Use of autologous blood as part of the perfusate for cardiopulmonary bypass: a priming technique

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In an attempt to replace the oncotic and protein coating capabilities of serum albumin in the perfusate, we estimated a priming protocol that used autologous blood as part of the perfusate solution. Prior to March 1, 1999, our standard priming protocol was 1650 ml of crystalloid with 250 ml of 5% serum albumin and 5000 units of heparin. After removing albumin from our prime, our standard protocol was altered to include 40 ml of the patient’s autologous blood in 1800 ml of crystalloid and 10000 units of heparin. To determine the intraoperative effects of using albumin/crystalloid primes (Group A), autologous blood/crystalloid primes (Group B) and crystalloid primes (Group C), a total of 178 patients were sequentially evaluated. Intraoperative parameters evaluated were total protein (TP), colloid osmotic pressure (COP), platelets (PLTs) and fluid requirements during cardiopulmonary bypass (CPB).

During an overlapping 12-month period of time, 1092 consecutive cardiac surgical cases using CPB (584 albumin prime; 508 autologous blood prime) were evaluated for clinical outcomes in terms of mortality and length of hospitalization. In addition, over a period of 15 months, 1458 patients in both the autologous blood/crystalloid group and the crystalloid only group were evaluated for the incidence of high-pressure excursions (HPE) after going on bypass. Comparative reviews of TP, COP and PLTs demonstrated no significant difference 10 min after the start of bypass between Groups A and B. However, in Group C, there was a statistically significant increase in the intraoperative fluid requirements during CPB, compared to both of the other groups. There was no significant difference in the incidence of HPE, with an occurrence of 1.04% in the crystalloid only group and 1.11% in the autologous blood/crystalloid group.

Autologous blood perfusates were identical to albumin perfusates in their platelet protection and reduction of fluid shifts during the intraoperative period. Perfusion (2002) 17, 211–216.

Introduction

Since the early 1970s, albumin has been added to priming solutions for two main reasons. The first, and what appeared to be the most important, was the fact that albumin had been shown to place a protein coating over the inner surfaces of extracorporeal devices and, thereby, prevent platelet destruction/activation at the start of bypass. The second reason was to provide an oncotic pressure (COP) to the priming fluid and, thereby, prevent large shifts of fluid from the intravascular space to the extravascular space, including the heart, lungs and brain.

The pressures of cost containment, medical/legal issues and public fear of disease transmission from blood-related products have forced cardiac centers to re-examine their stand on albumin in the prime. After removing albumin, many primes now consist of a variety of solutions, such as crystalloids (pH and non-pH balanced), Pentaspan®, Hespan®, Hartmann’s solution, Dextran 40, Dextrose 5%, Haemaccel, Gelofusine® and autologous blood. According to a 1998 survey of 52 cardiac centers throughout North America, 55.8% of the respondents had stopped using albumin in their priming solutions for CPB.

In the absence of albumin as part of the perfusate, platelet protection afforded by the protein coating of extracorporeal circuitry may be compromised. Even as little as 0.75 g of albumin has been shown to provide some platelet protection at the start of CPB.

As previously indicated, there have been many publications demonstrating the platelet-sparing effects of adding albumin to the priming solutions. For example, many have shown greater decreases in platelet counts when albumin was not part of the priming fluids. This was clearly demonstrated when
either crystalloids alone or crystalloids/synthetic volume expanders were used in the primes as an alternative to albumin.\textsuperscript{17,18}

In a three-part trial, we examined 1) the intraoperative effects of using autologous blood in the perfusate as it relates to albumin and crystalloid perfusates, 2) the clinical outcomes of two perfusate groups, 3) the incidence of HPE during CPB, comparing crystalloid and autologous blood perfusates.

**Part 1**

On March 1, 1999, we eliminated 12.5 g of serum albumin from our prime and replaced it with 40 ml of the patient’s (autologous) heparinized blood in an attempt to produce the same passivating effects on extracorporeal surfaces that the serum albumin exhibited. We examined a total of 178 patients for the hematological effects of using albumin primes (n=63), autologous blood primes (n=63) and crystalloid only primes (n=52) by examining the COP, TP, Plts and volume requirements (VR) during the course of CPB.

