Comparison of Two Colloid Constituents in Prime Solutions and the Effect on Blood Loss Following Cardiopulmonary Bypass

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ABSTRACT

A retrospective study was conducted on a population of 24 patients who had undergone coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB). This population is divisible into two groups that differ in prime constituents. Group A used 500cc of 6% Hydroxyethyl starch (Hespan) as the colloid, and Group B used 150cc of 25% albumin. No statistically significant differences were found in the preoperative demographics. All of these cases were done using the same perfusion technique and equipment. Intraoperative values displayed levels of significant difference (p <.05) between the two groups with respect to 1) bypass platelet count; and 2) greater usage of protamine in Group A.

Group A Hespan = Platelet count x 1000/ml was 99.90+/- 32.4, Blood loss (cc's) was 1033.3+/-305.5, Protamine:Heparin ratio was 1.41:1.0 +/- .37
Group B Albumin = Platelet count x 1000/ml was 153.84 +/- 34.17; Blood loss was 929.6+/- 105.4; Protamine:Heparin ratio was 1.01:1.0 +/- .43

In the postoperative phase which ended when the chest tube was removed, levels of significant difference were as follows:

Group A Hespan = Platelet Ct.#2 x 1000/ml was 124.87 +/- 30.62, Blood loss (cc's) was 1390.25 +/- 405.78, PPF Admin. ratio was 1417 +/- 506.32.
Group B Albumin = Platelet count x 1000 ml was 159.71 +/- 41.22; Blood loss = 1087.0 +/- 385.72, PPF Admin. ratio was 875 +/- 291.94.

From this study it seems as though there are two factors contributing to the increased blood loss seen in Group A that may result from Hespan usage - the intraoperative and postoperative decreased platelet count and the increased amount of protamine used. Furthermore, Group A patients required substantially more PPF postoperatively.

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INTRODUCTION

A retrospective study was undertaken on 24 patients operated on by two different surgical groups. The purpose of the study was to determine whether the difference in prime constituents could be a contributing factor in postoperative blood loss. The groups differed only in Hespan/Albumin as the colloid additive in the prime solution.

Two demographically equivalent groups were selected retrospectively for the study, and involved only patients that had been subjected to coronary artery bypass grafting (CABG). Group A used 500cc., 6% Hydroxy-ethyl starch (Hespan) while Group B used 150cc., 25% human albumin as the primary colloid of the priming solution. The remainder of the prime used by both surgical groups included approximately 2,000cc. Ringer's, 10,000 units of Heparin, 50 mEq. of sodium bicarbonate and 12.5 grams of Mannitol.

Ideally, the priming solution should preserve the interstitial-intravascular fluid balance when the circulating plasma volume is suddenly increased with the onset of bypass. Twenty-five percent albumin, which was used by Group B is a highly soluble protein, supplies the oncotic equivalency of five times its volume in human plasma.[1] Not only does it prevent the rapid trans-capillary shift of fluid volume to the interstitial spaces, it is also believed to reduce platelet adhesion on the internal surfaces of the cardiopulmonary bypass circuit (CPB) [2-5] though the latter effect remains controversial.[3]

Hespan, which was used by Group A, is a synthetic colloid plasma volume expander which approximates the action of albumin, and has been considered a safe and effective lower cost replacement for albumin.[6] The large quantities necessary for bypass have been linked to the disruption of the coagulation mechanism postoperatively.[3,7] This study was undertaken to determine if any significant finding existed between these two groups with respect to the colloids used in the prime.

MATERIALS AND METHODS

In order to rule out factors that may have inadvertently affected blood loss in the postoperative period, patients medical records were reviewed to determine and define a consistent patient population for study. The patients chosen had undergone a CABG for the first time, no patients were on chronic preoperative anticoagulation therapy, none required intra-aortic

balloon pumping or any other blood pump assist devices during their hospital stay and all recovered from their surgery to be discharged (**Table 1** displays the demographics).

The same CPB equipment was utilized for all patients in the study, this included COBE CML II [a] membrane oxygenator, along with the Bio-Medicus PB-80[b] blood pump, William Harvey[c] arterial line filter, Sarns MP-4[d] cardioplegia delivery system and a custom tubing pack with pre-bypass filtration. The CPB circuit priming solution was prepared as previously described for the two groups being compared. Perfusion technique was similiar for each patient. Pump time did not exceed 120 minutes, patients were cooled to approximately 28°C, automated activated coagulation times (A-ACT) were maintained at greater than 480 seconds, arterial pressure was maintained between 50-70 mm/Hg and heparin reversal was achieved utilizing protamine sulfate. Blood work, which included arterial blood gases, electrolytes, hemoglobin/hematocrit and platelet counts were analyzed one hour prior to bypass, at least twice during bypass (cold and warm) and following bypass before the patient's transfer to the intensive care unit. No major intraoperative difficulties with bleeding or problems maintaining acceptable CPB parameters were found in the patients being reviewed.

