystalloid Priming in Cardiac Surgery Patients with Cardiopulmonary Bypass

Huey-Ling Liou[1], Chun-Che Shih[2], Yann-Fen C. Chao[3], Nien-Tsung Lin[4], Shau-Ting Lai[5], Shu-Hua Wang[6], and Hsing I Chen[7]

[1]*Department of Nursing, Taipei Veterans General Hospital, Taipei 11217*
[2]*Institue of Clinical Medicine, National Yang-Ming University, Taipei 11221*
Division of Cardiovascular Surgery, Taipei Veterans General Hospital, Taipei 11217
[3]*Department of Nursing, Mackay Medical College, New Taipei City 25245*
[4]*Department of Microbiology, Immunology and Molecular Medicine, Tzu Chi University, Hualien 97004*
[5]*Division of Cardiovascular Surgery, Taipei Veterans General Hospital, Taipei 11217*
[6]*Department of Anesthesiology, Taipei Veterans General Hospital, Taipei 11217*
and
[7]*Institue of Physiological and Anatomical Medicine, Tzu Chi University, Hualien 97004*
Taiwan, Republic of China

Abstract

Cardiac surgery with cardiopulmonary bypass (CPB) induces a systemic inflammatory response syndrome that may contribute to postoperative morbidity and mortality. We investigated the inflammatory responses to colloids compared to crystalloid priming in cardiac surgery patients with cardiopulmonary bypass. Thirty patients undergoing coronary artery bypass grafting (CABG) preparing for CPB were randomized into Ringer's solution (RS), 10% hydroxyethyl starch (HES) or 25% human albumin (HA) group. Serum concentrations of tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6) and interleukin-10 (IL-10) were measured before CPB, at the end of CPB and 1, 6 and 12 h after CPB. Serum C-reactive protein (CRP) was determined pre-operatively and then daily for 2 days. Body-weight gain was significantly decreased on the day after surgery in the HES group than in the RS group. Volume priming in CPB for CABG patients using HA or HES preparation had less tendency for intense inflammatory response with lower levels of TNF-α, IL-1β, IL-6 and higher levels of IL-10 compared to patients treated with RS. HES prime had lower levels of circulating CRP than in patients treated with HA or Ringer prime on the second post-operative day. Our data indicate that volume priming using colloid during CPB in CABG patients might exert beneficial effects on inflammatory responses.

Key Words: cardiac surgery, cardiopulmonary bypass, priming solutions, inflammatory response

Introduction

Cardiac surgery with cardiopulmonary bypass (CPB) induces a systemic inflammatory response syndrome (SIRS) that may contribute to the development of postoperative complications (13, 15). These deleterious effects of CPB may cause complement activation, release of oxygen-free radicals and other mediators such as cytokines (13). Different pro- and anti-inflammatory mediators, including tumor necrosis factor-α, TNF-α; interleukin-1β, IL-1β; interleukin-6, IL-6 and interleukin-10, IL-10, are involved

Corresponding author: Hsing I Chen, M.D., Ph.D., Professor, Institute of Physiological and Anatomical Medicine, Tzu Chi University, No. 701, Sec. 3, Jhongyang Rd., Hualien 97004, Taiwan, ROC. Tel: +886-3-8560824, Fax: +886-3-8573075, E-mail: chenhi@mail.tcu.edu.tw
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and their release is regulated by intracellular transcription factors (15). Cytokines are intercellular messengers produced by tissues in response to trauma by surgery or other stimuli (15). The role of cytokines in the pathophysiology of the CPB-related acute-phase reaction has been studied (11, 15). This complex sequence of events is responsible for many complications observed after CPB. Loss of vascular tone, capillary fluid leakage and leukocyte extravasation lead to organ dysfunction (13).

Colloid solution used in CPB purging has been shown to reduce neutrophil and complement activation (9, 24). Boldt *et al*. (6) founded lower plasma levels of pro-inflammatory cytokine IL-6 and anti-inflammatory cytokine IL-10 after CPB in the high-dose hydroxyethyl starch (HES) CPB priming compared with the albumin-based CPB priming. Tamayo *et al*. (25) showed that priming with gelatin *vs*. Ringer lactate produced no significant differences in the plasma levels of IL-6, IL-8, TNF-α, C-reactive protein (CRP) and complement in patients undergoing coronary artery bypass grafting (CABG) with CPB. Otherwise, the effect of priming fluids for CPB on the inflammatory response has not been extensively examined. The major aim of the present study was to investigate inflammatory response in colloids compared to crystalloid priming in cardiac surgery patients with CPB.

