Non-invasive assessment of shunt and ventilation/perfusion ratio in neonates with pulmonary failure

H L Smith, J G Jones

Abstract

Aims—To make non-invasive measurements of right to left (R-L) shunt and reduced ventilation/perfusion ratio (V\textsubscript{A}/Q) in neonates with pulmonary failure and to examine sequential changes in these variables after treatment.

Methods—Twelve neonates with pulmonary failure were studied. They ranged in gestational age from 24 to 37 (median 27) weeks and were 1–39 (median 4) days old. Shunt and reduced V\textsubscript{A}/Q were derived from their effects on the relation between inspired oxygen pressure (PIO\textsubscript{2}) and arterial oxygen saturation measured with a pulse oximeter (Sp\textsubscript{O}2). Pairs of PIO\textsubscript{2} v Sp\textsubscript{O}2 data points were obtained by varying PIO\textsubscript{2} in a stepwise fashion. A computer algorithm based on a model of pulmonary gas exchange fitted a curve to these data. With PIO\textsubscript{2} on the abscissa, an increase in shunt produced a downward movement of the curve, whereas reducing V\textsubscript{A}/Q to < 0.8 shifted the curve to the right. The right shift gives a variable that is inversely related to V\textsubscript{A}/Q, the PIO\textsubscript{2} – P\textsubscript{o}2 difference, where P\textsubscript{o}2 is mixed capillary oxygen pressure.

Results—Ten of the 12 infants on the first study day had large shunts (range 5.9–31.0%, median 19.9%, normal < 8%) and large PIO\textsubscript{2} – P\textsubscript{o}2 differences (range 9.7–64.4 kPa, median 19.8 kPa, normal < 7 kPa) equivalent to a median V\textsubscript{A}/Q of 0.2 (normal median V\textsubscript{A}/Q = 0.8). Sequential improvement in shunt and V\textsubscript{A}/Q were shown in most infants after treatment. Sudden large changes in these variables were shown in two infants.

Conclusion—This simple non-invasive method distinguishes between shunt and reduced V\textsubscript{A}/Q in neonates with pulmonary failure.

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Keywords: shunt; V\textsubscript{A}/Q; non-invasive; oxygen saturation

A reduced ventilation/perfusion ratio (V\textsubscript{A}/Q) and an increased shunt cause quite different, but characteristic, effects on the relation between inspired oxygen pressure (PIO\textsubscript{2}) and arterial oxygen saturation measured with a pulse oximeter (Sp\textsubscript{O}2). A reduced V\textsubscript{A}/Q in the absence of shunt reduces both alveolar oxygen (P\textsubscript{A}O\textsubscript{2}) and oxygen saturation but increasing the PIO\textsubscript{2} washes out alveolar nitrogen, restores P\textsubscript{A}O\textsubscript{2}, and corrects desaturation. In contrast, an isolated shunt reduces oxygen saturation, but increasing PIO\textsubscript{2} does not correct this because the shunted blood is never exposed to the increased PIO\textsubscript{2}. The non-shunted blood is almost fully saturated, and even administering 100% oxygen adds only a small amount of dissolved oxygen, which cannot compensate for the effect of the shunt.

It may be important in neonates to differentiate between a reduced V\textsubscript{A}/Q and a shunt. For example, in an animal model of surfactant deficiency when surfactant was administered into the airways either as a bolus or as an aerosol, V\textsubscript{A}/Q worsened with the former but improved with the latter. There may also be a prognostic significance of different degrees of

Figure 1 (A) Increasing shunt (from 0 to 40%) lowers the curve. (B) Reducing V\textsubscript{A}/Q from 0.8 to 0.1 shifts the curve to the right. The right shift of each PIO\textsubscript{2} v Sp\textsubscript{O}2 curve from the position of the dissociation curve (dashed line) is the PIO\textsubscript{2} – P\textsubscript{o}2 difference in kPa which includes P\textsubscript{A}O\textsubscript{2}/R. The 0.8 curve represents the normal lung which intercepts a PIO\textsubscript{2} of 21 kPa (vertical line) at 97% Sp\textsubscript{O}2.
VA/Q and shunt. However, existing methods of quantifying the relative contributions to oxygen desaturation of VA/Q and shunt are not suitable for routine clinical application in neonates.4–8

