Hemodilution, blood transfusion, and regional oxygenation

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Acute hemodilution in a chronic polycythemic patient may be deleterious
Chapter 7
Introduction
A few data from animal studies in an acute polycythemic model showed that this situation was associated with a decreased cardiac output (CO) and increased systemic vascular resistance (SVR) because of an increased blood viscosity.\textsuperscript{1-3} However, the concept of decreased CO and increased SVR with polycythemia, as hypothesized in the literature, was never confirmed in man and especially not in relation to chronic polycythemia. In contrast to polycythemia, acute isovolemic hemodilution leads to an increase in CO, a decrease in SVR, and finally an increase in the oxygen extraction. These observations are summarized in the concept of an optimal hematocrit range for maximum oxygen transport. However, there is no report in the literature on the effects of acute isovolemic hemodilution, starting with chronic polycythemia and ending with a hematocrit well below normal value, while monitoring systemic hemodynamic and oxygenation parameters. We describe the treatment and the effects of acute hemodilution in a patient with chronic polycythemia undergoing surgery for an erythropoietin producing renal tumor.

Case report
An 80-year-old woman was to be operated for an erythropoietin producing renal tumor. Physical examination and laboratory tests on admission revealed an arterial blood pressure 160/75 mmHg, an erythropoietin level of 116 U l\textsuperscript{-1} (normal range: 1-10 U l\textsuperscript{-1}), and a Ht of 62 %. The ECG showed signs of left ventricular hypertrophy. The patient was treated with nifedipin and atenolol for chronic hypertension. Since polycythemia needed correction before surgical intervention, it was decided to perform acute isovolemic hemodilution just prior to surgery, which would also result in a quantity of autologous blood for retransfusion during surgery if acute bleeding should occur.
Chapter 7

After having obtained informed consent, and before anesthesia was induced, venous and arterial cannules were inserted, including a pulmonary artery thermodilution catheter (Edwards 7 Fr; Baxter Healthcare Corp, USA) through the right jugular vein. Baseline measurements of the mean arterial blood pressure (MAP), pulmonary artery pressure (PAP), pulmonary artery wedge pressure (PAWP), central venous pressure (CVP), and cardiac index (CI) were made before anesthesia. Arterial and mixed venous blood samples were obtained for the determination of hemoglobin (Hb), Hb oxygen saturation, Ht, PO₂, PCO₂, and pH. From this data, systemic vascular resistance index (SVRI), pulmonary vascular resistance index (PVRI), left ventricle stroke work index (LVSWI), systemic oxygen delivery (DO₂), oxygen consumption (VO₂), and oxygen extraction ratio (O₂ER) were calculated. In addition, whole blood and plasma viscosity, including erythrocyte aggregability, were measured. The microcirculation (sublingual mucosa) was visualized using orthogonal polarization spectral (OPS) imaging (Cytoscan, Cytometrics, PA, USA).

Anesthesia was induced with thiopental 5 mg kg⁻¹, fentanyl 2 μg kg⁻¹, and rocuronium 0.5 mg kg⁻¹. Following tracheal intubation, the lungs were ventilated with a mixture of oxygen in air (FiO₂: 0.4), maintaining normocapnia. Anesthesia was maintained with isoflurane 0.4-0.7 % and fentanyl; muscle relaxation was maintained with rocuronium. After induction of anesthesia, isovolemic hemodilution was performed by withdrawal of blood and simultaneous infusion of a gelatin solution (Gelofusine®) in a ratio of 2:3. Following baseline measurements after induction of anesthesia, all measurements were repeated after exchange of 500, 1000, 1500, 2000, and 2500 ml, and after retransfusion of 500 ml autologous blood. A selection of the parameters is depicted in table 7.1.