Materials and Methods

Patient Population

This prospective study was approved by the Institutional Ethical Board of the hospital. Patients who were included into the study were asked to give written informed consent. Subjects scheduled for elective coronary artery bypass grafting surgery without any known immune or hypothalamic-pituitary-adrenal axis dysfunctions were enrolled in the study. Patients with a history of myocardial infarction in the 6 weeks before surgery were excluded. Exclusion also included patients with emergency surgery, previous heart surgery, valve combined CABG and valve surgery and left ventricular ejection fraction less than 0.30. Other exclusion criteria were: congestive heart failure, exogenous hormone therapy, chronic renal failure (creatinine > 2.0 mg/dl), history of malignancy, signs of acute infection or inflammation, malnutrition and diabetes mellitus type I. Sample size calculations were based on a two-side α error at 0.05 and power of 80%. The study required personnel of multiple disciplines to conduct different experiments and to include analysis of data obtained from previous studies (6, 11, 13, 15). Accordingly, we calculated for treatment effect sizes of 20%. A sample size of 30 patients (10 per group) was required in this study. Thirty patients preparing for first-time CABG surgery were randomly assigned *via* the sealed-envelope method to receive one of three prime solutions for the CPB pump: (1) Group 1 (RS), Ringer's solution 950 ml, N = 10; (2) Group 2 (HES), 500 ml of 10% hydroxyethyl starch 200/0.5 diluted in 450 ml of Ringer's solution, N = 10; (3) Group 3 (HA), 150 ml of 25% human albumin diluted in 800 ml of Ringer's solution, N = 10 (Fig. 1).

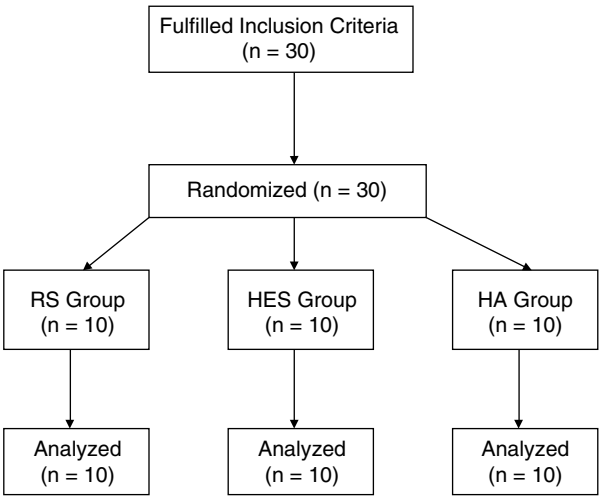

Fig. 1. Flow diagram of patient recruitment, randomization and analysis. RS, Ringer's solution; HES, 10% hydroxyethyl starch; HA, 25% human albumin.

Anesthesia

Patients received flunitrazepam, morphine and atropine intramuscularily for premedication. The anesthetic technique was standardized and consisted of 5 μg/kg fentanyl, 0.3 mg/kg diazepam and 0.1 mg/kg pancuronium to perform intubation. Fentanyl at 7-10 μg/kg was administered before sternotomy. Anesthesia was maintained using continuous infusions of sufentanil (0.1 mg/kg/h) and midazolam (0.03 mg/kg/h). Repetitive doses of pancuronium (0.03 mg/kg) were given on an hourly basis to maintain adequate neuromuscular blockade. During CPB, body temperature was kept at 34°C. Colloidal fluids (25% albumin, 10% HES) and norepinephrine were given to maintain mean arterial pressure above 60 mmHg during CPB. Leukocyte-depleted packed red blood cells (PRBCs) were given when hemoglobin was less than 7 g/dl.

Cardiopulmonary Bypass Technique

The CPB comprises a roller pump (Sarns Inc., Ann Arbor, MI, USA), membrane oxygenator (Hiltie

7000; Medos, Medizintechunk, AG, Stolberg, Germany), cardiotomy reservoir (Medos, Medizintechunk, AG, Stolberg, Germany) and a tubing set (Hym) including an arterial filter (Gish Biomedical, Santa Ana, CA, USA). Standard cannulation of the ascending aorta and the right atrium was performed. After starting the CPB at a flow rate of 2-4 L/min/m^2, the body was cooled to 32°C - 34°C in all patients. For cardioplegia, 1,000 to 1,500 ml of ice-cold cardioplegia (Hospira Inc, Chicago, IL, USA) was used. The priming fluid of the extracorporeal circulation circuit consisted of RS, HES or HA (950 ml) in three different groups. Mannitol (3 ml/kg), $NaHCO_3$ (5 ml/kg) and heparin (5,000 IU) were added.