We have described129 a simple non-invasive method for the calculation of shunt and reduced VA/Q in adults which entails the simultaneous measurement of two variables, the inspired oxygen partial pressure (PIO2) and oxyhaemoglobin saturation using pulse oximetry (SpO2). By changing the inspired oxygen partial pressure, pairs of PIO2 and SpO2 values are obtained. The curve relating PIO2 to SpO2 reflects the shape of the dissociation curve but always lies to the right, and its shape and position vary considerably when gas exchange is impaired.1 2 9–11 Thus, with PIO2 on the abscissa:

+ Increasing the shunt from 0 to 40% displaces the PIO2 vs SpO2 curve downwards (fig 1A).
+ Reducing VA/Q from 0.8 to 0.1 shifts the curve to the right (fig 1B) because the oxygen gradient increases between PIO2 and PAO2 (or Pc ¯O2, the mixed capillary oxygen).
+ Increasing alveolar CO2 also shifts the curve to the right by PCO2/R, where R is the gas exchange ratio. The right shift due to PCO2/R is small, typically 6 kPa, compared with the effect of reducing VA/Q from 0.8 to 0.1, which causes a shift of 28 kPa.

Note that, in fig 1B, the PIO2 vs SpO2 curve representing a VA/Q of 0.8 corresponds to the curve in normal subjects and gives an SpO2 of 97% breathing air.

We studied a group of neonates with pulmonary failure to see if we could derive shunt and VA/Q from the PIO2 vs SpO2 data pairs despite the expected circulatory and ventilatory instabilities in such infants. We then examined the day to day changes to see if we could show sequential improvements in shunt and VA/Q with continuing treatment.

Methods

Patients

Twelve neonates, each with pulmonary failure requiring mechanical ventilation, were studied after local ethics committee approval had been obtained and informed consent obtained from the parents. In seven of these babies, up to four repeat studies were performed at intervals of up to 23 days.

The babies were being treated in the Neonatal Intensive Care Unit, Rosie Maternity Hospital, Addenbrooke’s Hospital, Cambridge. All but one of the infants were preterm and admitted for treatment for respiratory distress syndrome (table 1). All infants were being ventilated through a tracheal tube. A consultant neonatologist not involved in this study managed ventilatory support. One infant, delivered at 37 weeks gestation (infant A), had developed hydrops foetalis after parvovirus infection in utero. In most infants, surfactant had been administered when appropriate through a tracheal tube. Arterial blood gas and

Table 1 Summary of the clinical information on the first day of the study

<table>
<thead>
<tr>
<th>Patient code</th>
<th>Days after delivery</th>
<th>Gestation (weeks)</th>
<th>Birth weight (kg)</th>
<th>Admission diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>4</td>
<td>37</td>
<td>3.94</td>
<td>Parvovirus infection Anaemia Hydramnios</td>
</tr>
<tr>
<td>B</td>
<td>33</td>
<td>28</td>
<td>0.86</td>
<td>RDS</td>
</tr>
<tr>
<td>C</td>
<td>8</td>
<td>27</td>
<td>0.69</td>
<td>RDS Surfactant x 2</td>
</tr>
<tr>
<td>D</td>
<td>3</td>
<td>31</td>
<td>1.0</td>
<td>RDS Surfactant x 3</td>
</tr>
<tr>
<td>E</td>
<td>2</td>
<td>27</td>
<td>0.86</td>
<td>RDS Surfactant x 4</td>
</tr>
<tr>
<td>F</td>
<td>39</td>
<td>29</td>
<td>0.84</td>
<td>RDS</td>
</tr>
<tr>
<td>G</td>
<td>7</td>
<td>31</td>
<td>1.56</td>
<td>RDS Surfactant</td>
</tr>
<tr>
<td>H</td>
<td>1</td>
<td>26</td>
<td>0.82</td>
<td>RDS Surfactant</td>
</tr>
<tr>
<td>I</td>
<td>4</td>
<td>26</td>
<td>0.68</td>
<td>RDS Surfactant</td>
</tr>
<tr>
<td>J</td>
<td>26</td>
<td>27</td>
<td>0.82</td>
<td>RDS Surfactant</td>
</tr>
<tr>
<td>K</td>
<td>1</td>
<td>24</td>
<td>0.55</td>
<td>RDS Surfactant</td>
</tr>
<tr>
<td>L</td>
<td>3</td>
<td>24</td>
<td>0.71</td>
<td>RDS, PDA Surfactant</td>
</tr>
</tbody>
</table>

