A COMPARISON OF 6% HYDROXYETHYL STARCH AND 5% ALBUMIN AS PRIME SOLUTIONS IN CARDIOPULMONARY BYPASS

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Colloids are useful in cardiac surgery to increase preload and improve cardiac output without having the risks associated with blood transfusions. Hydroxyethyl starch or hetastarch (HES), a synthetic colloid for intravascular volume expansion, was compared with our standard priming solution containing lactated Ringer's solution in 30 patients (15 in each group) undergoing coronary artery bypass operations. Demographic characteristics of all the patients were similar without any statistical significance. Group A received 6% HES containing prime fluid and group B received lactated Ringer's solution containing prime solution. Clinical and laboratory observation and comparisons were carried out for the following factors: preoperative and postoperative hematocrit, BUN, creatinine, sodium, potassium, PTT, aPTT, fibrinogen, ALP, SGOT, SGPT, total protein, albumin, postoperative urine output, factor VIII and postoperative blood loss. There were no complications attributed to colloid administration. The only significant differences noted were in post-bypass fibrinogen, albumin, SGOT and cost to the patients for each prime. In the view of its safety, easy use and low cost, hydroxyethyl starch is thought to be a suitable colloid for being used in priming fluids for cardiopulmonary bypass (CPB).

Key words: ***Open heart surgery, hemodilution, prime solution, hydroxyethyl starch***

Albumin and hydroxyethyl starch are volume expanders used in cardiac surgery to optimize preload and cardiac output. It was found that the use of colloidal agents in extracorporeal circuits were effective in reducing hepatic, renal and hematological alterations usually associated with CPB (1). Hydroxyethyl starch is a synthetic plasma volume expander derived

from amylopectin, having an average molecular weight of about 460.000 daltons. 6% hetastarch solution has colloid properties that approximate those of human albumin. HES has a fast and short duration of action and elimination half-life (1,2). The studies have shown that HES produced significant volume expansion without adverse effects (3). Hydroxyethyl starch has been shown to be a safe and effective plasma expander in hypovolemic postoperative patients (4), and has been used successfully for preoperative isovolumic hemodilution (5).

This prospective study was carried out to compare the efficacy and safety of 6% HES with standard lactated Ringer's solution as prime solutions for patients undergoing open heart surgery.

MATERIAL AND METHODS

A prospective, randomized study involving 30 adult patients undergoing elective uncomplicated CABG surgery between September 1991 and July 1992, were divided into two study groups (15 in each group).

There were 23 male and 7 female patients with an age range of 34 to 67 years (mean age 54.63±9.51), Group A consisted of 15 patients who received 6% HES (Plasmasteril, Fresinius Laboratorius, Paris) containing prime solution and group B consisted of 15 patients who received our standard prime solution containing lactated Ringer's solution. The patient characteristics were similar with no statistical significance (Table 1). All patients were NYHA functional status 1 or 2 without the evidence of left ventricle dysfunction as clinically manifested by the symptoms of congestive heart failure. Patients were to be excluded for the following reasons: prior cardiac surgery, insulin-dependent diabetes, preoperative hematocrit less than 39%, myocardial infarction during the study period, significant coagulopathy at the baseline period. Radial artery and pulmonary artery catheters were placed in all patients before the surgery. Anesthesia consisted of diazepam (10 mg/kg) supplemented with 2.5% sodium thiopental and muscle relaxation was by succinylcholine. Before CPB, patients received only lactated Ringer's solution infusion. Activated clotting time (ACT) was measured in all patients before heparinization and maintained at greater than 400 seconds during CPB. All operations were performed by the same team of surgeons. Hypothermic, hemodilutional CPB was instituted using a membrane oxygenator (Shiley S-100), heat exchanger and roller pumps with arterial blood filters on either the suction or arterial lines of the circuit. Cold blood cardioplegia and topical hypothermia was used during a single period of aortic cross-clamping. Flow was maintained at 2.0 to 2.2 l/min/m2 at moderate hypothermia (28°C to 33°C) and aortic mean pressure was maintained between 50 and 70 mm Hg. The perioperative variables of the patients were shown in Table 2.

After the termination of CPB, the content of the pump-oxygenator was returned to the patient. Lactated Ringer's solution was

Table 1. Baseline and preoperative patient variables in Groups A and B.