Measurement of Cytokine and CRP

Blood was withdrawn from the radial catheter and collected in plastic tubes containing plastic pearls and allowed to clot at room temperature. Following centrifugation, serum samples were stored in polypropylene tubes at -70°C until use. Serum concentrations of TNF-α, IL-1β, IL-6 and IL-10 were measured using quantitative sandwich enzyme immunoassay techniques. Results were presented as picograms per milliliter (pg/ml). Commericial kits for TNF-α, IL-1β, IL-6 (Pierece Endogen, Rockford, IL, USA) and IL-10 (RayBio, Norcross, GA, USA) were used. All data represent the means from duplicate measurements. The interassay coefficient of variation for TNF-α, IL-1β, IL-6 and determinations were less than 10%. Normal values (measured in 6 healthy volunteers) was < 5.7 pg/ml for TNF-α, < 7.2 pg/ml for IL-1β, 0 pg/ml for IL-6 and IL-10. CRP was assayed with the image immunochemistry system and calibrator 5 plus by rate nephelometry (Beckman Coulter, USA). All laboratories testing performed by personnel were blinded to patient information and study objectives.

Postoperative Management

All patients, anesthetists, surgeons and cardiovascular intensive care unit (CVSI) staffs were all blinded to the solution type. The subjects were admitted to the CVSI and treated as per standard clinical practice. The physicians responsible for post-operative care of the patients were blinded with respect to the study group. Tracheal extubation was performed when hemodynamics were stable, temperature was 36°C (rectal temperature), and there was adequate spontaneous breathing (PaO_2 >80 mmHg with Fio2 0.3, breathing frequency < 15/min). After surgery, packed RBCs were given when hemoglobin was less than 9 g/dl, and fresh frozen plasma (FFP) was given when there was excessive bleeding (> 400 ml/h) in the presence of an activated partial thromboplastin time 60 s. Platelet concentrates were given when bleeding continued (400 ml/h) despite a normal clotting time. Epinephrine or dopamine was given when MAP was < 60 mmHg and cardiac index was < 2.5 l/min/m^2 despite administration of IV volume (crystalloid, 25% albumin, 10% HES) to reach pulmonary capillary wedge pressure (or central venous pressure) > 16 mmHg.

Endpoints

The primary endpoints were comparison of serum concentrations of TNF-α, IL-1β, IL-6 and IL-10 before CPB, at the end of CPB, 1, 6 and 12 h after CPB, and comparison of CRP between pre-operation and daily after operation for two days in the HES or HA priming group *vs*. the RS priming group. Secondary endpoints were analyses of the relationships between cytokines and CRP after CPB at specific time points.

Statistical Analysis

Data are presented as means ± standard error of mean (SEM). Statistical analysis was performed with SPSS software (SPSS Inc, Chicago, IL, USA). Mann-Whitney U test was used to test the difference between HES or HA priming group *vs*. RS priming group regarding demographic and clinical characteristics of patients, appropriate peri-operative data, post-operative body weight gain and fluid balance. A non-parametric analysis for pre-CPB and post-CPB, CRP of pre-operative and 1 and 2 post-operative days was conducted by Mann-Whitney U test to compare the difference between means in the HES or HA priming group *vs*. the RS priming group. Pearson correlation analyses were performed to determine the associations between cytokine levels and CRP of 1 and 2 post-operative days. Statistical significance was defined as a value of $P < 0.05$.

Results

Demographics, Clinical Characteristics and Operative Data

Patients did not differ with regard to demographics, clinical characteristics and operative data (Table 1). No complications occurred and all patients survived in CVSI.

