Effects of polycythaemia and haemodilution on circulation in neonates

Verena H A Mandelbaum, Carlos D Guajardo, Mathias Nelle, Otwin Linderkamp

Abstract
Haemodilution in nine neonates resulted in significant mean (SEM) decrease of packed cell volume (0.67 (0.01) to 0.55 (0.01)) and increases in cardiac output (250 (16) to 308 (25) ml/min/kg) and blood flow velocities of the internal carotid artery and the coeliac artery (+20%). However, red cell flows in the aorta, carotid and coeliac arteries did not change during haemodilution, thereby indicating that haemodilution did not improve oxygen transport.

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Neonatal polycythaemia increases the risk of pulmonary hypertension, renal failure, necrotising enterocolitis, cerebral ischaemia, intracranial haemorrhage, and developmental retardation. The clinical manifestations of polycythaemia result from the rise in blood viscosity. Previous studies have shown that cardiac output and cerebral blood flow velocity in polycythaemic neonates increased more than 30% during isovolaemic haemodilution (partial exchange transfusion). Blood flow in gastrointestinal arteries of polycythaemic infants has not been studied. However, experiments in puppies have shown that polycythaemia decreases gastrointestinal blood flow by more than 40%. The present study was designed to evaluate the effects of polycythaemia and haemodilution on cardiac output and blood flow velocities of cerebral and coeliac arteries in newborn infants.

Subjects and methods
Nine neonates with a packed cell volume above 0.60 and signs of polycythaemia (for example, cyanosis, increased respiration rate, or jitteriness) were studied at between 4 and 120 hours of birth (polycythaemic group). Their gestational age ranged from 33 to 41 weeks and their birth weight ranged from 2800 to 4410 g. Nine healthy neonates with gestational age of 34 to 40 weeks and birth weight of 2900 to 3800 g with a packed cell volume below 0.60 were studied at between 6 and 120 hours of birth (control group). The study protocol was approved by the ethical committee of the University Hospital Centre of Heidelberg. Informed consent was obtained from the parents in each case. In each group, five infants were born by caesarean section, and four were delivered vaginally. All infants had birth weights appropriate for their gestational age (10th to 90th centile according to the Munich charts). The umbilical cords were clamped within 20 seconds of birth. In the polycythaemic infants, isovolaemic haemodilution was performed with serum (Biseko, Biotest) via an umbilical vein catheter. The haemodilution procedure lasted about two hours and was continued until the packed cell volume was about 0.55.

Cardiovascular measurements in the polycythaemic infants were done before and one to two hours after haemodilution. During the examinations, infants were either sleeping or quiet and in supine position. Blood flow velocities and cardiac output were measured using an Interspec XL pulsed Doppler ultrasound system (Interspec Inc). Details of the cardiac output method have been reported elsewhere. Systolic blood flow velocities were measured using a 5.0 MHz pulsed Doppler transducer. The arteries were identified by duplex scan mode. The right and left internal carotid artery were localised via the anterior fontanelle. As there were no significant differences between the two internal carotid arteries, the mean velocities of both arteries were calculated for each infant. The coeliac artery was localised by ultrasound from a longitudinal abdominal section and blood flow velocity was determined close to the origin of the artery from the abdominal aorta.

Packed cell volume was determined by the microhaematocrit method. Mean arterial blood pressure was measured in the right and left upper arm using an oscillometric technique (Dinamap 847, Critikon). Systemic flow resistance was calculated as mean pressure to cardiac output ratio.

