Clinical aspects of blood activation in open-heart surgery

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Citation for published version (APA):

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Chapter 7

Cell saver device efficiently removes cell-derived microparticles during cardiac surgery

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INTRODUCTION

At the end of cardiac procedures assisted by cardiopulmonary bypass (CPB), a large volume of diluted blood (0.75-1.5 L) remains within the extracorporeal circuit. To reduce transfusion requirements, this blood can be used for autotransfusion with or without processing. One of the options for processing is the use of a Cell Saver device (Haemonetics, Braintree, Mass) that concentrates erythrocytes and discards plasma. During CPB, elevated numbers of cell-derived vesicles, microparticles, are present that promote coagulation and inflammation. The aim of this study was to determine the effects of a Cell Saver device on microparticle counts during a cardiac operation. Heparin and prothrombin fragment F1+2 were measured as controls for the efficient removal of low-molecular-weight substances.

PATIENTS AND METHODS

Patients for elective coronary artery bypass grafting assisted by CPB (n=13) were included after signed informed consent. This study was approved by the Medical Ethics Committee of the Academic Medical Center (Amsterdam, The Netherlands). Blood was collected before and after processing with a Cell Saver device (Cell Saver 5). Cell counts were determined on a Celldyn 4000 hematology analyzer (Abbott, Mijdrecht, The Netherlands). Microparticles, prothrombin fragment F1+2, and heparin were determined as described previously. Concentrations of heparin, microparticles, and F1+2 were corrected for hematocrit. Data were analyzed with SPSS version 11.0 (SPSS, Inc., Chicago, Ill) and presented as medians (interquartile range). The paired-samples t test or Wilcoxon signed rank test was used whenever appropriate.

RESULTS AND DISCUSSION

All data are summarized in Table 1. Processing with the Cell Saver device decreased blood volume about 2-fold from 850 mL to 440 mL. As expected, the hematocrit increased from 0.26 (before) to 0.55 (after cell salvage; p<0.001). The recovery of the erythrocytes was almost 100% (p=0.161). In contrast, about 89% of the platelets (p<0.001) and 31% of the leukocytes (p<0.001) were removed by the Cell Saver device.
Cell saver device removes microparticles

**Table 1. Cell saver device data.**

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
<th>Removal (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Volume (mL)</strong></td>
<td>850 (796-934)</td>
<td>440 (323-481)</td>
<td>53 (46-63)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Hematocrit (L/L)</strong></td>
<td>0.26 (0.24-0.26)</td>
<td>0.55 (48-0.60)</td>
<td>NA</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Erythrocytes (mL)</strong></td>
<td>217 (199-246)</td>
<td>199 (178-253)</td>
<td>3 (-5-17)</td>
<td>0.161</td>
</tr>
<tr>
<td><strong>Thrombocytes (10^9)</strong></td>
<td>140 (85-179)</td>
<td>16 (10-21)</td>
<td>89 (79-91)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Leukocytes (10^9)</strong></td>
<td>4.7 (3.1-6.0)</td>
<td>3.8 (1.5-4.0)</td>
<td>31 (18-45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Heparin (10^3 IU)</strong></td>
<td>1765 (1666-2053)</td>
<td>9 (4-11)</td>
<td>100 (99-100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>F1+2 (nmol)</strong></td>
<td>2.47 (0.50-7.39)</td>
<td>0.04 (0.03-0.05)</td>
<td>98 (92-99)</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>EryMP (10^7)</strong></td>
<td>128 (37-292)</td>
<td>5 (2-5)</td>
<td>97 (86-99)</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>PMP (10^7)</strong></td>
<td>147 (93-191)</td>
<td>1 (1-2)</td>
<td>99 (98-99)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are presented as medians (interquartile ranges). NA, not applicable; F1+2, prothrombin fragment; EryMP, erythrocyte-derived microparticles; PMP, platelet-derived microparticles.

Small molecules like heparin and F1+2 were removed efficiently by 100% (p<0.001) and 98% (p=0.003), respectively. The data demonstrating the efficiency of the Cell Saver device to recover erythrocytes and to remove platelets, leukocytes, and heparin are all in
close agreement with data provided by the manufacturer in the Cell Saver 5 Equivalence Validation Report of September 20, 1993 (95.8% erythrocyte recovery; 82% and 24.3% for platelets and leukocytes, respectively; 97.8% for heparin).

Cell-derived microparticles are, on average, smaller in diameter than platelets and range in size from about 100 nm to 1.0 μm. Thus, the largest microparticles may overlap in size with platelets, which on average range in size from 1.0 μm to 5.0 μm. Both erythrocyte-derived microparticles and platelet-derived microparticles were removed efficiently (97% and 99%; p=0.002 and p<0.001, respectively). Interestingly, the efficiency of the Cell Saver device to remove platelet-derived microparticles as well as erythrocyte-derived microparticles was significantly increased compared with the efficiency to remove thrombocytes (p=0.019 and p=0.002, respectively; Wilcoxon signed rank test. Thus, cell-derived vesicles, which on average are smaller in diameter than thrombocytes, are removed more efficiently from blood by a Cell Saver device than thrombocytes in a clinical setting.

This study is the first to directly evaluate the efficiency of a Cell Saver device to remove cell-derived microparticles from patient blood. Our data show that a Cell Saver device efficiently reduces the numbers of coagulation- and inflammation-promoting microparticles. From these data we cannot exclude that microparticles may bind to cells present within the blood, or that low numbers of microparticles are generated by cell activation during the passage of blood through the Cell Saver device.
REFERENCES

