Adding Hetastarch to the Adult Cardiopulmonary Bypass Prime Does Not Affect Patient Outcomes

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ABSTRACT

Hespan™ (hetastarch), a synthetic colloid, is often used in priming cardiopulmonary bypass circuits. The purpose of this study is to determine the efficacy of adding hetastarch to the prime compared to adding no hetastarch. Twenty-four adult patients undergoing cardiopulmonary bypass received Hespan™ in the prime, while twenty-nine patients did not. Outcomes were compared using paired t-test, analysis of variance, analysis of covariance, and descriptive statistics, where p<0.05 was considered significant. There were no significant differences in change in lung compliance, weight gain, time on the ventilator, or length of stay in the intensive care unit. Adding colloids to the adult CPB prime does not improve patient outcomes over priming exclusively with crystalloids.

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INTRODUCTION

Osmosis, as described by Starling, is the movement of water from a region with a low concentration of non-permeating solute, to a region with a high non-permeating solute concentration. This flow of water carries with it any dissolved solutes to which the membrane is highly permeable. It is this concept that determines fluid movement across the capillary. Plasma inside the capillary, as well as the interstitial fluid outside the capillary, contains large amounts of permeating solutes, or crystalloids. Since the capillary is permeable to crystalloids, no difference in water concentration is created (1). However, the plasma proteins, or colloids, are essentially non-permeating and have a very large concentration inside the capillary, and exert colloid osmotic or oncotic pressure (COP) (2). Under normal circumstances, this difference in protein concentration favors flow of interstitial fluid into the capillary (1).

The effect of crystalloids and colloids in fluid balance is essential when choosing the constituents for cardiopulmonary bypass (CPB) priming solutions. Priming the extracorporeal circuit with non-blood solutions has contributed greatly to the safety of cardiopulmonary bypass. Not only does priming with crystalloid and/or colloids reduce the use of homologous blood products, it also allows for hemodilution, which will decrease the hematocrit and thus viscosity and resistance to blood flow (3).

Choosing the optimal priming solution for the extracorporeal circuit should be based primarily on patient safety. Decreasing the risk for edema is an important goal (4). Lacy and Wright suggest that colloid solutions are preferred over crystalloid solutions for priming cardiopulmonary bypass circuits and for postoperative resuscitation following myocardial revascularization (5). Smiley reported that priming with crystalloids allows for elevations in extracellular sodium and water during CPB (6). Boldt, et al. concluded that using large volumes of crystalloid results in marked hemodilution with severe reduction in COP, followed by impairment of pulmonary function in the post bypass period (7). Unfortunately, priming with either crystalloid or colloid solutions immediately leads to dilution of serum proteins once bypass is initiated (4), and thus a decrease in COP, which may contribute to edema and altered lung function (8).

Byrick, et al. found that accumulation of pulmonary extravascular water, after coronary artery bypass grafting, is not affected by priming the extracorporeal circuit with either colloid or crystalloid solutions (9). Lumb, when comparing two different colloids, noted a significant increase in extravascular lung water (EVLW) associated with a decreasing serum COP, and an increasing alveolar-arterial difference in oxygen tension (AaDO₂) immediately after bypass (10). Yet, there was no significant accumulation of lung water measured postoperatively in the ICU. Overall, the literature does not provide a clear superiority of any priming solution over another. There have been several studies performed to compare one crystalloid-colloid combination against another (5, 10), as well as studies to determine which colloid solution is safest and most effective (11, 15).

Hetastarch is an artificial colloid, derived from a waxy starch, composed almost entirely of amylopectin (package insert). Hespan™, 6% hetastarch in 0.9% NaCI, has colloidal properties that approximate those of 5% albumin. Palazzo, et al. found that although the COP in hetastarch prime was slightly less than that in the albumin prime prior to CPB, the patient’s COP during and after bypass were not significantly different (12). Thompson and Walton (13), and Lamke and Liliedahl (14), concluded that Hespan™ was comparable to 5% albumin, and superior to crystalloid with regard to plasma volume expansion. Therefore, hetastarch may be considered an effective colloid for pump priming as well as an effective plasma expander for postoperative cardiac patients.

Several studies have indicated that hetastarch is an acceptable substitute for 5% albumin in pump priming solutions (11, 12, 15). However, there is still controversy over patient outcomes when pure crystalloids are used for priming compared to various crystalloid-colloid combinations. The cost of colloids can vary from fifty to one hundred dollars, per five hundred milliliters, compared to only five to thirty dollars per liter for crystalloid. With the recent focus on reducing costs in health care, the necessity for the addition of colloids to the prime should be evaluated. If there is no clinical advantage for the patient the increase in cost may not be justified.

