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_{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_{A}/Q were derived from their effects on the relation between inspired oxygen pressure (P_{O2}) and arterial oxygen saturation measured with a pulse oximeter (SpO2). Pairs of P_{O2} v SpO2 data points were obtained by varying P_{O2} in a stepwise fashion. A computer algorithm based on a model of pulmonary gas exchange fitted a curve to these data. With P_{O2} on the abscissa, an increase in shunt produced a downward movement of the curve, whereas reducing V_{A}/Q to < 0.8 shifted the curve to the right. The right shift gives a variable that is inversely related to V_{A}/Q, the P_{O2} − P_{O2} difference, where P_{O2} 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 P_{O2} − P_{O2} differences (range 9.7–64.4 kPa, median 19.8 kPa, normal < 7 kPa) equivalent to a median V_{A}/Q of 0.2 (normal median V_{A}/Q = 0.8). Sequential improvement in shunt and V_{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_{A}/Q in neonates with pulmonary failure.

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Keywords: shunt; V_{A}/Q; non-invasive; oxygen saturation

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Figure 1 (A) Increasing shunt (from 0 to 40%) lowers the curve. (B) Reducing V_{A}/Q from 0.8 to 0.1 shifts the curve to the right. The right shift of each P_{O2} v SpO2 curve from the position of the dissociation curve (dashed line) is the P_{O2} − P_{O2} difference in kPa which includes P_{O2}/R. The 0.8 curve represents the normal lung which intercepts a P_{O2} of 21 kPa (vertical line) at 97% SpO2.
V_{A}\/Q and shunt. However, existing methods of quantifying the relative contributions to oxygen desaturation of V_{A}\/Q and shunt are not suitable for routine clinical application in neonates.

We have described a simple non-invasive method for the calculation of shunt and reduced V_{A}\/Q in adults which entails the simultaneous measurement of two variables, the inspired oxygen partial pressure (P_{IO2}) and oxyhaemoglobin saturation using pulse oximetry (SpO_{2}). By changing the inspired oxygen partial pressure, pairs of P_{O2} and SpO_{2} values are obtained. The curve relating P_{O2} to SpO_{2} 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. Thus, with P_{IO2} on the abscissa:
- Increasing the shunt from 0 to 40% displaces the P_{IO2} = SpO_{2} curve downwards (fig 1A). This reflects the inability of an increase in P_{IO2} to compensate for an increase in shunt.
- Reducing V_{A}\/Q from 0.8 to 0.1 shifts the curve to the right (fig 1B) because the oxygen gradient increases between P_{O2} and P_{A\text{-}O2} (or P_{a\text{-}O2}, the mixed capillary oxygen). Increasing alveolar CO₂ also shifts the curve to the right by P_{CO2}/R, where R is the gas exchange ratio. The right shift due to P_{CO2}/R is small, typically 6 kPa, compared with the effect of reducing V_{A}\/Q from 0.8 to 0.1, which causes a shift of 28 kPa.
- Note that, in fig 1B, the P_{IO2} = SpO_{2} curve representing a V_{A}\/Q of 0.8 corresponds to the curve in normal subjects and gives an SpO_{2} of 97% breathing air.

We studied a group of neonates with pulmonary failure to see if we could derive shunt and V_{A}\/Q from the P_{O2} = SpO_{2} 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 V_{A}\/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 with intrauterine growth retardation and were admitted for ventilation 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 arterial pressure were 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.

<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</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.
haemoglobin values were recorded independently as part of routine clinical management. Monitoring included measurement of inspired oxygen concentration and arterial saturation using the integral gas analyser in the Draeger Babylog 8000 ventilator (to give FiO2 or PIO2) and an Ohmeda Biox 3700e pulse oximeter (to give SpO2). The Draeger automatically calibrates itself every 24 hours—for example, at 1100, using piped air and 100% oxygen. Each calibration takes 90 seconds and the instrument is accurate to 5% full scale deflection—that is, 21(1)kPa. The instrument sounds an alarm if the calibration exceeds this range. The routine arterial blood gas results were used periodically to check the pulse oximeter reading. Pulse oximeters are accurate to ±1% in the normal range but much less at low SpO2 (see Discussion).

PROCEDURE

PIO2 was varied in steps to cause the SpO2 to vary between 85% and 96%. This level of oxygen has been used in previous research in the measurement of cerebral blood flow using near infrared spectroscopy. The PIO2 was never reduced below 21 kPa.