**Part 2**

Patient outcomes in terms of mortality and morbidity were examined in 1092 consecutive cases, that is, in 584 consecutive patients prior to March 1999 (albumin prime) and in 508 consecutive patients after March 1999 (autologous blood prime).

**Part 3**

Over the past few years, the phenomenon of HPE has been well documented\textsuperscript{14,19,20} in the absence of albumin. It has been shown to occur in all oxygenators, with all primes and probably in all centers\textsuperscript{15,20} when albumin is eliminated from the prime. Even though HPE detection is easiest in positive displacement pumps when pre- and post-membrane pressures are measured, a 1998 survey of 52 cardiac centers found that 80.8% of these centers measured only post-membrane pressures, 7.7% only pre-membrane pressures and 3.8% did not measure pressures at all.\textsuperscript{15} Therefore, we decided to do a retrospective look at the incidence of HPE over a period of 15 months, which included 1458 CPB patients using either crystalloid only or autologous blood priming solutions.

**Methods and materials**

**Part 1**

One hundred and seventy-eight patients, divided into three groups (A, B, C), were evaluated for four recognized blood parameters and three accepted priming solutions for the adequacy of perfusion. In Group A, prior to the discontinuation of serum albumin from the prime, 63 consecutive adult patients were examined for TP, COP, Plts and VR 10 min after going on CPB. The perfusate consisted of 250 ml 5% serum albumin, 1550 ml of crystalloid (Normosol R) and 5000 units of heparin. All cases were isolated from cardiotomy suction blood entering the perfusate prior to going on bypass. In Group B, after hospital and divisional approval, the policy of putting albumin into the circulating prime was discontinued. The albumin portion of the prime was replaced with 40 ml of the patient’s (autologous) blood and circulated with 1800 ml of Normosol R and 5000 units heparin. To obtain the latter, the attending perfusionist would prepare a 60-ml syringe with 5000 units of heparin and give it to the anesthesiologist for withdrawal of this autologous blood prior to systemic heparinization. The 40-ml sample of blood would then be injected into the circulating crystalloid prime and allowed to circulate for approximately 30 min. Using the latter protocol, 63 consecutive adult patients were again examined in this group for TP, COP, Plts and VR, 10 min after the start of CPB. In Group C, the same data were also collected on 53 adult patients, using 1800 ml of Normosol R only and 5000 units heparin as the perfusate composition. Exclusion criteria involved all those patients receiving homologous blood or homologous blood products in any of the three groups examined.

**Part 2**

Prior to March 1999, 584 consecutive patients using albumin primes were compared to 504 consecutive patients after March 1999 using autologous blood primes, in terms of morbidity and mortality. Variables evaluated included patient demographics, type of procedure, mortality and length of hospitalization (Table 1).

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<th>Table 1 Patient demographics (N=1088)</th>
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COPD=chronic obstructive pulmonary disease; NYHA=New York Heart Association; EF=ejection fraction; HTN=hypertension; PVD=peripheral vascular disease.
Part 3
A retrospective analysis of 1458 cases using both autologous blood and crystalloid only primes, spanned over a period of 15 months, and focused on the occurrences of HPE as reported by the attending perfusionist. Criterion used for the definition of HPE was a rising pressure differential that exceeded 225 mmHg within the first 30 min of CPB, and a decrease in the platelet count of greater than 55% (when measured).

Cardiopulmonary bypass
The oxygenator used in all cases was the Sorin Monolyth with a hard-shell venous reservoir. CPB was conducted using the Sorin CAPS and Sorin SIII Heart Lung machines (Sorin Biomedica, USA). Sorin’s blood cardioplegia, at a ratio of 4:1, was also used in all cases. All blood samples were collected from the CPB circuit 10 min after the start of bypass and all patients were not actively cooled at the start of bypass, but allowed to drift to a temperature of 31–32°C. TPs were measured using the Beckman-Coulter Synchron CX7, and total Plts were measured using the Beckman-Coulter STKS, and uncorrected for hemodilution. COP was estimated using modifications of TP calculations as described by Beshere et al.5 and Blackwell et al.6 VRs were determined by using the total priming volume and all volumes added by the perfusionist during the course of CPB. All ACTs were measured using kaolin activators with the Medtronic Hemotec (Englewood, CA) HRACT cartridges, and all cases exceeded an activated clotting time (ACT) value of 480 s prior to the start of bypass.