Difference in Fluid Balance and Body Weight Gain

The need for 25% albumin was significantly higher at the day after surgery in the patients treated with RS or HES priming than those treated with HA priming (Table 2). Use of packed red cells and plate-

Table 1. Demographics, clinical characteristics and operative data

	RS Group (N = 10)	HES Group (N = 10)	HA Group (N = 10)
Age (yr)	62.4 ± 2.9	69.8 ± 2.7	64.1 ± 4.3
Male Sex, n (%)	8 (80.0)	7 (70.0)	9 (90.0)
Diabetes mellitus, n (%)	1 (10)	2 (20)	3 (30)
Hypertension, n (%)	5 (50)	3 (30)	5 (50)
LVEF (%)	53.0 ± 2.3	54.7 ± 4.5	49.7 ± 4.6
FEV1/ FVC (%)	77.4 ± 1.8	69.2 ± 2.5	74.1 ± 0.9
APACHE II			
Admission ICU	24.0 ± 1.0	23.8 ± 1.2	22.4 ± 1.5
1 day ICU	17.2 ± 1.2	17.3 ± 1.4	14.9 ± 0.9
2 day ICU	11.0 ± 1.2	10.7 ± 1.1	11.4 ± 0.9
Ischemic time (minute)	82.2 ± 8.7	93.4 ± 7.1	95.5 ± 9.4
Bypass time (minute)	141.2 ± 17.3	143.8 ± 11.3	158.1 ± 15.9
Time to tracheal extubation (hours)	22.8 ± 2.5	38.3 ± 9.4	40.1 ± 19.1
Length of ICU stay (days)	2.8 ± 0.5	6.2 ± 2.9	3.4 ± 0.7
Length of postoperative hospital stay	10.5 ± 1.8	9.3 ± 1.1	11.2 ± 3.4
ICU mortality (n)	0	0	0

Values are expressed as numbers (%), or means ± SEM. APACHE II, Acute Physiology and Chronic Health Evaluation II; LVEF, left ejection fraction; FEV1/FVC, force expiratory volume/forced vital capacity. Comparison of the difference between groups. Differences between groups are not significant ($P > 0.05$).

lets was not significantly different among the three groups. However, the use of fresh frozen plasma was significantly higher during surgery in the patients treated with RS priming than those treated with HA priming (Table 2). Catecholamine usages were not significantly different among the three groups (Table 2). Total fluid intake balance was not significantly different among the three groups during surgery and in the post-operative day. Body weight gain was significantly lower the day after surgery in patients treated with HES priming than those treated with RS priming (Fig. 2). The body weight gain was not different between the RS and HA priming groups.

Changes of Levels of Plasma Cytokines (TNF-α, IL-1β, IL-6, IL-10)

Plasma cytokine levels were significantly different over times within groups ($P < 0.05$). Patients in the RS priming group had higher TNF-α, IL-1β and IL-6 levels at the beginning of reperfusion to 1 and 6 h after reperfusion than in patients in the HA and HES priming groups (Figs. 3, A, B and C). There was no significant difference among the groups. IL-10 significantly increased in all patients. The IL-10 level was significantly higher at the beginning of reperfusion (after CPB) to 1 h after CPB in the HA and HES priming groups compared to those in the RS priming group (Fig. 3D).

Changes of CRP

CRP increased to high levels after CPB in all groups (Table 3). The CRP levels were significantly lower at the second day after surgery in patients treated with HES priming than those treated with RS or HA priming (11.7 mg/dl *vs*. 18.3 mg/dl, 11.7 mg/dl *vs*. 16.6 mg/dl). The level of TNF-α after CPB was positively correlated with CRP in the first day after surgery (Fig. 4A). The level of IL-10 1 h after CPB was significantly negatively correlated with CRP on the second day after surgery (Fig. 4B).

Discussion

Hypo-oncotic primes may be associated with interstitial fluid expansion with subsequent widespread organ tissue edema. The sole use of crystalloid prime was associated with an increased post-operative weight gain (20). Several studies have demonstrated the beneficial effects of albumin CPB prime on the reduction in weight gain by attenuating the decrease of colloid osmotic pressure and serum albumin level in young children or adults after CPB (1, 19). Although these observations may be caused by oncotic properties of albumin, others effects may be caused by antioxidant and free radical-scavenging properties of albumin (10). Another study has demonstrated that CPB–prime using 10% HES improved cardiac index and reduced gain in body weight in the early post-pump period (11). It has been shown that HES may exert protective effects on endothelial function, for example, by beneficially altering endothelial cell integrity re-

Table 2. Fluid treatment during perioperative, first postoperative and second postoperative day

