Respiratory failure: two forgotten concepts

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Dum spiro, spero
(while I breathe, I hope)

‘Blood gases please’ is a frequently requested investigation. But physicians in specialties other than critical care/emergency and respiratory medicine often find it difficult to interpret the results. The aim of this article is to help physicians in the diagnosis and treatment of patients with hypoxia.

The textbook definition of respiratory failure is an arterial partial pressure of oxygen (P_{\text{a}}O_{2}) of less than 8kPa when breathing room air; it is divided into type I and II depending on the level of P_{\text{a}}CO_{2}. Does this mean that if a patient has a P_{\text{a}}O_{2} of 10kPa, then you do not have to be too concerned because they are not in respiratory failure? Perhaps it is wise to avoid an exact definition of respiratory failure as any deviation from normal could be serious, and to think instead of impaired gas exchange. Also, even when there is a small or significant degree of respiratory impairment, how bad is it for the patient? In the first half of this paper, we will look at how we can sometimes be misled by arterial blood gases and miss significant degrees of gas exchange impairment. In the second half, we will go on to show that in certain clinical situations, correcting the hypoxaemia may not be the most important thing to do.

Detecting impaired gas exchange (A-a gradient)

A 25 year old girl is seen in A&E with sudden onset of pleuritic chest pain and slight shortness of breath. Her oxygen saturations on air are 98%, but the casualty officer was wise enough to do blood gases which showed P_{\text{a}}O_{2} of 12kPa and P_{\text{a}}CO_{2} of 3.5kPa on room air. Is this abnormal, and if so, how abnormal?

Significant degrees of gas exchange impairment are often missed because the P_{\text{a}}O_{2} does not appear to be abnormal or oxygen saturations on pulse oximetry are normal. A more accurate way of assessing gas exchange is to calculate the alveolar-arterial oxygen gradient (D(A-a)O_{2}, or A-a gradient). The alveolar-arterial oxygen gradient is the drop in the partial pressure of oxygen between alveolar gas and arterial blood. This fall in P_{\text{a}}O_{2} is not caused by impaired diffusion of oxygen from the alveolar membrane to pulmonary capillaries, but is due to ventilation perfusion mismatch within the lungs. Ventilation excess perfusion in the lung apices (V/Q>1), and the lung bases are well perfused but poorly ventilated (V/Q<1).

Overall, because there is more lung in the bases, the average V/Q ratio is 0.8. This gives rise to a physiological right to left shunt, with the admixture of well oxygenated blood from the apices mixing with poorly oxygenated blood from the lung bases occurring in the left atrium. Almost all causes of hypoxaemia (except that due to hypoventilation), are due to an increase in V/Q mismatch, and the A-a gradient is a measure of this mismatch.

The use of mmHg as the unit of gas partial pressures made calculations of A-a gradient difficult and perhaps this is why it has not been commonly used. However, now that the use of kiloPascals (kPa) is commonplace for arterial blood gas analysis, the calculation of A-a gradient is simple and can be put to everyday use. The A-a gradient or D(A-a)O_{2} is based on the alveolar air equation from which we can predict alveolar PO_{2} (P_{\text{A}}O_{2}) from the partial pressure of inspired oxygen (P_{\text{i}}O_{2}) and the respiratory exchange ratio (R) which is usually 0.8.

\[
P_{\text{A}}O_{2} = P_{\text{i}}O_{2} - \frac{1}{R} + P_{\text{a}}CO_{2} \frac{F_{\text{O}_{2}}}{R}
\]  

(Alveolar Air Equation)

where P_{\text{i}} is the partial pressure of a gas in the alveoli, and F_{\text{O}_{2}} is the fraction of inspired oxygen.

Luckily, we do not have to use this equation as most of the term on the right is negligible and the equation can thus be simplified to:

\[
P_{\text{A}}O_{2} = P_{\text{i}}O_{2} - P_{\text{a}}CO_{2} / R
\]  

(Simplified Alveolar Air Equation)

or even more simply:

\[
P_{\text{A}}O_{2} = P_{\text{i}}O_{2} - (P_{\text{i}}CO_{2} \times 1.2)
\]

where 1/R = 1/0.8 = 1.25, but 1.2 can be used to simplify calculations further. Alveolar CO_{2} is practically the same as arterial CO_{2} so P_{\text{a}}CO_{2} = P_{\text{A}}CO_{2}.

The partial pressure of inspired oxygen (P_{\text{i}}O_{2}) is very simple to calculate. Atmospheric pressure at sea level is 101kPa and oxygen comprises 20.8% of the atmosphere. Thus, the partial pressure of O_{2} in inspired room air is 20.8% of 101kPa or near enough 21kPa. Therefore, P_{\text{i}}O_{2} approximates to the fraction of inspired O_{2} at sea level. So breathing 28% oxygen (F_{\text{O}_{2}} = 28%) gives a P_{\text{i}}O_{2} of 28kPa at sea level.

For a normal young adult with a P_{\text{A}}O_{2} of 13kPa, P_{\text{a}}CO_{2} 5kPa breathing air, the A-a gradient is:

\[
= P_{\text{i}}O_{2} - P_{\text{a}}O_{2}
= P_{\text{i}}O_{2} - (P_{\text{i}}CO_{2} \times 1.2) - P_{\text{a}}CO_{2}
= 21 - (5 \times 1.2) - 13
= 2kPa
\]

To put this into words, the A-a gradient is the inspired level of oxygen, minus the arterial CO_{2} multiplied by 1.2, minus the arterial O_{2}.

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The normal A-a gradient is about 2kPa. This value increases with age as V/Q worsens and may be up to 4kPa in a 70yr old with no respiratory disease (Table 1). Any increase from these values is caused solely by ventilation perfusion mismatch. The calculation of the A-a gradient is most accurate when performed on room air but is less reliable when the F\textsubscript{O}\textsubscript{2} is above 28%.