The purpose of this study is to test the efficacy of the colloidal properties of hetastarch, when used in the CPB pump prime, compared to no hetastarch, as determined by change in patient lung compliance, weight gain, time on the ventilator, and length of stay in ICU. The null hypothesis is that there is no difference in patient weight gain, change in lung compliance, time on the ventilator, and length of stay in ICU when hetastarch is used, as opposed to no hetastarch in the prime, for cardiopulmonary bypass.

MATERIALS AND METHODS

Fifty-three consecutive adult patients undergoing CPB with one of four cardiac surgeons were prospectively studied. Patients with preexisting anemia or coagulopathies, such as thrombocytopenia, were not included in the study. One patient was excluded due to operative complications, which led to an extended period on the ventilator in the ICU.

The patients were divided into two groups based on the use of hetastarch in the extracorporeal circuit (ECC) prime. The pump was routinely primed with 1800ml of Plasmalyte A® for three surgeons. The fourth surgeon required 500ml of Hespan™ to replace 500ml of Plasmalyte A for his patients. No changes

a Baxter Healthcare Corp., Deerfield, IL
b DuPont Pharmaceuticals, Wilmington, DE
in surgical protocol were made with inclusion in this study. Management of anesthesia and conduct of CPB were the same for all patients. Any differences in surgeon protocol were taken into account during statistical analysis.

Preoperative hematocrit, platelet count, coagulation studies (PT and PTT), and lung compliance \[C = \Delta \text{volume (L)} / \Delta \text{pressure (cmH}_2\text{O)}\] were recorded. Intraoperative information recorded included: type and amount of additional volume added, total urine output, use of aminocaproic acid, trasylol, cross clamp and pump time. Postoperative measurements included: lung compliance, type and amount of fluid/blood products administered, hours on the ventilator, and length of stay (LOS) in the intensive care unit (ICU). Compliance change was found by subtracting preoperative compliance from postoperative compliance. Data such as patient weight, PT, PTT, platelet count, hematocrit, urine output, and chest tube drainage were measured at twelve, twenty-four hours and postoperative days two through five to assess volume and coagulation status.

The main outcomes of interest were change in lung compliance, LOS in ICU, ventilator time, and weight change. Fifty-three patients in the study provided a statistical power greater than eighty percent to detect clinically significant differences in these parameters. The data was statistically analyzed by t-tests and analysis of variance (ANOVA). Analysis of covariance (ANCOVA) was also used to control for potential confounding variables, such as surgeon, oxygenator type, cross-clamp, and CPB time. A p value of less than 0.05 was considered significant.

**RESULTS**

Table 1 illustrates the descriptive data of the study population for the two groups either receiving or not receiving hetastarch in the CPB prime. There were no significant differences in the patient population with respect to age and weight, but there were significantly more males in group 1 (p = 0.01). Group 1 originally had significantly longer cross clamp and CPB times. However, there were no significant differences in cross clamp or CPB times once surgeon was removed as a confounding variable. Length of stay in ICU was not significantly different between the two groups.

Time on the ventilator was shorter in group 2 (p < 0.01), but was not statistically significant once surgeon was considered as a confounding variable (Figure 1).

No significant differences were found in preoperative coagulation measurements, or postoperative chest tube drainage at twelve and twenty-four hours as illustrated in Table 2.

A significant difference was seen in the amount of

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**Table 1. Patient Data and Operative Outcomes**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>GROUP 1 (n = 29)</th>
<th>GROUP 2 (n = 24)</th>
<th>Adjusted p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>60.3 ± 14.6</td>
<td>64.3 ± 10.9</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79.6 ± 18.5</td>
<td>74.4 ± 13.2</td>
<td>NS</td>
</tr>
<tr>
<td>Cross clamp (min)</td>
<td>99.3 ± 26.9</td>
<td>63.9 ± 18.4</td>
<td>0.00 0.58</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>136.1 ± 42.5</td>
<td>89.5 ± 26.1</td>
<td>0.00 0.15</td>
</tr>
<tr>
<td>Time on vent (hrs)</td>
<td>13.2 ± 4.5</td>
<td>10.7 ± 3.3</td>
<td>0.03 0.91</td>
</tr>
<tr>
<td>LOS in ICU (hrs)</td>
<td>28.9 ± 13.6</td>
<td>24.2 ± 6.7</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Adjusted p value: the p value once confounding variables are statistically taken into account.

