Effect of blood transfusion on the carbon monoxide transfer factor of the lung in man

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Summary

1. Ten studies were performed on nine patients with haematological disorders but with normal lungs, who required intermittent blood transfusions. The transfer factor for carbon monoxide and uptake of carbon monoxide per unit lung volume ($K_{CO}$) were measured with the single breath technique before and at various intervals after transfusion.

2. The mean haemoglobin concentration increased from 7.7 to 11.1 g/dl.

3. The $T_{1}CO$ increased according to a formula based on the Roughton & Forster (1957) diffusion equations, $T_{1}CO$ (standardized) = $T_{1}CO$ (observed).$(10.2 + Hb)/1.7 Hb$, where haemoglobin (Hb) is expressed as g/dl.

4. The correlation between measured and predicted values was slightly better if changes in alveolar volume were taken into account, by using the $K_{CO}$ value.

Key words: anaemia, blood transfusion, carbon monoxide, lung, pulmonary function tests.

Introduction

The measurement of the transfer factor of the lung for carbon monoxide provides valuable information on the state of the lungs in disease. The dependence of this index on haemoglobin concentration has been demonstrated previously in patients with chronic anaemia (Guleria, Pande, Markose, Gupta & Jain, 1971; Oinakara, Blumenthal, Johnston, Kauffman & Solnick, 1970) and polycythaemia (Herbert, Weill, Stuckey, Urner, Gonzales & Ziskand, 1965; Burgess & Bishop, 1963).

Serial measurements of the carbon monoxide-diffusing capacity in an individual play an important role in the assessment of patients in whom day-to-day changes in carbon monoxide uptake may occur. For example, in the presence of pulmonary haemorrhage, the uptake of carbon monoxide per unit of lung volume ($K_{CO}$) may rise to two or three times the base-line value (Ewan, Jones, Rhodes & Hughes, 1976). Thus repeated measurements of the $K_{CO}$ can monitor disease activity in patients with Goodpasture's syndrome.

Many patients with pulmonary haemorrhage require blood transfusion. Since the correction factor for haemoglobin concentration in general use in the calculation of carbon monoxide uptake has only been verified in patients with iron-deficiency anaemia, in whom gradual changes in haemoglobin concentration occurred (Cotes, Dabbs, Elwood, Hall, McDonald & Saunders, 1972), it was important to ascertain whether the same relationship was valid when rapid changes occurred as the result of blood transfusion. The correction factor used by Cotes et al. (1972) was

Abbreviations: $T_{1}CO$, transfer factor (diffusing capacity) for carbon monoxide; $K_{CO}$, transfer factor per unit alveolar volume ($T_{1}CO$/alveolar volume); $FEV_{1.0}$, forced expired volume in 1 s; $VC$, vital capacity.

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based on the diffusion equation for carbon monoxide transfer from alveolar gas to pulmonary capillary blood worked out by Roughton & Forster (1957), who showed that the transfer of carbon monoxide was dependent on the diffusing capacity of the alveolo-capillary membranes, the rate of reaction of carbon monoxide with haemoglobin and the quantity of haemoglobin present in the pulmonary capillary bed (see the Theory section).

Rankin, McNeill & Forster (1961) studied five patients before and after blood transfusion. The diffusing capacity for carbon monoxide rose after transfusion, but this increase was greater than that predicted either by the Roughton & Forster (1957) relationship, or that found when chronic anaemias were corrected. However, their measurements were often made on ill and shocked patients, and the initial value for diffusing capacity may possibly have been low from haemodynamic changes. We have applied the correction factor for haemoglobin based on the Roughton & Forster (1957) equation to patients whose haemoglobin had changed rapidly as a result of blood transfusion, but whose clinical status was otherwise unaltered.

Methods

The subjects were fit and co-operative, with no history of recent acute blood loss. They ranged in age from 25 to 75 years, most being in the younger age group. They had no evidence of pulmonary disease. Mean FEV1/VC ratio was 81% (range 73–87%). Two had a reduction of vital capacity (83 and 79% predicted). All, except one, had had previous multiple blood transfusions. Nine patients were studied; diagnoses, change in the haemoglobin concentration after transfusion and the time interval between the completion of the transfusion and transfer-factor measurements are shown in Table 1. Patient no. 2 was studied on two separate occasions (Table 1: 2a, 2b). Six of the patients were admitted to hospital as day cases for the transfusion and all were fit and mobile. They received between 1500 and 2000 ml of whole blood or the equivalent of packed cells, at a maximum rate of infusion of 150 ml/h. The mean rise in haemoglobin after transfusion was 3·3 ± 1·3 SD g/dl.