	RS Group (N = 10)	HES Group (N = 10)	HA Group (N = 10)
Priming solution	RS 950 ml	RS 450 ml + HES 500 ml	RS 800 ml + HA 150 ml
Intravenous 10% HES (ml)			
POD0	400.0 ± 66.7	300.0 ± 110.6	150.0 ± 76.4
POD	375.0 ± 119.5	400.0 ± 66.7	260.0 ± 114.7
POD1	175.0 ± 80.7	100.0 ± 66.7	100.0 ± 66.7
25% Albumin (ml)			
POD0	5.0 ± 5.0	0	0
POD	75.0 ± 15.4	70.0 ± 11.1	5.0 ± 5.0*†
POD1	0	30.0 ± 21.3	0
Medical treatment			
Packed red cell (ml)			
POD0	585.0 ± 330.5	739.0 ± 591.3	210.0 ± 123.1
POD	216.0 ± 81.5	338.0 ± 119.7	226.0 ± 82.0
POD1	34.0 ± 34.0	0	170.0 ± 57.2
Fresh frozen plasma (ml)			
POD0	243.0 ± 118.1	75.0 ± 53.4	0**
POD[a]	215.0 ± 113.1	63.0 ± 42.5	270.0 ± 121.5
Platelet (ml)			
POD0	100.0 ± 66.7	0	0
POD	0	32.0 ± 32.0	0
Total fluid (ml)			
POD0	3857 ± 400.9	3788 ± 314.3	3785 ± 331.1
POD	4137 ± 426.6	3950 ± 377.8	3649 ± 254.9
POD1	2309 ± 259.5	3015 ± 397.3	2580 ± 268.8
Catecholamines (μg/kg/minute)[a]	0	1.4 ± 1.4	0.05 ± 0.05

Values are means ± SEM. POD0, during surgery; POD, the day after surgery; POD1, the first day after surgery; [a]Data collected during first three postoperative days; Catecholamines, epinephrine + norepinephrine. Comparison of the difference between RS group *vs*. HES or HA group is shown by $*P < 0.05$, $**P < 0.001$; comparison of the difference between HES *vs*. HA group is shown by $^{\dagger}P < 0.001$.

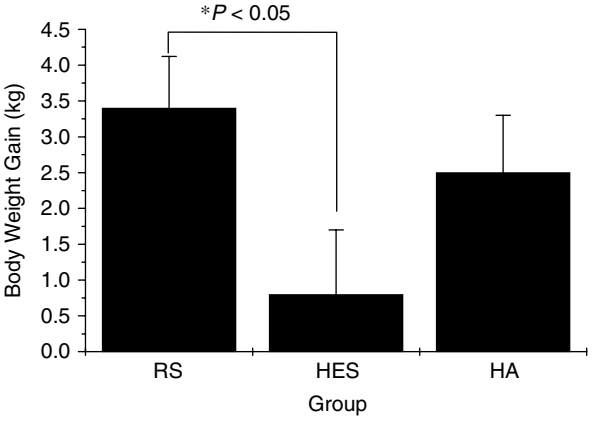

Fig. 2. Comparison of in body weight gain between groups on the day after surgery (N = 10 in each of the three groups). Values are means ± SEM; RS, Ringer's solution; HES, 10% hydroxyethyl starch; HA, 25% human albumin. $*P < 0.05$ indicates significant difference between the RS and the HES priming groups. There was no difference between RS *vs*. the HA priming group and HES *vs*. the HA priming group.

sulting from O_2 free radical scavenging or by stabilization of fragile cell membranes (2). From a clinical point of view, CPB has been shown to be associated with several adverse effects with post-pump syndromes. Colloid infusions are routinely administered to patients with systemic circulatory disorders on the preceding days when there is sufficient cardiac output and restored organ perfusion. In our study, the need for 25% albumin was significantly higher on the day after surgery in the patients treated with RS or HES priming than those treated with HA priming. However, our present study revealed that body weight gain was significantly decreased on the day after surgery in patients treated with HES priming than those treated with RS priming. It is possible that the HES group received more albumin after surgery. Accordingly, HES and albumin exerted additive effects on oncotic pressures in this group. Body weight gain was not significantly different between the HES and HA priming groups.

