Selection of optimal quantity of hydroxyethyl starch in the cardiopulmonary bypass prime

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Ringer’s solution prime reduces colloid osmotic pressure and causes edema during cardiopulmonary bypass, while hydroxyethyl starch (HES) can be used to attenuate this effect. Fifty patients were classified into five equal groups: Group I (preoperative patients) is the control group and the other four groups (II, III, IV, V) received different volume ratios of Ringer’s solution to HES (1:0, 2:1, 1:2, 0:1, respectively). This study was aimed at evaluating the optimal quantity of HES regarding body fluids expansion, ventilation and recovery time, blood rheologic properties, clotting parameters, platelet counts, blood loss and red blood cell membrane properties. The results showed a reduction in interstitial fluid (ISF) expansion, changes in blood rheologic properties with the increase in HES quantity and shorter ventilation and recovery times in Groups IV and V. We concluded that the optimal HES quantity in the prime is two thirds, which insures an 83% reduction of ISF relative to Group II, shorter ventilation and recovery times and avoidance of the hazards of high levels of HES. Perfusion (2004) 19, 41-45.

Introduction

Hemodilution using Ringer’s solution as prime for cardiopulmonary bypass (CPB) during open-heart surgery reduces plasma colloid osmotic pressure (COP),¹ which can lead to edema in many tissues and results in organ dysfunction after CPB.² Thus, hydroxyethyl starch (HES) was preferred as a prime solution in order to avoid the fall in plasma COP and decrease water flow out of the vascular system (edema).³ At the same time, HES affects the coagulation system by decreasing coagulation factor level⁴ and reducing platelet (Plt) function by coating the platelet surface.⁵ It also affects blood rheologic properties and may affect the red blood cell (RBC) membrane properties.

Using crystalloid (Ringer’s solution) or colloid (HES) as CPB prime is still controversial and remains a topic for debate. Many studies are available to support or refute the use of the two types of solution, so the truth must lie somewhere in between.⁶

Therefore, the aim of the present study was to evaluate the optimal quantity of HES in the CPB prime considering the different effects on body fluid expansion during CPB, ventilation and recovery times, blood rheologic properties, clotting parameters, Plt count, blood loss and RBC membrane properties.

Methods

This study was conducted at the Kasr Al-Aini Hospital after the approval of the Cardiothoracic Surgery Department (Faculty of Medicine, Cairo University) and the Local Ethics and Research Committee. Written informed consent was obtained from each patient included in this study.

Fifty patients undergoing open-heart surgery for valve replacement and coronary artery bypass grafting (necessitating CPB) were divided into five equal groups. Group I (Cpl) is the control group (pre-operative patients). Groups II, III, IV and V received different volume ratios of Ringer’s solution to HES (1:0, 2:1, 1:2, 0:1, respectively). The HES (HAES-steril®; Fresenius AG, Bad Homburg, Germany) used in the study has an average molecular weight of 200 000 Da and a molar substitution of 0.55.

All patients had normal hepatic and renal functions and a hematocrit of less than 25%, and were undergoing first-time open-heart surgery with no previous history of capillary leakage disease or

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pulmonary dysfunction. Prothrombin concentration was not less than 85%.

Plasma volume (PV) was estimated by radioactive iodinated \(^{131}\)I human serum albumin (HSA) [200 g/L, CSL Ltd, Australia, Reg. No. 20759/99]\(^6\) using the single injection method.\(^7\) HSA acts as a tagged material since it is stable and has a suitable physiological behavior.

Extracellular fluid (ECF) volume was estimated by inulin (L. light & Colnbrook Co. Ltd., UK) using the single injection method. Inulin concentration in blood samples was estimated in vitro using the anthrone method.\(^8\) Interstitial fluid (ISF) volume is the difference between the ECF volume and PV.

Plasma and blood viscosities were measured using a standard Ostwald’s viscometer and the erythrocyte sedimentation rate (ESR) was measured using Westergren’s method.\(^9\)

Prothrombin concentration (PC) was measured using thromborel S (Dade Behring Marburg GmbH) and activated partial thromboplastin time (aPTT) was measured using pathromtin SL (Dade Behring Marburg GmbH). Plt counts were performed automatically using the Sysmex Automated Hematology Analyzer K-1000 (TOA Medical Electronics Co., Ltd., Kobe, Japan). Total blood loss is the sum of the blood in surgical sponges and suction traps.

