Heparin Content of Cell-Salvaged Blood After Cardiopulmonary Bypass

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ABSTRACT

Blood remaining in the extracorporeal circuit (ECC) is frequently concentrated and washed before transfusion to the patient after termination of cardiopulmonary bypass. As additional doses of protamine are often administered to reverse the effects of suspected heparin content of this blood, we determined activated clotting times (ACTs) and heparin concentration pre and post cell salvaged blood administration. After a 1 liter normal saline wash, administration of the cells obtained using the Cobe Baylor Rapid Autologous Transfusion (BRAT) system caused no change in either patient ACT (p=0.19) or plasma heparin concentrations. We conclude that additional protamine administration is unwarranted after transfusion of concentrated, washed red blood cells (RBCs) from the ECC with the Cobe BRAT cell salvage device.

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INTRODUCTION

The risks of homologous blood product exposure have led to widespread use of blood conservation techniques. Intraoperative blood salvage can be accomplished in cardiac surgery by transfusing the blood remaining in the extracorporeal circuit (ECC) following aortic cannula removal. One potential drawback is the effect of the residual heparin in the extracorporeal blood. Some clinicians administer additional protamine to counteract this presumed heparin. However, we believe that the blood preparation cycle in cell salvage machines reduces the heparin to inconsequential concentrations negating requirements for further protamine. Minimal heparin effect in the cell salvaged blood has been previously shown with the Haemocell® device (1). The purpose of this study was to extend analysis to a different device, using a larger patient sample.

MATERIALS AND METHODS

After review by the Institutional Committee for the Protection of Human Subjects, 99 patients undergoing elective cardiopulmonary bypass (CPB) were studied. In all patients, heparinization was achieved with 300 IU/kg of porcine heparin a and further doses as required to maintain the ACT>400 seconds throughout bypass. No dose adjustments were required for patients receiving heparin preoperatively. Heparin effect was reversed with protamine in a 1 mg/100 IU (initial heparin dose) ratio after successful weaning from CPB.

Activated clotting time was measured with a Hemochron device b that underwent daily clot detector sensitivity and commercial controls testing, and monthly temperature calibration testing for the duration of the study period. Heparin concentrations were measured with the Hepcon Hemostasis Management System c. The device uses heparin/protamine titration to semiquantitatively determine heparin concentration by adding different amounts of protamine to fixed aliquots of heparinized blood in four cuvettes containing a fixed quantity of thromboplastin. The Hepcon underwent routine heat block temperature verification and cleaning as specified by the manufacturer. The low heparin assay cartridge was used for heparin concentration determinations. This cartridge displays results at 0.4 U/ml intervals between 0.0 U/ml and 1.2 U/ml.

The standard CPB circuit included a membrane oxygenator d and a centrifugal pump e, and was primed with crystalloid, albumin, and mannitol to a total volume of 1800 ml. Surgical preference dictated bypass temperature which ranged from 28°C to 35°C.

Following removal of the aortic cannula and protamine administration, residual and previously salvaged blood was processed with a Cobe Baylor Rapid Autologous Transfusion System (BRAT) f, a semi-continuous flow centrifugation cell saver device. A 1 liter normal saline (NS) wash was performed, and the cell salvaged blood was reinfused after protamine administration.

The following blood samples were taken: post-induction baseline ACT (pre-sternotomy), ACT three minutes after heparin administration, ACT and heparin concentrations after 30 minutes on CPB, three minutes after protamine administration, and three minutes after transfusion of the cell salvaged blood. All samples were taken from a central line after 10 ml dead space withdrawal. Heparin and protamine were administered through a separate line to avoid potential contamination of blood samples.

Activated clotting times were subjected to analysis of variance with individual comparisons using Bonferroni's corrected Students t-test. Significance was assessed with p<0.05.

RESULTS

Patient demographics and surgical details are included in Table 1. The heparin and protamine doses (Table 2) reflect our current practice to reverse heparin effects with a 1 mg protamine/100 IU heparin dose.