Our study showed that levels of TNF-α and IL-

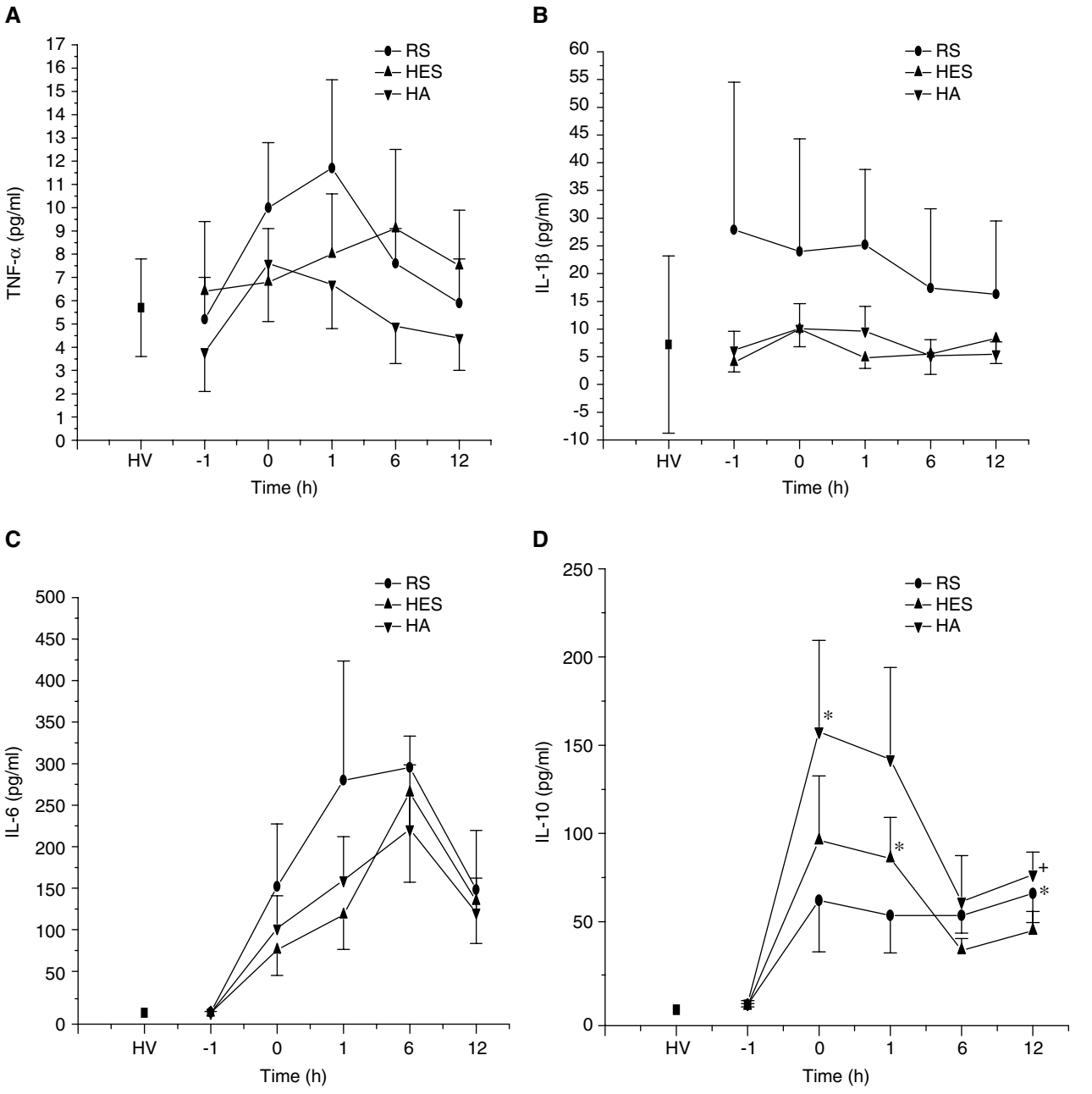

Fig. 3. Comparison of plasma levels of tumor necrosis factor-α (TNF-α, A), interleukin-1β (IL-1β, B), interleukin 6 (IL-6, C) and interleukin 10 (IL-10, D) of the pre-operative level (-1) and at various time points (0, 1, 6 and 12 h) after CPB among groups (N = 10 in each of the three groups). Data are means ± SEM; RS, Ringer's Solution; HES, 10% hydroxyethyl starch; HA, 25% albumin; HV, healthy volunteer; Significantly difference between RS priming group *vs*. HA and HES priming group is shown by $^{*}P < 0.05$). Significant difference between HA priming group *vs*. HES priming group is shown by $^{+}P < 0.05$. There was no significant difference among the groups in TNF-α, IL-1β and IL-6. There was a significantly higher level of IL-10 after CPB to 1 h after CPB in HA and HES priming groups compared to that in the RS priming group.