Variable	Group A (n=15)	GroupB (n=15)
Sex		
Male	%79	%81
Female	%21	%19
Age (y)	54.13±9.41	55.11±9.47
Weight(kg)	84.8±13.9	81.6±11.0
BSA(m^2)	1.85±0.16	1.82±0.2

Data are presented as percentage or mean ± standard deviation.
BSA: body surface area.

Table 2. Perioperative variables in Groups A and B.

	Group A	GroupB
Cross-clamp time (min)	59±28	51±25
CPB time (min)	55±10	65±8
IMA/Patient	1	1
Total bypass grafts	3.0±1.1	3.1±1.2

Data are presented as mean ± standard deviation.
CPB: Cardiopulmonary bypass
IMA: Internal mammarian artery

administered if there was insufficient volume to terminate the bypass. Dopamine or 10% $CaCl_2$ was used if necessary, for patient safety. Heparin was reversed with sufficient protamine to have ACT recover to within 10% of pre-heparinization levels.

Ten milliliters of blood was collected from a central venous catheter for clinical and laboratory observations and comparisons of the following factors: preoperative and postoperative levels of hematocrit, BUN, plasma creatinine, plasma sodium, plasma potassium, prothrombin time (PTT), activated prothrombin time (aPTT), fibrinogen, alkaline phosphatase (ALP), serum glutamic-oxalacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), total protein, postoperative urine volume (24 hour) blood loss (4 and 24 hours) and factor VIII.

For statistical evaluations Student's t test was used. All data were presented as mean±standard deviation. The probabilities less than 0.05 were used to indicate significance.

RESULTS

Thirty-three patients enrolled in the study, 16 patients received 6% HES and 17 patients received lactated Ringer's solution. One patient in the HES group was excluded from the study since he had a baseline PTT greater than 1 1/2 times the upper limit of normal. Two patients in the 5% albumin group were excluded from the study for, one had a re-operation because of excessive postoperative bleeding and the second had a baseline platelet count of 52.000. Among the 30 patients taken into the study (15 in each group), there was no hospital deaths and no adverse reactions were observed. One patient in 5% albumin group, required intra-aortic balloon pump, which was unrelated to the study.

Analysis of preoperative variables are shown in Table 3. We found no statistical difference in post-bypass hematocrit, creatinine, sodium, potassium, urine volume, PTT, aPTT, blood loss, ALP, BUN, SGPT, total protein and factor VIII ($p>0.05$) (Table 3). A significant

Table 3. Preoperative and postoperative variables in Groups A and B.

	Group A	Group B
Hematocrit		
Prebypass	41.51±1.86	42.06±2.02
Postbypass	36.17±3.08	38.87±1.96
Bun		
Prebypass	12.47±3.58	13.93±5.4
Postbypass	4.40±4.05	17.33±3.96
Creatinine		
Prebypass	1.06±0.30	1.07±0.30
Postbypass	1.01±0.27	1.03±0.24
Sodium		
Prebypass	141.07±2.05	141.53±1.96
Postbypass	137.07±3.13	134±3.20
Potassium		
Prebypass	4.35±0.44	4.47±0.42
Postbypass	4.28±0.36	4.15±0.44
PTT		
Prebypass	13.00±0.93	13.19±0.91
Postbypass	16.60±1.18	16.4±1.24
aPTT		
Prebypass	36.13±4.37	37.3±3.62
Postbypass	43.33±4.35	43.67±4.24
Fibrinogen		
Prebypass	186.47±18.72	204.00±38.54
Postbypass	361.20±47.45	308.80±39.76 *
ALP		
Prebypass	54.47±9.09	53.25±12.54
Postbypass	55.60±7.78	57.53±12.55
SGPT		
Prebypass	16.93±5.09	18.40±3.85
Postbypass	17.60±10.43	19.73±10.43
SGOT		
Prebypass	29.07±8.62	33.80±10.11
Postbypass	36.00±6.90	42.87±11.44 *
Total protein		
Prebypass	5.55±0.37	5.45±0.36
Postbypass	5.93±0.30	5.48±0.33
Chest tube drainage (ml)		
At 4th hour	174.67±61.63	190.67±93.7
At 24th hour	548.00±126.33	574.00±206.87
Urine output(ml)		
Immed. after bypass	725.33±484.97	761.33±378.34
Postop.24 hour	2943.33±1339.60	2857.33±1126.34
Factor VII		
Prebypass	137.3±42.1	134.1±54.3
Postbypass	121.3±34.6	127.8±31.8
Albumin		
Prebypass	3.45±0.25	3.47±0.25
Postbypass	3.30±0.23	3.45±0.18