Results
The packed cell volume decreased from mean (SEM) 0.67 (0.01) (range 0.63 to 0.70) before isovolaemic haemodilution to 0.55 (0.01) (range 0.52 to 0.58) after the procedure (table). Cardiac output and blood flow velocities of the internal carotid artery and the coeliac artery were significantly decreased in the polycythaemic infants when compared with the control group. During haemodilution, the blood flow parameters in the polycythaemic group increased to the values of the control group. The increase in cardiac output was mainly due to a rise in stroke volume, whereas the heart rate increased only slightly. Red blood cell flow was calculated as the product of cardiac output or blood flow velocity times packed cell volume. These calculated red cell flow values and systolic blood pressure were similar in polycythaemic and control infants and did not change with haemodilution. Systemic blood flow resistance
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<table>
<thead>
<tr>
<th></th>
<th>Control infants</th>
<th>Polycythaemic infants</th>
<th>Difference</th>
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<tbody>
<tr>
<td></td>
<td>Before haemodilution</td>
<td>After haemodilution</td>
<td></td>
</tr>
<tr>
<td>Packed cell volume (PCV)</td>
<td>0.54 (0.01)*</td>
<td>0.67 (0.01)</td>
<td>0.55 (0.01)</td>
</tr>
<tr>
<td>Systolic blood pressure (P, mm Hg)</td>
<td>54 (1)</td>
<td>58 (5)</td>
<td>57 (2)</td>
</tr>
<tr>
<td>Stroke volume (mL/kg)</td>
<td>2.4 (0.1)*</td>
<td>2.0 (0.2)</td>
<td>2.4 (0.2)</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>124 (3)</td>
<td>122 (4)</td>
<td>127 (3)</td>
</tr>
<tr>
<td>Cardiac output (Q, mL/min/kg)</td>
<td>296 (14)*</td>
<td>250 (16)</td>
<td>308 (25)</td>
</tr>
<tr>
<td>Red cell flow (Q×PCV)</td>
<td>159 (11)</td>
<td>167 (10)</td>
<td>171 (12)</td>
</tr>
<tr>
<td>Systemic flow resistance (R=Q/P)</td>
<td>18 (1)*</td>
<td>26 (9)</td>
<td>19 (2)</td>
</tr>
<tr>
<td>Blood flow velocities (cm/sec)</td>
<td>42 (3)</td>
<td>34 (2)</td>
<td>41 (4)</td>
</tr>
<tr>
<td>Internal carotid artery (ICA)</td>
<td>24 (2)</td>
<td>23 (2)</td>
<td>22 (2)</td>
</tr>
<tr>
<td>Coeliac artery (CA)</td>
<td>68 (3)*</td>
<td>58 (3)</td>
<td>69 (3)</td>
</tr>
<tr>
<td>CA×PCV</td>
<td>36 (2)</td>
<td>39 (2)</td>
<td>38 (2)</td>
</tr>
</tbody>
</table>

Data are mean (SEM) 95% confidence intervals around the mean values and the mean differences can be calculated as 2×SEM. *p<0.05 when compared to the polycythaemic infants before haemodilution. An unpaired t test was used to compare control and polycythaemic infants and a paired t test was used to test for changes in the measured parameters in the polycythaemic infants during haemodilution.

(blood pressure/cardiac output) decreased with haemodilution according to the rise in cardiac output.

Discussion

From the present data we conclude that cardiac output and blood flow velocities in cerebral and gastrointestinal arteries of polycythaemic neonates increase significantly as a result of isovolaemic haemodilution. However, systemic red cell blood transport was not affected by polycythaemia and haemodilution. Assuming that the blood flow velocities in the cerebral and coeliac arteries reflect the actual blood flows, red cell flows to the brain and the gastrointestinal tract were also not altered by haemodilution (table). Swetnam et al observed that cardiac output increased by 32% and systemic oxygen transport increased by 13% immediately after exchange transfusion. This may be explained by a higher packed cell volume (mean 0.72) before haemodilution.

Systemic blood flow resistance (computed as systolic blood pressure to cardiac output ratio) decreased with haemodilution according to the rise in cardiac output (table). Flow resistance is often used as an indicator of vessel diameter, but in circular vessels it is the product of blood viscosity and vascular hindrance (that is, vessel geometry). In the present study, blood viscosity was not measured. However, blood viscosity calculated from previously published nomograms decreased by the same percentage (~20%) as systemic flow resistance. This suggests that the decrease in systemic flow resistance during haemodilution was due to a decrease in blood viscosity, whereas vascular hindrance probably remained unchanged.

In human adults, systemic red cell flow and red cell transport to most organs tend to decrease at packed cell volume values above 0.55, whereas our results suggest that in neonates red cell flow does not change up to a packed cell volume of 0.70. Different circulatory responses of adults and neonates to polycythaemia may be due to altered vessels in adults or to favourable rheological properties of neonatal blood. Blood viscosity in neonates decreases less with rising packed cell volume than in adults when viscosity measurements are done in a narrow tube with a diameter of 50 μm. In these narrow tubes, transport of neonatal blood does not significantly change when the packed cell volume is increased from 0.50 to 0.70, whereas in adults red cell transport decreases at packed cell volumes above 0.60.

We conclude that polycythaemia and haemodilution in neonates do not affect systemic, cerebral, and gastrointestinal oxygen transport in neonates as long as the packed cell volume does not exceed 0.70.

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