RBC membrane properties were estimated using the osmotic fragility test.\(^9\) In the differential osmotic fragility curves, C% is the NaCl concentration at which hemolysis starts to occur. This value indicates the relative permeability of the RBC membrane. Also, the width at half maximum \(W_{hmax}\) of the differential curves is observed to estimate the relative elastic limit of the RBC membrane.

## Results

All groups (Gp) undergoing this study have similar patient demographic characteristics with no statistical differences, as presented in Table 1.

Body volume estimation (Table 2) showed a high increase in ECF for GpII \((p < 0.0025)\) and GpIII \((p < 0.025)\) relative to GpI (control patients, preoperative group) accompanied by a high increase in ISF \((p < 0.0001)\) for the same groups. In contrast, there was a nonsignificant increase \((p > 0.005)\) in ECF and ISF for GpIV and GpV relative to GpI. The reduction in PV in all groups was insignificant except in GpII, which showed a significant reduction.

As shown in Figure 1, the expansion in GpV (received 100% HES) is considered as the baseline for the edema that occurred in all groups due to capillary permeability. The ISF increase in GpIII and GpIV relative to GpV is not in correlation with the quantity of added HES. Also, the figure illustrates the percentage changes in ECF, ISF and PV for GpII to GpV with respect to the preoperative group (GpI).

In GpII (0% HES), maximum edema occurred. Consequently, it was expected that if one-third of HES was added to two-thirds Ringer’s solution (GpIII), 65% of ISF expansion would occur and similarly, 35% expansion would occur in GpIV.

Figure 2 shows the correlation between the previously mentioned expected and measured increases in ISF versus the quantity of HES added. The ISF increase in GpIV was 15% of that in GpII, i.e., there was an 85% reduction of formed edema in GpII instead of the expected 65%.

The data listed in Table 3 was found to give a linear relationship between HES added and plasma and blood viscosities, while it gave an exponential relationship for ESR values.

There were insignificant differences between the groups in PC, aPTT and Plt count, as presented in Table 4.

The osmotic fragility test shows a decrease in RBC membrane permeability and elasticity for all groups (Table 5).

Consciousness level and neurologic function were total in all patients of the four groups (GpII–GpV). Other intraoperative and postoperative clinical parameters are presented in Table 6. There were insignificant differences for these parameters among the

<table>
<thead>
<tr>
<th>Variable</th>
<th>GpI (control)</th>
<th>GpII</th>
<th>GpIII</th>
<th>GpIV</th>
<th>GpV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female/male</td>
<td>5/5</td>
<td>5/5</td>
<td>6/4</td>
<td>5/5</td>
<td>4/6</td>
</tr>
<tr>
<td>Age (year)</td>
<td>45.6±13.5</td>
<td>44.2±14.32</td>
<td>43.1±14.25</td>
<td>41.7±12.7</td>
<td>43.5±12.3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.5±19.35</td>
<td>81±21.1</td>
<td>77.4±25.83</td>
<td>69.5±13.75</td>
<td>70.6±13.95</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164.2±18.3</td>
<td>161.8±19.2</td>
<td>162.6±11</td>
<td>166±10.51</td>
<td>172±9.84</td>
</tr>
<tr>
<td>Body surface area (m(^2))</td>
<td>1.75±0.17</td>
<td>1.82±0.17</td>
<td>1.81±0.27</td>
<td>1.78±0.20</td>
<td>1.86±0.16</td>
</tr>
<tr>
<td>Type of surgery (CABG*/valves)</td>
<td>–</td>
<td>3/7</td>
<td>4/6</td>
<td>2/8</td>
<td>3/7</td>
</tr>
</tbody>
</table>

* Coronary artery bypass graft surgery.
four groups, except for ventilation and recovery times for GpIV and GpV ($p < 0.05$) relative to GpII and GpIII.

As presented in Table 7, fluid balance is significantly high in GpII ($p < 0.05$) and GpIII ($p < 0.001$) in comparison with GpIV and GpV. Urine output was less for GpV, but it was statistically insignificant. Blood loss was significantly high in GpV relative to GpII and GpIII ($p < 0.01$).