RDS, Respiratory distress syndrome; PDA, patent ductus arteriosus.
Table 2 Details of shunt and right shift of the PIO2 vS pO2 curve

<table>
<thead>
<tr>
<th>Patient*</th>
<th>Shunt (%)</th>
<th>Shunt 95% CI</th>
<th>Shift (kPa)</th>
<th>Shift 95% CI</th>
<th>( r^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>A 4</td>
<td>30.7</td>
<td>29.3 to 32.2</td>
<td>64.4 (&lt;0.05)</td>
<td>61.8 to 67.1</td>
<td>0.73</td>
</tr>
<tr>
<td>A 5</td>
<td>27.3</td>
<td>26.4 to 28.3</td>
<td>61.8 (0.27)</td>
<td>14.5 to 19.1</td>
<td>0.78</td>
</tr>
<tr>
<td>A 10</td>
<td>20.1</td>
<td>18.6 to 21.8</td>
<td>11.4 (0.49)</td>
<td>8.3 to 14.5</td>
<td>0.89</td>
</tr>
<tr>
<td>B</td>
<td>10.8</td>
<td>7.8 to 13.7</td>
<td>13.5 (0.4)</td>
<td>11.5 to 15.6</td>
<td>0.83</td>
</tr>
<tr>
<td>C</td>
<td>20.1</td>
<td>18.2 to 21.9</td>
<td>17.5 (0.25)</td>
<td>16.1 to 18.8</td>
<td>0.8</td>
</tr>
<tr>
<td>D</td>
<td>17.1</td>
<td>16.0 to 18.2</td>
<td>19.8 (0.2)</td>
<td>18.7 to 20.8</td>
<td>0.93</td>
</tr>
<tr>
<td>E 2</td>
<td>19.7</td>
<td>17.0 to 22.5</td>
<td>58.5 (&lt;0.05)</td>
<td>55.1 to 61.9</td>
<td>0.92</td>
</tr>
<tr>
<td>E 3</td>
<td>23.1</td>
<td>22.3 to 23.8</td>
<td>26.9 (0.14)</td>
<td>25.5 to 28.4</td>
<td>0.86</td>
</tr>
<tr>
<td>E 9</td>
<td>23.5</td>
<td>22.7 to 24.3</td>
<td>56.2 (&lt;0.05)</td>
<td>55.2 to 57.1</td>
<td>0.93</td>
</tr>
<tr>
<td>E 25</td>
<td>16.1</td>
<td>13.2 to 18.8</td>
<td>29.0 (0.13)</td>
<td>26.8 to 31.3</td>
<td>0.72</td>
</tr>
<tr>
<td>F 39</td>
<td>26.5</td>
<td>25.6 to 27.5</td>
<td>34.6 (0.1)</td>
<td>31.5 to 37.7</td>
<td>0.97</td>
</tr>
<tr>
<td>F 43</td>
<td>11.2</td>
<td>9.3 to 13.2</td>
<td>10.3 (0.5)</td>
<td>7.1 to 13.5</td>
<td>0.94</td>
</tr>
<tr>
<td>G</td>
<td>21.5</td>
<td>20.2 to 22.8</td>
<td>19.1 (0.2)</td>
<td>16.2 to 21.95</td>
<td>0.92</td>
</tr>
<tr>
<td>H 1</td>
<td>31.0</td>
<td>30.0 to 32.0</td>
<td>53.9 (&lt;0.05)</td>
<td>50.5 to 57.3</td>
<td>0.99</td>
</tr>
<tr>
<td>H 4</td>
<td>5.9</td>
<td>5.0 to 6.7</td>
<td>9.7 (0.55)</td>
<td>9.0 to 10.4</td>
<td>0.99</td>
</tr>
<tr>
<td>I 4</td>
<td>21.6</td>
<td>20.8 to 22.4</td>
<td>26.6 (0.15)</td>
<td>24.9 to 28.2</td>
<td>0.96</td>
</tr>
<tr>
<td>I 8</td>
<td>7.3</td>
<td>5.3 to 9.2</td>
<td>13.7 (0.4)</td>
<td>13.4 to 14.1</td>
<td>0.93</td>
</tr>
<tr>
<td>J 26</td>
<td>13.3</td>
<td>11.8 to 14.7</td>
<td>22.9 (0.18)</td>
<td>22.2 to 23.5</td>
<td>0.93</td>
</tr>
<tr>
<td>J 27</td>
<td>19.0</td>
<td>18.0 to 20.0</td>
<td>22.0 (0.18)</td>
<td>22.5 to 23.5</td>
<td>0.95</td>
</tr>
<tr>
<td>K</td>
<td>28.0</td>
<td>27.0 to 28.8</td>
<td>48.2 (0.35)</td>
<td>47.2 to 50.2</td>
<td>0.97</td>
</tr>
<tr>
<td>L 3</td>
<td>17.1</td>
<td>16.1 to 18.0</td>
<td>18.6 (0.22)</td>
<td>17.6 to 19.5</td>
<td>0.95</td>
</tr>
<tr>
<td>L 7</td>
<td>18.4</td>
<td>17.6 to 19.2</td>
<td>19.7 (0.2)</td>
<td>17.9 to 21.5</td>
<td>0.96</td>
</tr>
</tbody>
</table>