Statistics
Descriptive statistics were obtained for all variables using the SAS software package (SAS, Cary, North Carolina). These included continuous and discrete variables that were analysed accordingly with a Student’s t-test, chi-square test and analysis of variance when involving more than two groups (ANOVA). Post hoc Fisher’s test of least significant difference (PLSD) was used to assess statistical significance, with \( p<0.05 \) being the limit of significance.

Results
Part 1
The data from 178 patients were examined and found to have no significant difference in the mean prebypass values for all three perfusate groups. Ten minutes after the start of CPB, TPs dropped to a median of 40±5.6 g/l in Group A, 38±4.6 g/l in Group B and 37±4.2 g/l in Group C (Figure 1). COP decreased to a median of 12.7±1.7 mmHg in Group A, 12.1±1.4 mmHg in Group B and 11.8±1.3 mmHg

Figure 1

Figure 2

Figure 3

Figure 4
in Group C (Figure 2). Plts decreased from a median of $207 \pm 56.9 \times 10^3$ to $124 \pm 39.6 \times 10^3$ in Group A, $221 \pm 68.6 \times 10^3$ to $138 \pm 45.8 \times 10^3$ in Group B and from $238 \pm 64.6 \times 10^3$ down to $127 \pm 43.5 \times 10^3$ in Group C (Figure 3). A significant difference was noted in the VRs of these three priming solution protocols at the end of CPB. The mean VR, including priming volume, of Group A was $2776 \pm 1240$ ml ($p=0.0005$), while the mean value of Group B was $2752 \pm 959$ ml ($p=0.0004$) compared to Group C, where the mean VRs on CPB were $3517 \pm 1133$ ml (Figure 4).

When comparing the 10-minute data using percentage drop in Plts, TP and COP (Figure 5), we found that Group A dropped by a mean of $39.4 \pm 14.7\%$, $42.5 \pm 8\%$ and $43.4 \pm 7.8\%$, respectively. These values in Group B were $41.5 \pm 13.9\%$ in Plts, $44.5 \pm 7.1\%$ in TPs and $43.4 \pm 6.9\%$ in COP. However, the data for Group C only showed a significantly greater drop of $46.8 \pm 10.6\%$ in Plts, $47.2 \pm 5.4\%$ in TPs and $45.7 \pm 5.5\%$ in COP.

**Part 2**

Five hundred and eighty-four consecutive patients prior to albumin prime, and 508 consecutive patients after autologous blood prime, were evaluated for patient outcome. Patient demographics were very similar in both groups and are illustrated in Table 1. The majority of procedures performed were coronary artery bypass grafts (CABG), with 73% in the albumin group, as compared to 70% in the blood prime group. The median length of hospitalization was 7 days in both groups ($p=ns$). The overall mortality was also not different between both groups, ranging from 3% to 6% ($p=ns$) (Figure 6).

**Part 3**

After eliminating albumin as part of the perfusate, there was an unexpected, yet noticeable, increase in the occurrence of HPE in both the crystalloid and autologous blood groups. This was evidenced by the occasional, yet dramatic, increases in pre-membrane pressures (>400 mmHg) and pressure differentials (pre-membrane–post-membrane pressure) exceeding 250 mmHg. In those instances where Plts were measured during this HPE occurrence, severe thrombocytopenia was found (Plts 17000–77000).

The retrospective examination of data in 1458 patients from March 1, 1999 to June 9, 2000 revealed that there was no significant difference in the 16 incidents of HPE that occurred in both Groups B and C. In Group B, there were 12 incidents of HPE that occurred in 1078 cases for an occurrence rate of 1.04%, or 1 in every 95 cases. In Group C, there were four incidents of HPE in 380 cases for an occurrence of 1.11%, or 1 in every 90 cases (Figure 7). The occurrence of HPE in Group A was never considered prior to the change in priming protocols to Groups B and C.