Immediately before transfusion, the FEV1 and vital capacity were measured with a bellows spirometer. The single-breath diffusing capacity for carbon monoxide (TLCO) was then measured three times (Ogilvie, Forster, Blakemore & Morton, 1957) with inspired concentrations of 0·3% carbon monoxide and 10% helium, and mean values were obtained. The mean coefficient of variation for these measurements was 5%. No correction for back pressure was included. Alveolar volume was measured simultaneously by single-breath helium dilution and results were thus obtained for TLCO and TLCO/alveolar volume (KCO). This procedure was repeated less than 1–96 h after transfusion (Table 1). The haemoglobin concentration was measured at the beginning of the transfusion for the first six patients, and within 4 h of these measurements in the others. In no patient were there clinical signs or symptoms of fluid overload.

Theory

Roughton & Forster (1957) described the overall diffusing capacity (transfer factor) of the lungs for carbon monoxide (TL) in terms of eqn. (1).

$$\frac{1}{T_L} = \frac{1}{D_m} + \frac{1}{\Theta V_c} \quad (1)$$

$1/D_m$ is the resistance of the membrane to diffusion, $V_c$ is the capillary blood volume and $\Theta$ is the rate of combination of carbon monoxide at a normal haemoglobin concentration. Cotes et al. (1972) measured the change in transfer factor after correction of chronic anaemia by iron replacement. They confirmed that the value of Roughton & Forster for $\Theta$ effectively defined the steady-state relationship of transfer factor to haemoglobin concentration. Thus:

$$\frac{1}{T_L} = \frac{1}{D_m} + \frac{1}{\Theta'[\text{Hb}].V_c} \quad (2)$$

where $\Theta'$ is the rate of combination of carbon monoxide at a normal haemoglobin concentration and [Hb] is the haemoglobin concentration as a fraction of normal (14·6 g/dl). $\Theta'$ depends on the plasma oxygen tension in alveolar capillaries, the capacitance coefficient of blood for carbon monoxide and the diffusion barrier of the erythrocyte membrane to gas transfer. We have followed Cotes et al. (1972), assuming a value of 1 for $\Theta'$ (breathing air) and expressing [Hb] in absolute terms as g/dl. A $D_m/V_c$ ratio of 0·7 was assumed, derived from studies of normal subjects (Frans, 1970). Thus by rearrangement of eqn. (2):

$$T_L\text{CO}(\text{standardized}) = T_L\text{CO}(\text{observed}). \frac{14·6a + \text{Hb}}{(1 + a)\text{Hb}} \quad (3)$$

where $a$ is the ratio $D_m/V_c$. 
Table 1. Details of patients, including haemoglobin concentrations before and after transfusion, and time interval between the end of transfusion and the measurement of diffusing capacity

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Diagnosis</th>
<th>Age (years)</th>
<th>Haemoglobin (g/dl)</th>
<th>Interval between transfusion and testing (h)</th>
<th>$\textit{T} _1\textit{CO}$ (mmol min$^{-1}$ kPa$^{-1}$)</th>
<th>$K_{CO}$ (mmol min$^{-1}$ kPa$^{-1}$ l$^{-1}$)</th>
<th>Change of alveolar volume (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
<td>After</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Paroxysmal nocturnal haemoglobinuria</td>
<td>24</td>
<td>9.8</td>
<td>12.7</td>
<td>&lt;1</td>
<td>11.52</td>
<td>10.46</td>
</tr>
<tr>
<td>2*</td>
<td>(a) Chronic myeloid leukaemia</td>
<td>55</td>
<td>10.3</td>
<td>12.1</td>
<td>&lt;1</td>
<td>5.72</td>
<td>5.53</td>
</tr>
<tr>
<td></td>
<td>(b) Chronic myeloid leukaemia</td>
<td>55</td>
<td>9.8</td>
<td>11.6</td>
<td>&gt;1</td>
<td>3.8</td>
<td>4.7</td>
</tr>
<tr>
<td>3</td>
<td>Multiple myeloma</td>
<td>58</td>
<td>8.1</td>
<td>14.2</td>
<td>&lt;1</td>
<td>4.66</td>
<td>5.39</td>
</tr>
<tr>
<td>4</td>
<td>Chronic myeloid leukaemia</td>
<td>25</td>
<td>7.0</td>
<td>10</td>
<td>&lt;1</td>
<td>5.64</td>
<td>7.1</td>
</tr>
<tr>
<td>5</td>
<td>Autoimmune haemolytic anaemia</td>
<td>45</td>
<td>7.0</td>
<td>9.7</td>
<td>&lt;1</td>
<td>6.58</td>
<td>8.94</td>
</tr>
<tr>
<td>6</td>
<td>Sideroblastic anaemia</td>
<td>76</td>
<td>6.3</td>
<td>9.4</td>
<td>&lt;1</td>
<td>3.37</td>
<td>4.28</td>
</tr>
<tr>
<td>7</td>
<td>Acute myeloid leukaemia</td>
<td>48</td>
<td>6.5</td>
<td>10.7</td>
<td>5</td>
<td>4.43</td>
<td>5.32</td>
</tr>
<tr>
<td>8</td>
<td>Erythrocyte aplasia</td>
<td>47</td>
<td>5.3</td>
<td>9.6</td>
<td>14</td>
<td>3.23</td>
<td>3.96</td>
</tr>
<tr>
<td>9</td>
<td>Goodpasture's syndrome</td>
<td>49</td>
<td>7.7</td>
<td>10.6</td>
<td>60</td>
<td>2.51</td>
<td>2.98</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td>47</td>
<td>7.8</td>
<td>11.1</td>
<td>5.12</td>
<td>5.87</td>
</tr>
</tbody>
</table>