\( V_{a}/Q \) is the ventilation to perfusion ratio in the ventilated but poorly perfused compartment and was derived from the mean shift—that is, \( PIO2 − PCO2 \) in kPa—using fig 2. The number after the patient code is the number of days after birth for repeat studies. \( r^2 \) indicates the goodness of fit of the gas exchange model to the PIO2 vS pO2 data points.

Figure 4 The PIO2 vS pO2 curves from all 12 infants on the first day that they were studied. In every case the curve is shifted to the right of the line marking a PIO2 of 21 kPa, indicating a large reduction in \( V_{a}/Q \) ratio. In infant L, there are two data sets, before (closed circles) and after tracheal aspiration (open circles).
Figure 2 gives the inverse relation between right shift—that is, $P_{O_2} - P_{O_2}$—and $V_a/Q$.

The term “virtual” is used if shunt and $V_a/Q$ are calculated with assumed values of haemoglobin, carbon dioxide ($P_{CO_2}$), respiratory quotient ($R$), and arteriovenous oxygen difference when the actual values are not available. In this study, $R$ and arteriovenous oxygen difference were assumed.

**Results**

Table 1 shows the admission diagnosis, gestational age, days after delivery, and weight of the 12 infants.

Figure 3 shows a $P_{O_2}$ v $S_{O_2}$ data set from infant I on the first study day (closed circles). A model curve (Mod) was fitted to these data by the computer algorithm which calculated a shunt value of 21.6%. A 21.6% shunt is shown by curve SH which, in the absence of $V_a/Q$ abnormality, asymptotes the dissociation curve D as shown in fig 3. The algorithm fits the SH curve to the data points by displacing it to the right of D by 26.6 kPa. This displacement is the $P_{O_2} - P_{O_2}$ difference, which represents the combined effects of a reduced $V_a/Q$ plus $P_{CO_2}/R$.