6 were increased after CPB. Previous studies demonstrated similar findings (7, 26). During CPB and cardioplegic arrest, the heart is essentially undergoing an ischemia/reperfusion injury. After removal of the aortic cross-clamp, there is pulmonary sequestration of neutrophils (26). Complement certainly has been implicated in the ischemia/perfusion injuries after CPB. However, the other inflammatory cytokines, including TNF-α and IL-6, may also play a role. IL-6 levels may correlate with the severity of tissue damage induced by surgery and the inflammatory response to CPB (30). Elevated IL-6 production has also been associated with poor outcomes (18). It has been demonstrated by Biffl *et al*. that IL-6 inhibited

Table 3. C-Reactive Protein (CRP)

		POD0	POD1	POD2
	Group			
CRP (mg/dl)	RS	0.6 ± 0.2	5.9 ± 0.5***	18.3 ± 1.3***†
	HES	1.1 ± 0.5	5.2 ± 0.3***	11.7 ± 1.7**
	HA	0.5 ± 0.2	6.9 ± 1.6**	16.6 ± 1.8***‡

Values are means ± SEM (N = 10 in each of the three groups). POD0, before operation; POD1, the first day after surgery; POD2, the second day after surgery. Comparison of the difference within groups *vs*. value at before operation is shown by $^{**}P < 0.01$, $^{***}P < 0.001$); comparison of the difference between RS *vs*. HES group is shown by $^{\dagger}P < 0.001$ and HA *vs*. HES group by $^{\ddagger}P < 0.05$.

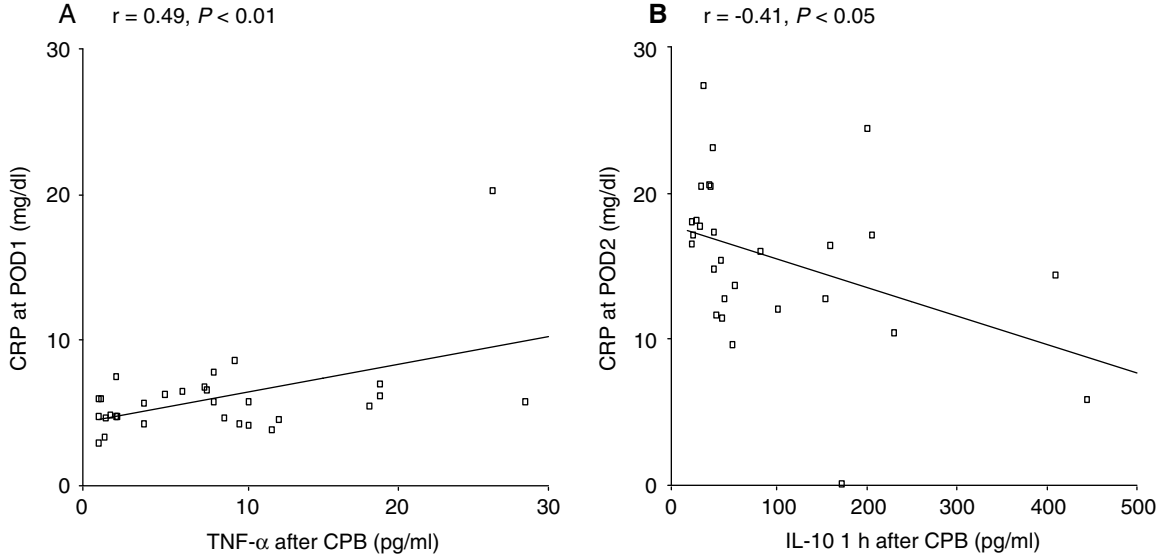

Fig. 4. Correlation of plasma levels of cytokines with CRP (C-reactive protein) at post-operative days in the overall study population. POD1, the first day after surgery; POD2, the second day after surgery. TNF-α (tumor necrosis factor-α) was positively correlated with CRP (r = 0.49, $P < 0.01$). IL-10 (interleukin 10) was negatively correlated with CRP (r = 0.41, $P < 0.05$).