**Conclusions**

Removal of serum albumin as part of the perfusate priming volume has left the perfusionist with several options in replacing the colloid component of this fluid. In the North American market, these colloid replacements are in the form of synthetic solutions such as Pentaspan® or Hespan®. Both of these solutions are excellent volume expanders, but do little for platelet protection at the start of bypass. In fact, Hespan has been implicated in some concerns revolving around postoperative blood loss. The use of 40 ml of autologous blood was determined prior to the change in priming protocols and was based on previously published findings that as little as 0.75 g albumin/2000 ml crystalloid was sufficient for platelet
protection. Since human blood contains 38–50 g albumin/l blood, it was determined that 40 ml of patient blood should provide 1.5–2.0 g albumin for every 2000 ml crystalloid prime.

As expected, we have shown that removal of colloids from the perfusate and using crystalloids only will result in significant VRs (mean 828 ml/patient) during the course of CPB. When compared to the albumin and autologous blood primes, there was also a greater decrease in the mean circulating platelet count at the start of bypass using crystalloid only primes, which is consistent with previously published reports. The same applied with the decrease in mean values for TPs and COPs in the crystalloid only primes.

The results of this analysis indicate that the use of autologous blood in the perfusate provides platelet protection that is closely related to that found with 250 ml of 5% serum albumin in the prime. It also appears that the fluid requirements for CPB are similar when using either albumin/crystalloid (2776±1240 ml) or autologous/blood crystalloid (2752±959 ml) as perfusates for bypass. Therefore, in respect to platelet protection and fluid requirements during CPB, autologous blood perfusates have shown to be adequate replacements for the loss of albumin in the prime. However, unlike albumin primes, there were the sporadic and unexpected occurrences of random HPE problems.

Another drawback to the use of autologous blood perfusates and crystalloid only perfusates resulted in the occasional significant drop in mean arterial pressure (MAP) that occurs at the start of CPB. This was an unexpected occurrence, and, therefore, no data were collected. The drops in MAP were often more resistant to vasopressor administration in the autologous blood group, but did not appear to have adverse affects on patient outcomes, as demonstrated in Part 2.

These findings suggest that crystalloid only prime is associated with a significantly higher use of volume added during the CPB run. This has potential clinical importance in terms of fluid overload which may lead to prolonged ICU stay, ventilator dependence, length of hospitalization and possibly death. Our clinical data support the finding that albumin primes and autologous blood primes result in comparable patient morbidity and mortality. Length of hospitalization was chosen as a variable because it represents a good surrogate for patient morbidity because these are likely to impact it. Our data demonstrate the safety of using autologous blood for possible protein coating of the membrane, avoiding the unnecessary use of blood products such as human albumin.

Although the occurrence of HPE was a rare phenomenon when albumin was added to the perfusates, it did become more prevalent when autologous blood and crystalloid only primes were used. In fact, the incidence of HPE was almost identical in both the autologous blood group (1.11% or 1 in every 90 cases) and the crystalloid only group (1.04% or 1 in every 95 cases).

The findings of HPE in this analysis do raise some unanswered questions. For example, it is well documented that HPE has a tendency to occur when commercial serum albumin is absent from the perfusate. But, as demonstrated in this three-part trial, the platelet protection afforded by albumin in the prime is almost identical to the platelet protection afforded by autologous blood in the prime. Yet, the occurrence of HPE was found with the autologous blood primes, and not the albumin primes. Is it possible that we have been focusing for far too long on the platelet-protective effects of commercial serum albumin, and not enough on albumin’s other significant benefit as a drug plasma-binding agent? The binding abilities of plasma proteins and hemoglobin are well known, but it is also well known that albumin has the unlimited ability to bind with most drugs in a patient’s circulation, even such drugs as anesthetic agents and antifibrinolytics. Therefore, in the absence of albumin-containing perfusates, are there more unbound drugs available in the patient’s circulation for interaction with extracorporeal foreign surfaces? Answers to these questions were beyond the scope of this trial, but create an area for further investigation into the sporadic occurrence of HPE.

References


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