CPB= cardiopulmonary bypass; hrs= hours; ICU= intensive care unit; kg= kilograms; LOS= length of stay; min= minutes; NS= not significant

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**Table 2. Coagulation and Hematological Data**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>GROUP 1</th>
<th>GROUP 2</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>preoperative Hct</td>
<td>35.5 ± 5.7</td>
<td>34.5 ± 6.3</td>
<td>NS</td>
</tr>
<tr>
<td>preoperative platelet (10^9/L)</td>
<td>274 ± 266</td>
<td>217.6 ± 76.7</td>
<td>NS</td>
</tr>
<tr>
<td>preoperative PT (sec)</td>
<td>12.44 ± 1.18</td>
<td>12.0 ± 0.9</td>
<td>NS</td>
</tr>
<tr>
<td>preoperative PTT (sec)</td>
<td>28.52 ± 5.74</td>
<td>34.9 ± 20.3</td>
<td>NS</td>
</tr>
<tr>
<td>12hr chest tube drainage (ml)</td>
<td>612 ± 127</td>
<td>492.6 ± 227</td>
<td>NS</td>
</tr>
<tr>
<td>24hr chest tube drainage (ml)</td>
<td>996 ± 272</td>
<td>666.3 ± 310</td>
<td>NS</td>
</tr>
</tbody>
</table>

Hct= hematocrit; hr= hour; PT= prothrombin time; PTT= partial thromboplastin time

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**Figure 1: Patient hours spent on the ventilator postoperatively according to surgeon.**

<table>
<thead>
<tr>
<th>TIME ON THE VENTILATOR</th>
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<tbody>
<tr>
<td>Hours</td>
</tr>
<tr>
<td>16</td>
</tr>
<tr>
<td>14</td>
</tr>
<tr>
<td>12</td>
</tr>
<tr>
<td>10</td>
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<td>8</td>
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<tr>
<td>6</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>0</td>
</tr>
</tbody>
</table>

n=13 surgeon 1  n=11 surgeon 2  n=4 surgeon 3  n=22 surgeon 4

TOV = time on the ventilator
Plasmalyte A and the amount of Hespan™ used to prime the CPB circuit. This difference was expected, as Group 2 replaced 500 ml of Plasmalyte A in the prime with 500 ml of Hespan™. The amount of crystalloid and hetastarch added during CPB was not significantly different. The amount of red blood cells added during CPB was not significantly different once surgeon and Hct were removed as confounding variables. The amount of hetastarch given by anesthesia in the operating room, urine output while on CPB, as well as twelve hour and postoperative day two outputs, were not significantly different as seen in Table 3.

Preoperative weight was recorded, as well as postoperative weight at twelve hours and postoperative day two, but was statistically insignificant, as seen in Table 4.

Weight change was also recorded by taking the difference in twelve hour postoperative weight minus preoperative weight, as well as postoperative day two minus preoperative weight. There were no significant differences in weight change observed in the two groups.

Group 2 had a significantly lower compliance preoperatively as seen in Figure 2. There were no statistical differences found between the groups in postoperative compliance as well as change in lung compliance.

**DISCUSSION**

There have been previous studies performed to evaluate Hespan™ and the literature seems to agree that it can be used as a safe and effective synthetic colloid. Because it has colloidal properties that approximate those of 5% albumin (12), its addition to the adult CPB prime has become routine in many hospitals. This study was performed to evaluate the effectiveness of adding hetastarch to the adult CPB prime by recording and statistically analyzing specific patient outcome parameters.

Based on our results, it is clear that postoperative change in lung compliance, weight gain, time on the ventilator, and even length of stay in ICU are all a function of the surgeon. The shorter bypass runs performed by surgeon four have statistically ruled out any significance for the use of hetastarch in the adult CPB prime. Any variable that was originally considered significant was shown to be not significant once the surgeon was statistically considered as a confounding variable.

Today, reducing the costs of health care has become essential. In this study, adding hetastarch to the prime did not improve...
patient outcomes, shorten the length of stay, or therefore reduce costs. If adding a colloid to the prime leads to a decreased risk of edema and thus a shorter time on the ventilator, shorter length of stay in ICU, and an overall quicker recovery for the patient, the additional expense of the colloid can be justified. Our results did not justify the use of hetastarch in the pump prime.

The search for the perfect priming solution continues. Based on the results collected in this study, we accept the null hypothesis that there is no difference in patient weight gain, change in lung compliance, time on the ventilator, and length of stay in ICU, when hetastarch is used, compared to no hetastarch, in the adult CPB prime. The addition of hetastarch to the prime does not result in any significant differences in patient outcomes than does priming exclusively with crystalloids. As a step towards cost containment, without jeopardizing patient safety, the addition of hetastarch to the adult CPB prime may be eliminated.

REFERENCES