DATA ANALYSIS AND INTERPRETATION

The pairs of PIO2 and SpO2 data points for each study were recorded and analysed using a computer algorithm which gave a curve representing a single solution for each subject’s data set. This curve is not a statistical line of best fit but is based on a model of gas exchange used by the computer algorithm to describe the PIO2 v SpO2 data points by two variables of gas exchange:

- virtual shunt using the shunt equation;
- the difference between inspired oxygen and mixed pulmonary capillary oxygen pressures (PIO2 − PaO2), a function of reduced V/Q and PCO2/R.

Table 2 Details of shunt and right shift of the PIO2 v SpO2 curve

<table>
<thead>
<tr>
<th>Patient*</th>
<th>Shunt (%)</th>
<th>Shunt 95% CI</th>
<th>Shift (kPa), (V/Q)</th>
<th>Shift 95% CI</th>
<th>r²</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>16.8 (0.2)</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 21.9</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>21.5 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>42.0 (0.35)</td>
<td>12.2 to 26.2</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>

*Patient code is the number of days after birth for repeat studies.

Figure 4 The PIO2 v SpO2 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/Q ratio. In infant L, there are two data sets, before (closed circles) and after tracheal aspiration (open circles).
Figure 5  Sequence of changes in $P_{io2}$ vs $P_{o2}$ data points and model fit in seven infants who were studied sequentially.

Figure 2 gives the inverse relation between right shift—that is, $P_{io2} - P_{o2}$—and $V_{a}/Q$.

The term "virtual" is used if shunt and $V_{a}/Q$ are calculated with assumed values of haemoglobin, carbon dioxide ($P_{CO2}$), 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 $P_{io2} \times P_{o2}$ 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 $P_{io2} - P_{o2}$ difference, which represents the combined effects of a reduced $V_{a}/Q$ plus $P_{CO2}/R$.

Table 2 gives the calculated values of shunt and right shift ($P_{io2} - P_{o2}$) for all these infants on the first study day. This also shows the $V_{a}/Q$ derived from $P_{io2} - P_{o2}$ and the $r'$ value, which is the goodness of fit of the model to the data points.\(^8\)

The values for shunt and right shift—that is, $P_{io2} - P_{o2}$ difference and thus $V_{a}/Q$—for each baby shown in table 2 all showed a good fit to the $P_{io2} \times P_{o2}$ data points indicated by the $r'$ value.\(^7\) 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 $P_{io2}$ of 21 kPa (air at sea level) and an $P_{o2}$ 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% $P_{o2}$, 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 $P_{CO2}/R$. 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 $P_{io2}$ 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 $P_{io2} - P_{o2}$ 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 $P_{io2} - P_{o2}$ 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
Assessment of shunt and VA/Q ratio

seen in a variety of adult patients with pulmonary
obtained from one subject during one data col-
lected period showed a very large reduction
as follows. (...)

SpO2 fell precipitously necessitating the in-
duction of impaired gas exchange: shunt and the
VA/Q distribution on the oxygen gradient and
the 95% confidence interval of shunt and
reduction in VA/Q (0.05 < VA/Q < 1). In all 12
infants, we found a good fit of the model to the
Pio2 v Spo2 data points. With a few exceptions
the curves were stable—that is, a single shunt
equation fitted all the Pio2 v Spo2 data points
obtained from one subject during one data col-
lection period. The results were similar to those
seen in a variety of adult patients with pulmo-
ary failure during anaesthesia, thoracotomy, and after fat embolism.

Reducing median VA/Q 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 simplis-
tic approach ignores the effect of an altered
VA/Q distribution on the oxygen gradient and
lumps together the effects of a reduced VA/Q
with those of a shunt. In infants with respiratory distress syndrome, the
nitrogen gradient method shows a considerable reduc-
tion in VA/Q, which explains about 30% of the
oxygen gradient. Not only were VA/Q ratios as low as 0.05, but also, in one case, this
accounted for almost the whole of an oxygen
gradient of 63 kPa. This large gradient is
similar in magnitude to the Pio2 − Pco2 differ-
ence seen in our infant A (table 2), which gave
a VA/Q of 0.05.

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

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

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ship between inspired oxygen partial pressure and arte-
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