RESULTS

In the immediate preoperative period, a comparison of platelet counts revealed that both groups were similiar. The mean platelet count in Group A (Hespan) was 220.81 (1000/ml)± 76.16 while the mean platelet count in Group B (Albumin) was 228.25±47.13 (**Graph 1**). During the intraoperative period a significant difference ($p < .05$) in the circulating platelet count was observed, where Group A fell to a mean of 99.90±32.4 while Group B decreased to an average of 153.84±34.17. Postoperatively, at the time the mediastinal chest tubes were removed, a substantial difference in platelet counts persisted, where Group A had a mean of 124.87±30.62 while Group B had an average of 159.71±41.22. Therefore, a consistent finding being that Group A had significantly fewer platelets after the administration of the priming solution through bypass. Another significiant intraoperative, post-perfusion finding included the difference between the two Groups in reversing anticoagulation with protamine. The Protamine:Heparin ratio of Group A was 1.4:1.0±.37 while Group B utilized 1.0:1.0±.43. A significant difference in postoperative blood loss, measured from mediastinal chest tube drainage existed between the two Groups. Group A had a mean blood loss of 1380.25cc±405.78cc. while Group B had a mean blood loss of 1087.00cc±385.72 (**Graph 2**). The increased blood loss reflects the dissimilarity between the two groups. One other significant difference ($p < .05$) observed postoperatively was the amount of plasma protein fraction (PPF) given. Group A patients required a mean of 1417cc±306.32 of PPF while the patients in Group B required a mean of 875cc±219.25 of PPF (**Graph 3**). Preoperative and postoperative prothrombin time (PT) and partial prothrombin time (PPT) results were not significant. Group A preoperative PT and PTT were 11.58 sec.±1.25 and 43.66 sec.±16.56. Group B preoperative PT and PTT were 11.50 sec.±.62 and 42.93 sec.±15.06. Postoperatively, Group A PT and PTT were 11.95 sec.± 1.05 and 34.44 sec.± 4.16 while Group B were 12.45 sec.± .96 and 33.91 sec. ± 4.33. Both Groups required a mean of 450cc of packed red blood cells (PRBC) for each patient during the postoperative period. Some investigators have found increased PT/PTT results and the need for greater amount of PRBC's postoperatively with the use of Hespan in CPB.[3,8,9]

DISCUSSION

The lower intraoperative and postoperative circulatory platelet counts observed with the use of Hespan in the CPB prime have also been reported in other clinical studies.[5,10] The exact mechanisms are not clear but Hespan may not effectively coat the surfaces of the CPB circuit to prevent platelet adherence.[3-5] An increased use of protamine, a weak anticoagulant, to reverse heparin anticoagulation may increase postoperative bleeding.[11] This higher protamine dose used by Group A may have been given because of increased bleeding in the early post-perfusion time period which could have resulted from the decreased platelet counts seen in these patients. In addition, though antithrombin III levels were not measured in this retrospective study, Hespan has been linked to lower antithrombin III levels postoperatively.[5,12] This effect may have added circulating heparin which would also require a higher dose of protamine to reverse.

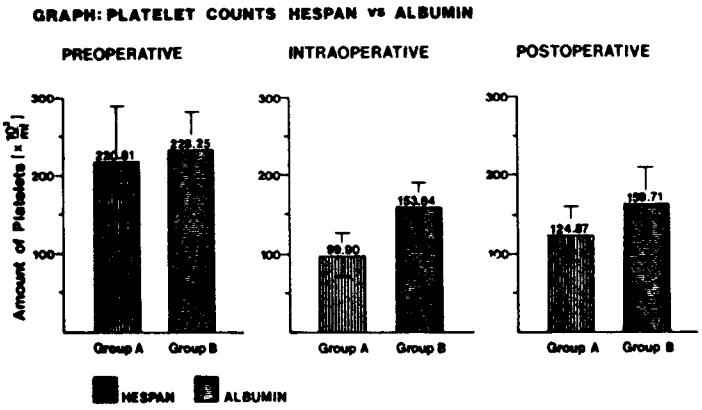
In three other studies comparing Hespan and albumin in CPB all had a greater blood loss postoperatively in their Hespan groups ranging from 12-24%.[5,10,13] The differences in blood loss between the two groups in the study was 22% higher in Group A (Hespan). The reason for the increased PPF usage in Group A (Hespan) may have been because it is a starch and not a protein. Its colloidal properties closely approximate those of human albumin, but it is not a protein, and proteins are least likely to leak through capillary pores into the interstitial spaces and those proteins that do leak eventually return to the circulation by the lymph vessels.[1] Proof that a polysaccharide starch like Hespan is less efficacious than human albumin in its postoperative colloidal effects is beyond the scope of this investigation, but Hespan has been linked to increased colloid requirements and weight gain postoperatively.[5]

Theoretically, if Hespan causes increased third spacing of fluids, circulating heparin would also travel to the interstitial fluid only to later re-enter the vascular space postoperatively and aggravate bleeding. Specific lowering of fibrinogen levels have also been noted with the use of Hespan raising suspicion of deleterious effects on hemostasis.[14] Others have suggested that Hespan's adverse effect on coagulation are dilutional,[5,12] but in the comparison here, total priming solution amounts were similiar, but protein concentrations were obviously different.