Table 1: Patient demographics and surgical procedures. Values are mean ± standard deviation.

| Age (years) | 59.5 ± 11.7 |
| M/F (Male/Female) | 64/35 |
| Height (meters) | 1.7 ± 0.1 |
| Weight (kg) | 83.3 ± 16.5 |
| CABG | 85 |
| Valve Replacement | 12 |
| Combined CABG & Valve | 2 |

Table 2: Heparin and protamine doses, and cell salvaged blood volume. Values are mean ± standard deviation.

| Heparin to patient (U) | 29,210 ± 8,804 |
| Heparin to pump (U) | 6,400 ± 1,700 |
| Protamine (mg) | 293 ± 73.6 |
| Cell salvaged volume (ml) | 506.6 ± 176.4 |
Heparin concentrations during bypass and ACTs post protamine administration were within acceptable range for CPB (Table 3). ACTs post protamine administration and post cell salvaged blood transfusion were not statistically different (p=0.19) but both were significantly less than the baseline pre-sternotomy ACT (p<0.05). Heparin concentrations were 0.0 U/ml post-protamine and post cell salvaged blood administration.

DISCUSSION

Blood conservation techniques, an essential part of surgical and anesthetic practice, include intraoperative blood salvage (2). In cardiac surgery, the blood remaining in the ECC after patient separation from CPB may be processed either by hemofiltration or more commonly with a cell salvage device. At our institution the Cobe BRAT is used; RBCs are concentrated by centrifugation and the acellular component removed by washing with 1 L NS as a previous study suggested that a >750 ml NS wash was required to effectively remove heparin (3). Previous practice involved regular protamine administration (50 mg) to reverse the presumed effects of heparin contaminating the final product. Although the potential risks of protamine administration (4), including systemic hypotension and pulmonary hypertension, are often correlated with initial protamine administration, it would still seem prudent to document heparin concentration of up to 0.2 U/ml as a previous study suggested that a NS wash volume of 750 ml produced heparin concentrations <0.04 U/ml using the Haemonetics Cell Saver® (3) in a study of only five patients. Use of a similar system in another study revealed a heparin concentration of 0.26 U/ml in the concentrated blood, resulting in effective administration of 182 U heparin to the patient (5). The same group documented patient heparin concentrations of 0.08 U/ml after transfusion of the cell salvaged (CS) blood in a separate study (6). The other groups in this study [hemofiltration, acute normovolemic hemodilution (ANV), ANV plus CS, ANV plus hemofiltration, plasmapheresis, and plasmapheresis plus CS] had similar heparin levels of 0.07-0.11 U/ml postoperatively. This suggests that there was no significant heparin contamination in the cell salvaged group. Our measured heparin concentration of 0.0 U/ml after transfusion of the cell salvaged unit, supports these findings. Bowie and Kemna have documented specificity and sensitivity of the Hepcon system with a coefficient of variation of 5% for heparin concentrations (7). However, individual heparin concentration of up to 0.2 U/ml are reflected as 0.0 U/ml in the low heparin assay cartridge of the Hepcon system, as the heparin concentrations are measured in 0.4 U/ml increments (personal communication, Medtronic Hemotec Inc., Engelwood, CO). Thus, it is possible that our measured heparin concentrations of 0.0 U/ml may not have reflected the absence of heparin. However, in conjunction with the normal ACT, the minimal measured heparin concentration was considered acceptable evidence for the absence of heparin.

The similar decrease in the post-protamine and post-autologous blood administration ACTs from pre-induction values has been previously noted by Gravlee, et al (8), who suggested that baseline ACT should be drawn after sternotomy because of possible surgical acceleration of coagulation.

We have shown in 99 patients that transfusion of cell salvaged blood that has been processed with the Cobe BRAT using a 1 liter NS wash after CPB weaning and protamine administration has no significant effect on plasma heparin concentrations or ACTs. Thus, there seems to be no justification for protamine administration after cell salvaged blood administration with the current technique of ECC blood salvage.

Table 3: Activated clotting time (ACT) and heparin concentrations. Values are mean ± standard deviation. NM = not measured

<table>
<thead>
<tr>
<th></th>
<th>ACT (seconds)</th>
<th>Heparin Concentration (U/ml)</th>
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<tbody>
<tr>
<td>Pre-heparin administration</td>
<td>141 ± 31#</td>
<td>NM</td>
</tr>
<tr>
<td>Post-heparin administration</td>
<td>621 ± 222</td>
<td>NM</td>
</tr>
<tr>
<td>Half hour on CPB</td>
<td>649 ± 197</td>
<td>2.7 ± 0.1</td>
</tr>
<tr>
<td>Post-protamine admin.</td>
<td>127 ± 16*</td>
<td>0.0</td>
</tr>
<tr>
<td>Post-cell salv. blood</td>
<td>128 ± 16*</td>
<td>0.0</td>
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</tbody>
</table>

# Baseline ACT > post protamine and post cell salvaged ACTs (p<0.05)
* No difference between post protamine and post cell salvaged ACTs (p=0.19)

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