Table 2 gives the calculated values of shunt and right shift ($P_{O_2} - P_{O_2}$) for all these infants on the first study day. This also shows the $V_a/Q$ derived from $P_{O_2} - P_{O_2}$ and the $r^2$ value, which is the goodness of fit of the model to the data points.

The values for shunt and right shift—that is, $P_{O_2} - P_{O_2}$ difference and thus $V_a/Q$—for each baby shown in table 2 all showed a good fit to the $P_{O_2}$ v $S_{O_2}$ data points indicated by the $r^2$ value. Figure 4 shows these data points and the computed curves for all 12 infants on the first study day. All these data are plotted on a grid where vertical and horizontal lines mark a $P_{O_2}$ of 21 kPa (air at sea level) and an $S_{O_2}$ of 90% respectively. Note that the normal curve, with a median $V_a/Q$ of 0.8, intersects the 21 kPa line at about 97% $S_{O_2}$, and this is equivalent to moving the dissociation curve (D in fig 3) to the right by about 6–7 kPa—for example, a normal $P_{CO_2}/R$. The 95% confidence intervals of the fit of the curve are shown for shunt (upper part of the curve) and right lateral shift (lower part of the curve).

Note that in every case the curve was shifted to the right of the vertical line marking a $P_{O_2}$ of 21 kPa (air at sea level). There was a good fit of the curve to the data points despite the considerable shunt and right shift, the most severe examples of which were in infants A, E, F, and H. Two curves are shown for infant L. The one on the right was recorded first and that on the left 20 minutes after tracheal suction (see discussion).

Seven babies were studied on more than one occasion (fig 5). Infant A, a neonate with hydrops foetalis secondary to anaemia following an intrauterine parvovirus infection, showed a considerable improvement from day 4 to day 5, and this improvement continued to day 10. The overall reduction in shunt was from 30.7% to 20.1%. More dramatically there was a decrease in $P_{O_2} - P_{O_2}$ from 64.4 kPa to 11.4 kPa, equivalent to an improvement in $V_a/Q$ from less than 0.05 to 0.49.

Infant E showed a very unstable clinical pattern with improvement (day 2 to day 3) followed by deterioration (day 3 to day 9). Eventually (day 25) there was the lowest value of shunt, 16.1%, but there was still a very large right shift—that is, a large $P_{O_2} - P_{O_2}$ difference—which our gas exchange model equated to the perfused alveoli having a $V_a/Q$ of 0.13.

Infants F and H showed a considerable improvement over the days they were studied, with a reduction in both the shunt and right shift to near normal values.

Infant I, a 26 week old neonate with infant respiratory distress syndrome, was the only baby studied while dependent on a high frequency oscillator. From day 4 to day 8 there was an improvement in both shunt and right shift (figs 4 and 5 and table 2). The shunt...
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decreased from 21.6% to 7.3% (normal), with the right shift being reduced from 26.6 kPa to 13.7 kPa—that is, a $V_a/V_i$ of 0.14 improving to 0.4.

Infant J showed deterioration in shunt from day 26 to 27. A normal echo ruled out a patent ductus arteriosus. However, this baby was hypotensive and had suspected necrotising enterocolitis. Infant L showed a more stable picture, with little change between days 3 and 7.

**Discussion**

Our gas exchange model derives two variables of impaired gas exchange: shunt and the $P_iO_2 - P_oO_2$ difference representing the effect of a reduced $V_a/V_i$ ($0.05 < V_a/V_i < 1$). In all 12 infants, we found a good fit of the model to the $P_iO_2$ v $P_oO_2$ data points. With a few exceptions the curves were stable—that is, a single shunt equation fitted all the $PIO_2$. This large gradient is low as 0.05, but also, in one case, this may have been caused by a VA/Q of 0.05 or 0.14 improving to 0.4.