Going back to the example of the 25 year old girl in A&E with a Pa\textsubscript{O}\textsubscript{2} 12.5 and Paco\textsubscript{2} 3.5 breathing room air, from the above equations:

\[
\text{A-a gradient} = 21 – (3.5 \times 1.2) – 12 = 4.8kPa
\]

Thus the A-a gradient is double what it should be despite the arterial blood gases appearing near normal, and therefore she has probably suffered a pulmonary embolus. Without this additional knowledge, she could easily have been sent home with apparently normal blood gases.

The calculation of the A-a gradient also illustrates the importance of documenting the level of inspired oxygen. Hypoxaemia in blood gases cannot be interpreted without knowledge of the F\textsubscript{O}\textsubscript{2}. Frequently, arterial blood gases are recorded in a patient’s notes without documentation of what that patient was breathing at the time.

How important is hypoxaemia?
The oxygen content of blood

Often when faced with a systemically sick hypoxic patient, we pay most attention to correcting the hypoxaemia thinking that this is what the patient needs most. However, this is not always the case. This can be easily demonstrated by remembering two important facts:

- Most of the oxygen is carried to the tissues by haemoglobin, not plasma. The vital organs need oxygen delivered to them by haemoglobin. Therefore, the delivery of oxygen to the tissues depends on the amount of haemoglobin, the amount of oxygen attached to haemoglobin and the cardiac output.
- The Hb-O\textsubscript{2} dissociation curve flattens after haemoglobin reaches 90% saturation (equivalent to a Pa\textsubscript{O}\textsubscript{2} of approximately 7.5kPa).

Each gm/dl of haemoglobin carries 1.34mls of O\textsubscript{2} when fully saturated (i.e. Sa\textsubscript{O}\textsubscript{2} = 100%). If the haemoglobin is only 95% saturated, then it carries 0.95 x 1.34 mlO\textsubscript{2}/gm. The oxygen content of one decilitre of blood can be calculated thus:

\[
\text{Hb} \times \text{SaO}_{2} \times 1.34 \text{ mlO}_{2}/\text{dl dissolved in plasma}
\]

With a normal haemoglobin of 14g/dl which is 100% saturated, the amount of oxygen attached to haemoglobin is 18.76 mlO\textsubscript{2}/dl. There is only 0.3ml of O\textsubscript{2} dissolved in 100ml of plasma at a Pa\textsubscript{O}\textsubscript{2} of 14kPa. Therefore, the amount of oxygen normally dissolved in plasma contributes less than 2% of the total oxygen content of blood and thus is a negligible amount.

In a sick, hypoxic patient with an Hb of 12g/dl and Pa\textsubscript{O}\textsubscript{2} of 8kPa (= Sa\textsubscript{O}\textsubscript{2} of 92%), one litre of blood contains:

\[
\begin{align*}
12 \times 0.92 \times 1.34 \times 10 \text{ (to convert to litres)} = 148 \text{ mlO}_{2}/\text{l}
\end{align*}
\]

The delivery of O\textsubscript{2} (DO\textsubscript{2}) to the tissues depends on the cardiac output, and if the patient is hypovolaemic this may be in the region of 4l/min (normal is about 5l/min at rest). Therefore, the oxygen delivery to the tissues is:

\[
148 \times 4 = 592 \text{ mlO}_{2}/\text{min}
\]

Increasing the Pa\textsubscript{O}\textsubscript{2} to 12 and thus the Sa\textsubscript{O}\textsubscript{2} to 97% with supplemental oxygen will increase the oxygen content of blood to:

\[
12 \times 0.97 \times 1.34 \times 10 = 156 \text{ mlO}_{2}/\text{l}
\]

and thus, the oxygen delivery with the same cardiac output of 4l/min to:

\[
156 \times 4 = 624 \text{ mlO}_{2}/\text{min}
\]

This is an increase of only 32 mlO\textsubscript{2}/min (a measly 5% improvement in oxygen delivery).

However, if instead of being given oxygen, the patient receives fluids to increase the cardiac output, the oxygen content of blood will remain at 148 mlO\textsubscript{2}/l as before, but after one litre of fluid the cardiac output may rise from 4 to 5l/min. The oxygen delivery now becomes:

\[
148 \times 5 = 740 \text{ mlO}_{2}/\text{min}
\]

This is an increase of 148 mlO\textsubscript{2}/min (a useful 25% improvement). Giving both oxygen and fluids increases the delivery of oxygen by 188 mlO\textsubscript{2}/min (32%). Thus the proportion of oxygen delivery contributed to by increasing the Pa\textsubscript{O}\textsubscript{2} or the Sa\textsubscript{O}\textsubscript{2} once it is already above the shoulder of the Hb-O\textsubscript{2} dissociation curve (about 8kPa and 92% Sa\textsubscript{O}\textsubscript{2}) is small compared with improving the cardiac output. Therefore, in the management of critically ill patients, as much if not more, attention should be paid to fluid resuscitation as to the normalisation of hypoxaemia.

Reference:

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Table 1. Change in predicted Pa\textsubscript{O}\textsubscript{2} and A-a gradient with age. A-a gradient calculated using I/R = 1.2. Predicted Pa\textsubscript{O}\textsubscript{2} = 0.133 (104 – 0.24 age)\textsuperscript{1}

<table>
<thead>
<tr>
<th>Age</th>
<th>Pa\textsubscript{O}\textsubscript{2} (kPa)</th>
<th>A-a Gradient (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>13.2</td>
<td>1.8</td>
</tr>
<tr>
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<td>12.5</td>
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</tr>
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</tr>
<tr>
<td>80</td>
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