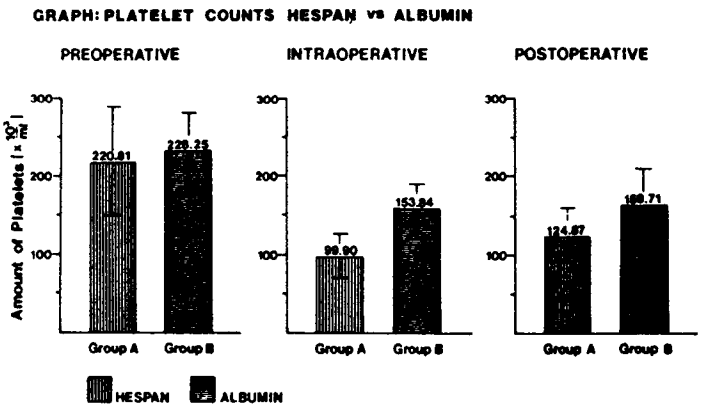
Hespan has been considered a lower cost replacement

a. COBE Laboratories, Lakewood, CO
b. Bio-Medicus, Eden Prairie, MN
c. William Harvey - C.R. Bard, Inc., Santa Ana, CA
d. Sarns/3M, Ann Arbor, MI

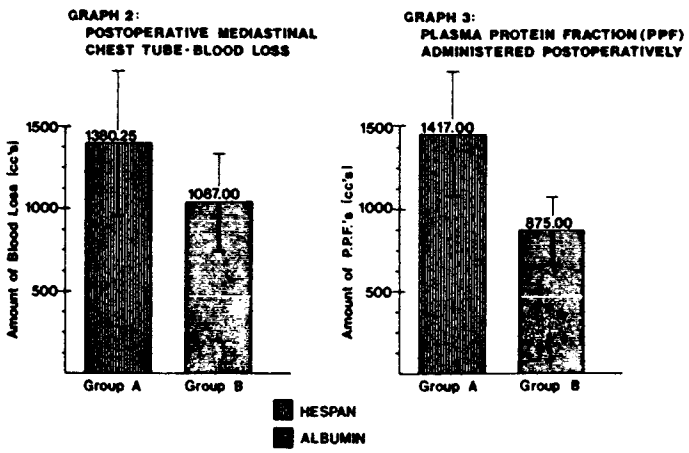
GRAPH 1



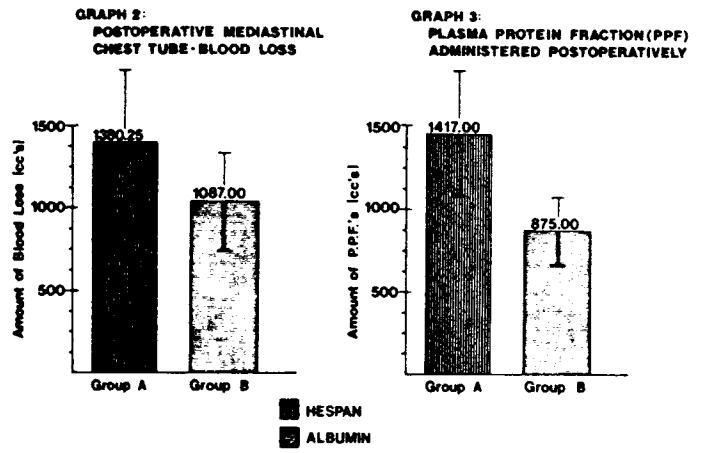
GRAPH 2



GRAPH 3



GRAPH 4



for albumin. At our institution, the patient charge for 150cc. albumin is $240 while 500cc. of Hespan is $110 - a substantial savings. Postoperatively, the Hespan group required more than 500cc. of PPF compared to the albumin group at a cost of $156 thereby eliminating any potential cost savings by using Hespan.

CONCLUSION

This study found significant differences in blood loss, in platelet counts during the intraoperative and postoperative period and in the amount of colloid therapy required postoperatively when comparing Hespan to albumin in the CPB prime solution. It appears that Hespan may not coat the artificial surfaces of the CPB circuit as well as albumin, causing platelet aggregation resulting in these lower intraoperative and postoperative platelet counts. The resultant disparity in blood loss of 303cc more in the Hespan group certainly raises doubt as to the safety and efficacy of Hespan as a replacement for albumin in the prime. Any cost savings realized by replacing albumin with Hespan is lost postoperatively due to the higher PPF requirements of Group A (Hespan) patients. Currently, at our institution, we have replaced Hespan with albumin in the prime solution of Group A patients, and are conducting a prospective study looking more closely at platelet function, coagulation parameters, colloid therapy and resultant blood loss as a follow-up to this investigation.

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