### Table 3 Blood and plasma viscosities; and ESR data for all groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>GpI (control)</th>
<th>GpII</th>
<th>GpIII</th>
<th>GpIV</th>
<th>GpV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood viscosity (poise)</td>
<td>0.0433 ± 0.0032</td>
<td>0.0251 ± 0.0029</td>
<td>0.0283 ± 0.0041</td>
<td>0.0333 ± 0.0054</td>
<td>0.0405 ± 0.0106</td>
</tr>
<tr>
<td>Plasma viscosity (poise)</td>
<td>0.0147 ± 0.00080</td>
<td>0.0101 ± 0.0037</td>
<td>0.0151 ± 0.0047</td>
<td>0.02 ± 0.0048</td>
<td>0.0266 ± 0.0032</td>
</tr>
<tr>
<td>ESR (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First hour</td>
<td>8 ± 0.44</td>
<td>6 ± 0.29</td>
<td>9 ± 0.45</td>
<td>15 ± 1.35</td>
<td>22 ± 1.86</td>
</tr>
<tr>
<td>Second hour</td>
<td>15 ± 0.9</td>
<td>13 ± 0.74</td>
<td>20 ± 1.63</td>
<td>29 ± 2.26</td>
<td>42 ± 2.71</td>
</tr>
</tbody>
</table>

ESR: erythrocyte sedimentation rate.

### Table 4 Clotting parameters, Plt count and blood loss for all groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>GpII</th>
<th>GpIII</th>
<th>GpIV</th>
<th>GpV</th>
</tr>
</thead>
<tbody>
<tr>
<td>PC (%)</td>
<td>95.6 ± 4.2</td>
<td>94.3 ± 4.5</td>
<td>91.8 ± 5.43</td>
<td>92.1 ± 3.67</td>
</tr>
<tr>
<td>(b)</td>
<td>75 ± 7.3</td>
<td>69.7 ± 5.44</td>
<td>70.6 ± 6.4</td>
<td>76.6 ± 9.42</td>
</tr>
<tr>
<td>Plt count</td>
<td>250.5 ± 34.52</td>
<td>228 ± 0.75</td>
<td>248.5 ± 34.13</td>
<td>240.6 ± 27.8</td>
</tr>
<tr>
<td>(b)</td>
<td>222 ± 31.64</td>
<td>181.5 ± 60</td>
<td>227.1 ± 37.2</td>
<td>230 ± 47.38</td>
</tr>
<tr>
<td>aPTT (second)</td>
<td>39 ± 3.03</td>
<td>37.2 ± 6.41</td>
<td>40.1 ± 5.7</td>
<td>41.9 ± 3.8</td>
</tr>
<tr>
<td>(b)</td>
<td>43.1 ± 7.7</td>
<td>46.3 ± 5.12</td>
<td>45.1 ± 3.2</td>
<td>48.1 ± 5.34</td>
</tr>
<tr>
<td>Blood loss (mL)</td>
<td>400 ± 22</td>
<td>401 ± 50</td>
<td>410 ± 48</td>
<td>469 ± 44</td>
</tr>
</tbody>
</table>

(a) Pre-CPB and (b) post-CPB.

PC: prothrombin concentration
Plt: platelet count
aPTT: activated partial thromboplastin time.
the vascular system and into the interstitium and a reduction of plasma COP. This is in agreement with Jansen et al.,\textsuperscript{10} who showed the role of COP in water movement out of the vascular system. In contrast, HES in GpIV and GpV reduces the net movement and interrupts the free movement of Ringer’s solution. This effect starts to appear when the quantity of HES is two-thirds of the prime.

The linear increase in plasma and blood viscosities (Table 3) is in agreement with that of Sade et al.,\textsuperscript{13} while the exponential increase in ESR is in agreement with Mishler.\textsuperscript{14}

The exponential decrease in the suspension stability of RBCs progressively increases the aggregation and sludging of RBCs, which produces a reduction in microcirculation blood flow and tissue perfusion.\textsuperscript{15}

The nonsignificant differences among the four groups with regard to PC, aPTT and Plt count are in agreement with London et al.,\textsuperscript{16} who reported on the safety of HES. On the other hand, GpV shows a large increase in blood loss, which may indicate a negative effect of HES on coagulation, which may be due to the higher HES dose or interference with clotting factors.

The decrease in membrane permeability and elasticity is in accordance with Kameneva et al.,\textsuperscript{17} who studied RBC deformability changes under the effect of mechanical stress and hypothermia and showed that each of these factors can cause a significant decrease in the deformability of RBCs (especially when acting synergistically).

The present study supports the prime mixture with a volume ratio of 1:2 Ringer’s solution to HES because it insures optimal reduction of edema formation, shorter ventilation and recovery times, a reduction in the expected hazards with a massive increase in ESR, which may be pronounced with absolute colloidal prime and avoidance of the negative effect of large doses of HES on the coagulation system.

**References**


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