* This patient was studied on two occasions (a, b).
Fig. 1 shows the expected change in transfer factor for carbon monoxide for an alteration in haemoglobin concentration as predicted by eqn. (3). In practice, results are corrected in order to correspond to an arbitrary normal haemoglobin of 14.6 g/dl. A similar curve can be drawn for $K_{CO}$. There is no theoretical justification for the linear correction which Dinakara et al. (1970) fitted empirically to their data.

Results

Observed values of $T_{L}CO$ and $K_{CO}$ before and after transfusion, uncorrected for changes in haemoglobin concentrations, show a rise in $T_{L}CO$ in all but two patients (Table 1). These two patients were among those tested immediately after transfusion and both showed a significant fall in alveolar volume at this time. All patients, however, showed a rise in $K_{CO}$ after transfusion. Thus, despite a fall in alveolar volume, the uptake of carbon monoxide of the ventilated alveoli rose as expected. Table 1 shows the change in alveolar volume after transfusion for all the patients. Since the vital capacity did not change, the falls in alveolar volume were caused by a fall in residual gas volume.

The values obtained for $T_{L}CO$ and $K_{CO}$, corrected for the differing haemoglobin concentrations by using eqn. (2), are plotted in Fig. 2. The values for $T_{L}CO$ and $K_{CO}$ before and after transfusion follow the line of identity, matching the predictions from the Roughton & Forster (1957) equation, especially for $K_{CO}$ which takes changes in alveolar volume into account. For $K_{CO}$, the regression equation is $K_{CO}$ (before transfusion) = 0.986 $K_{CO}$ (after transfusion) + 0.056 ($r = 0.968$). The intercept did not differ significantly from zero ($P > 0.1$) and the regression coefficient was not significantly different from 1.0 ($P > 0.1$).

Discussion

These results demonstrate that the commonly used correction factor for haemoglobin may be applied in patients who have recently received a blood transfusion. A fall in alveolar volume was seen in several patients who were studied immediately after
transfusion, which may be due to an increase in central blood volume, with or without some alveolar oedema. The most marked change in alveolar volume, however, occurred in the youngest patient in the group and the oldest subject showed no significant change. Maldistribution of gas in the lung may also account for this change, perhaps associated with bronchial constriction; an allergic phenomenon could be responsible. However, there was no significant fall in the values for FEV₁₀ and residual volume did not rise. When these changes in alveolar volume are used in the derivation of the value for $K_{CO}$, the correlation of the results with the change in haemoglobin concentration improved.

The correction factor used in this study assumes a $D_m/V_e$ ratio of 0.7. Changes in the pulmonary capillary volume might also occur with blood transfusion, and hence change the value for this ratio. In eqn. (3) the $D_m/V_e$ ratio appears in both the numerator and denominator and so changes would need to be large to influence the usefulness of the prediction. Nevertheless, in patients who have large alterations in pulmonary capillary blood volume due to shock or cardiac failure, the correction factor may not be valid.

The permeability of the erythrocyte membrane relative to that of the cell interior is assumed to be infinite in this situation and this is reflected in the value given for the $D_m/V_e$ ratio. Nevertheless, even if a lower, and possibly more accurate, value for the permeability of the cell interior to carbon monoxide is taken (Holland, 1969) this would not significantly affect the results.

The Roughton & Forster (1957) equation appears to define the relationship between haemoglobin and carbon monoxide uptake well, when acute changes occur as the result of transfusion. The correction factor may then be used with confidence provided that the patient has no gross alteration in his haemodynamic state.

References


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