At baseline a CI above the normal range and a low SVRI were found, which is in contrast to what was expected. Exchange of up to 2000 ml blood resulted in a decrease in Ht from 59 to 34 %. During hemodilution, CI
### Table 7.1. Systemic hemodynamic and oxygenation parameters during hemodilution.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>pre-an</th>
<th>post-an</th>
<th>-500</th>
<th>-1000</th>
<th>-1500</th>
<th>-2000</th>
<th>-2500</th>
<th>-500</th>
<th>post-op</th>
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<tr>
<td>Ht</td>
<td>59</td>
<td>57</td>
<td>49</td>
<td>41</td>
<td>39</td>
<td>34</td>
<td>30</td>
<td>37</td>
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<td>121</td>
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<td>84</td>
<td>100</td>
<td>114</td>
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<td>77</td>
<td>101</td>
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<td>73</td>
<td>60</td>
<td>69</td>
<td>74</td>
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<td>60</td>
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<td>79</td>
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<td>PAWP</td>
<td>16</td>
<td>16</td>
<td>12</td>
<td>19</td>
<td>25</td>
<td>23</td>
<td>23</td>
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<td>12</td>
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<tr>
<td>CI</td>
<td>4.71</td>
<td>4.71</td>
<td>4.27</td>
<td>5.29</td>
<td>5.27</td>
<td>4.41</td>
<td>4.43</td>
<td>5.34</td>
<td>7.5</td>
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<td>SVRI</td>
<td>1883</td>
<td>1561</td>
<td>1384</td>
<td>1286</td>
<td>1457</td>
<td>1215</td>
<td>1046</td>
<td>1228</td>
<td>906</td>
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<tr>
<td>PVRI</td>
<td>271</td>
<td>187</td>
<td>187</td>
<td>197</td>
<td>197</td>
<td>200</td>
<td>216</td>
<td>165</td>
<td>96</td>
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<tr>
<td>P_{O_2}</td>
<td>5.9</td>
<td>7.4</td>
<td>7.4</td>
<td>7.3</td>
<td>7.0</td>
<td>6.8</td>
<td>6.8</td>
<td>6.1</td>
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<tr>
<td>S_{O_2}</td>
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<td>88</td>
<td>87</td>
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<td>85</td>
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<tr>
<td>DO_{2}</td>
<td>957</td>
<td>925</td>
<td>760</td>
<td>827</td>
<td>778</td>
<td>567</td>
<td>479</td>
<td>744</td>
<td>710</td>
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<td>VO_{2}</td>
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<td>93</td>
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<td>103</td>
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<td>11</td>
<td>13</td>
<td>14</td>
<td>15</td>
<td>12</td>
<td>18</td>
<td>14</td>
</tr>
</tbody>
</table>

Before induction of anesthesia (pre-an), after induction of anesthesia (post-an), during hemodilution, where (-) denotes the withdrawal and (+) the administration of blood, and finally post-operative (post-op). ([normal values])

Ht: hematocrit (%), MAP: mean arterial pressure (mmHg), HR: heart rate (beats per minute), PAWP: pulmonary artery wedge pressure (mmHg), CI: cardiac index (l min\(^{-1}\)m\(^2\)), SVRI: systemic vascular resistance index (dyn s cm\(^{-5}\)m\(^{-2}\)), PVRI: pulmonary vascular resistance index (dyn s cm\(^{-5}\)m\(^{-2}\)), P_{O_2}: mixed venous P_{O_2} (kPa), S_{O_2}: mixed venous saturation (%), DO_{2}: systemic O_{2} delivery (ml min\(^{-1}\)m\(^2\)), VO_{2}: systemic O_{2} consumption (ml min\(^{-1}\)m\(^2\)), O_{2}ER: systemic O_{2} extraction ratio (%).
Figure 7.1. Images of the sublingual microcirculation using OPS imaging (Cytoscan).