Reducing median $V_a/V_i$ below unity causes a considerable increase in oxygen gradient. However, some workers, as recently as 1995, have assumed that the entire oxygen gradient is explained only by a shunt. This simplistic approach ignores the effect of an altered $V_a/V_i$ distribution on the oxygen gradient and lumps together the effects of a reduced $V_a/V_i$ with that of a shunt. In infants with respiratory distress syndrome, the nitrogen gradient method shows a considerable reduction in $V_a/V_i$, which explains about 30% of the oxygen gradient. Not only were $V_a/V_i$ ratios as low as 0.05, but also, in one case, this accounted for almost the whole of an oxygen gradient of 65 kPa. This large gradient is similar in magnitude to the $P_iO_2 - P_oO_2$ difference seen in our infant A (table 2), which gave a $V_a/V_i$ of 0.05.

In some of our infants, the increase in shunt (> 30%) and reduction in $V_a/V_i$ (< 0.05) were considerable, the gas exchange abnormalities being as great as those previously seen during thoracic anaesthesia in adults in whom a considerable part of the lung was collapsed.

Some infants showed considerable variability in the $P_iO_2$ v $P_oO_2$ data. Three examples are as follows. (a) Infant L at the start of the data collection period showed a very large reduction in $V_a/V_i$ causing a right shift of 40 kPa but with a very small shunt (fig 4). After tracheal aspiration, there was an improvement in $V_a/V_i$ but with an increase in shunt from 6.6 to 17% (open circles fig 4). (b) In infant J, there were two episodes of sudden hypoxaemia when the $P_oO_2$ fell precipitously necessitating the inspired oxygen concentration to be increased to 60%. These episodes may have been caused either by a transient opening of an R-L shunt or, more likely, a fall in cardiac output causing an increased shunt effect. (c) At times, in an otherwise stable data set, there was more than 21.6% variability in $P_oO_2$. This was particularly so when we were measuring $P_oO_2$ on the steep part of the $P_iO_2$ v $P_oO_2$ curve. This was consistent with our previous observations in postoperative adult patients, for whom we reported a very unstable pattern of $P_oO_2$ when the $P_iO_2$ lay on the steep part of the $P_iO_2$ v $P_oO_2$ curve.

Severinghaus and Naifeh examined the accuracy of pulse oximeters. They found that the probe is accurate to ±1% in the normal range, but, with a sudden hypoxic episode, an $SpO_2$ reading of 55% may be 7% lower than the actual $SaO_2$ value. Because such inaccuracy occurs only on the very steep part of the oxyhaemoglobin dissociation curve, this has little effect on the derivation of the $P_iO_2$ v $P_oO_2$ curve in our studies. The derived $P_iO_2$ v $P_oO_2$ curve based on our model of gas exchange obviously does not fit every data point, and the $r^2$ value and the 95% confidence interval of shunt and right shift of the curve describe this variability (table 2).

The fetal dissociation curve is shifted to the left of the adult curve with a $P_{ao}$ of 2.7 kPa compared with the adult value of 3.6 kPa. This difference is reduced after birth and after blood transfusion. This means that the median value of the variable $P_iO_2 - P_oO_2$, which for the whole study was 1.8 kPa, may have been underestimated by less than 1 kPa.

The model is sensitive to a reduced haemoglobin concentration and low cardiac output. The haemoglobin value for each infant was recorded from routine samples taken on the day of the study, and these values were used in the calculation of shunt and $V_a/V_i$. A cardiac output equivalent to an arteriovenous oxygen difference of 5 ml/dl was assumed.

We conclude that the method shows that the gas exchange model based on the oxyhaemoglobin dissociation curve provides a good fit to the $P_iO_2$ v $P_oO_2$ data in the circumstances of our study. The model gave a non-invasive measurement of shunt and reduced $V_a/V_i$ in neonates during mechanical ventilation and allowed the prediction of the effect on $P_oO_2$.

We thank Drs James Powell and Jackie Gedney for their assistance with this study. Dr Wilf Kelsall was consultant neonatologist at Addenbrooke’s hospital in whose care were the infants described in this paper.


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