* $p<0.05$ vs control

difference was observed in the cost to the patient for each prime. In our department, hetastarch containing prime costs 30$ per patient, whereas our standard, albumin containing prime costs 42$ Per patient.

DISCUSSION

Hemodilution has been used for clinical CPB for more than two decades and it has reduced the incidence of transfusion reactions, transmission of viral hepatitis and other related clinical problems with the use of extracorporeal circuit (6). In addition, hemodilution increases urine output, decreases the incidence of postoperative oliguria and acute renal failure, increases the clearances of Na, K, creatinine and water (6).

Colloids are important adjuncts to cardiac surgery (7). They increase intravascular volume and maintain colloid oncotic pressure without the risk of infection inherent in blood products (8). Albumin and hetastarch have been used successfully for this purpose in open heart surgery. Both crystalloid and colloid containing priming solutions have been used for hemodilution during clinical CPB.

With crystalloid primes during and immediately after CPB, there is an increase in water and sodium uptake and they prevent extravasation of the fluids throughout the CPB (9,10).

Although the patient's blood volume is decreased after the operation, the volume of the extracellular fluid is increased partly because colloids prevent extravasation. It was also observed in the literature and in our study that need for transfusion to maintain central venous pressure was lower in patients with HES (9). Mishler and associates (1) found that the use of colloidal agents in extracorporeal circuits was effective in reducing hepatic, renal and hematological alterations usually associated with CPB. We compared 15 patients who received HES with 15 patients who received lactated Ringer's solution during CPB. None of the patients who have received either HES or Ringer's solution showed left ventricular failure or any other organ disease. All patients received similar volume of the fluids. Therefore, we believe that the groups are comparable. It is widely accepted that CPB cause an increase in the levels of creatinine, BUN, SGOT, SGPT and decrease in the levels of sodium and potassium. In our study, there was no clear difference between the two groups in the preoperative levels of BUN, SGOT and fibrinogen. Usually liver enzymes, especially SGPT increases after CPB, although increased in our study, there was no difference between the groups. But SGOT levels were lower in the HES group, the same results were observed in the other studies as well (11,12). When compared with lactated Ringer's solution containing priming solution, no significant difference was found according to hematocrit levels when 6% HES was used. Similar results were observed in Robert's and William's studies (12,13). The effect of volume expanders on coagulation remains as the most important consideration, particularly in open heart surgery patients whose coagulation is already disturbed by heparinization and CPB.

All colloids cause a dilutional decrease in clotting factor concentrations if administered in sufficient volumes. Dextran has been shown to lower factor VIII activity (4,5). It has also been shown to interfere with stable clot formation and enhance fibrinolysis (14,15).

When HES was taken into regard, there is still controversy on its effects on coagulation components. Although Strauss et al. (16,17) showed specific decrease in F VIII, Mostrioanrini et al. (9) observed no changes in F VIII and platelet count. In our study, we observed no difference in FVIII and platelet count between the groups. We suggest that HES has no direct effect on factor VIII activity in particular or coagulation in general at the amounts used in our study. There was no clinically significant bleeding in either of the groups and there was no statistically significant difference between the groups.

Robert et al. (13) found no significant difference in postoperative blood loss, PTZ, aPTT and fibrinogen levels when HES was used as the prime solution. Similar results were observed by the others as well (11,18,19). We found that fibrinogen levels were 15% lower in the HES group in

comparison to the group that has received albumin. This difference was statistically significant ($p<0.05$) but showed no effect on post operative bleeding.

In conclusion, HES was shown to be a suitable colloid for volume expansion in cardiac surgery. Therefore, it is possible to say that HES is as effective as and much more economical than albumin, without having any adverse or allergic reactions; and it does not have the risks that accompany albumin administration.

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