neutrophil apoptosis *in vitro*. They have also proposed that circulating IL-6 in critically ill patients may limit neutrophil apoptosis and prolong its toxic effects (4) whereas, transfusion of blood may contribute to immunomodulation (21). In the present study, the RS priming group received significantly more FFP transfusion. The results may be attributed to an increased inflammatory response in the RS priming group. Anti-inflammatory cytokines such as IL-10 may significantly abrogate these complications. In our study, IL-10 was peaked from the beginning of reperfusion and remained at a high level during the 12-h period after CPB. It has been demonstrated that IL-10 mediates inhibition of generation of oxygen free radicals in macrophages in response to lipopolysaccharide through IκB-α degradation (8). The effects of these priming fluids on the immunologic response have not been extensively examined. In the present study, TNF-α, IL-1β and IL-6 increased slightly in the RS priming group compared with the HA and HES priming groups. However, the extent of increase was not statistically significant. IL-10 increased at reperfusion to 1 h after CPB in the HA and HES priming groups as compared with the RS priming group. Nevertheless, the level of IL-10 significantly increased at reperfusion to 1 h after CPB in HA and HES priming groups. These findings are consistent with other investigations suggesting potential beneficial effects on inflammation from HES and albumin (6, 27, 28). The mechanisms by which albumin and HES enhanced IL-10 production are unclear and deserve further investigation.

CRP is a risk marker and plays a role in the pathogenesis of inflammation and atherosclerosis. It is synthesized and secreted mainly by hepatocytes in response to IL-6 and either IL-1 or TNF-α (3, 14). CRP activates complement, increases phagocytic activity of neutrophils, increases respiratory burst of neutrophils and induces expression of adhesion molecules, synthesis of tissue factor, cytokines from

monocytes and platelet aggregation (17). In our study, the level of TNF-α after CPB was positively correlated with CRP on the first day after surgery. The level of IL-10 at 1 h after CPB was inversely correlated with CRP on the second day after surgery. How cytokines affect CRP has not been fully explored. Several studies have reported that CRP induces pro-inflammatory cytokines in the major cells involved in atherosclerosis (23, 29). A study has provided evidence that CRP, by decreasing IL-10, alters the anti-inflammatory/pro-inflammatory balance and attenuates inflammation, which is pivotal in atherothrombosis (22). Importantly, elevated serum levels of IL-10 are associated with a significantly improved outcome of patients with acute coronary syndrome (ACS) or CABG, supporting the concept that the balance between pro- and anti-inflammatory cytokines is a major determinant of outcome in these patients (12, 16). Boldt *et al*. (5) reported the influence of different volume replacement strategies on inflammation and endothelial activation in the elderly undergoing major abdominal surgery. Plasma CRP, IL-6 and IL-8 levels increased significantly in both crystalloid groups (lactic Ringer, normal Saline) than in the HES 130/0.4 treated group. We showed in the present study that CRP was significantly lower on the second day after surgery in patients treated with HES priming than those treated with RS or HA priming.

The optimal priming fluid in cardiac surgery is still a topic of debate. In a meta-analysis that included 21 controlled trials with 1,346 patients for cardiac surgery with CPB, the albumin and crystalloid groups were similar in time to tracheal extubation, intensive care unit and hospital stay (19). In the present study, there was also no difference in time to tracheal extubation, intensive care unit and hospital stay among the three groups.

Our data indicate that the HA and HES groups have lower levels of pro-inflammatory cytokines, although the levels were not statistically significant. Patients in the RS priming group had a higher levels of TNF-α, IL-1β and IL-6 at the beginning of reperfusion to 1 and 6 h after reperfusion than in patients in the HA and HES priming groups (Figs. 3A-3C). There was no significant difference among the groups. The IL-10 level was significantly higher at the beginning of reperfusion (after CPB) to 1 h after CPB in HA and HES priming groups compared to that in RS priming group (Fig. 3D). Limitations of the study are that the pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) increased slightly in the RS priming group compared with the HA and HES priming groups. It is possible that the small sample size is not enough to assess the difference in pro-inflammatory cytokines between the colloids and crystalloid groups. Further investigations with larger sample sizes are required. The present study revealed that CRP level on the second day after surgery in the HES group was significantly lower than HA or RS group. CRP level also correlated well with the TNF-α and IL-10 levels. In conclusion, colloid priming during CPB might exert beneficial effects on inflammatory responses.

Acknowledgments

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