A The microcirculation of the presented polycythemic patient before induction of anesthesia, and B the microcirculation of a healthy, normocytic volunteer. These images clearly show an increased number of microcirculatory networks with significantly dilated venules in the polycythemic patient as compared to normal. During the whole procedure this image did not change.
Hemodilution and polycythemia

increased only slightly despite a further decrease in SVRI. PAWP and CVP increased. Because of just a slight increase in CI, in combination with the decreasing arterial oxygen content (CaO₂), the DO₂ gradually decreased and the low O₂ER at baseline increased from 10 to 15%. The very high whole blood viscosity returned to normal values at a Ht of 34%.

Upon further hemodilution (to Ht 30%), VO₂ suddenly decreased to a value of 40% of baseline, while the O₂ER remained at a low level (12%). At this last step of hemodilution, MAP fell to 77 mmHg, which was accompanied by acute ST depression and inverse T waves on the ECG. Because of these sudden changes, it was decided to retransfuse 500 ml of autologous blood to a Ht of 37%. Upon retransfusion, the ECG abnormalities disappeared and VO₂ increased above post-anesthetic baseline values.

OPS imaging showed an increased number of microcirculatory networks with significantly dilated venules as compared to normal (figure 7.1). During the whole procedure this image did not change.

After retransfusion the surgical procedure was started. Because of metastases, surgery was discontinued after obtaining some tissue samples from the tumor. The postoperative course was uneventful and treatment with chemotherapy was started.

Discussion

It is generally accepted that isovolemic hemodilution is accompanied by an increase in CO, whereas hemoconcentration (e.g. chronic polycythemia) results in a decrease in CO, due mostly to changes in SVR, caused by differences in blood viscosity. However, in the present chronically polycythemic patient, systemic baseline parameters were not conform this theory: the CI was not decreased but elevated and the SVRI was not increased but below normal levels. Together with the OPS images, these findings are suspect for shunting of blood at tissue level, which may explain the fixed low O₂ER, decreased SVRI despite high viscosity, and conse-
quentley the high CI. The images, as well as the O2ER, remained unchanged during hemodilution, suggesting that the possible shunting persisted. The observations during isovolemic hemodilution in our patient did not confirm the hypothesis of an optimal hematocrit range for tissue oxygenation. As blood is bypassing the capillary beds, more oxygen ends up at the venous side of the vascular bed, without being utilized by the tissues, as reflected in the present case by the P, O₂ and S, O₂. Even when the VO₂ started to decrease at Ht 34 % (Hb: 9.5 g dl⁻¹), indicating that oxygen uptake had reached a state of oxygen supply dependency, P, O₂ and S, O₂ showed little change. The critical level of hemodilution at Ht 34 % is in contrast with previous reports, where in anesthetized animals¹,³,⁵,⁶ and humans⁷ a critical Ht of 9 - 12 % could be demonstrated. At further hemodilution to a Ht of 30 %, VO₂ decreased severely and cardiac ischemia became apparent on the ECG registration, indicating that in our patient at an Ht of 30 % (Hb: 8.0 g dl⁻¹) myocardial oxygenation was already compromised. In a recent study of hemodilution down to a Hb level of 5.2 g dl⁻¹ in awake volunteers, 3 out of 55 subjects showed ECG changes, but not before a Hb level between 5.0 and 6.7 g dl⁻¹.⁸ Administration of 500 ml autologous blood not only restored the hemodynamics but also led to an overshoot in VO₂, which might very well have served to meet a possible oxygen debt.

Based on the above data, it may be hypothesized that chronic polycythemia is compensated for by peripheral shunting of the blood. This adaptional response to conditions of increased blood viscosity does not seem to change during acute hemodilution, thereby decreasing the tolerance for acute isovolemic hemodilution. One might argue that advanced age or the chronic use of a β-blocking agent may have influenced the critical point of hemodilution. However, in clinical studies it has been demonstrated that the compensatory mechanisms are independent of these factors.⁹,¹⁰

In conclusion, from the results of the presented case it may be hypothesized that chronic polycythemia is compensated by peripheral shunting, of
which the exact nature is subject for further investigation. Meanwhile one should be cautious with acute hemodilution to subnormal levels in chronically polycythemic patients, since this may well be deleterious for the patient.

References


