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_aO_2) of less than 8kPa when breathing room air; it is divided into type I and II depending on the level of P_aCO_2. Does this mean that if a patient has a P_aO_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

Key Points

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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_aO_2 of 12kPa and P_aCO_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_aO_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 PO_2 is not caused by impaired diffusion of oxygen from the alveolar membrane to pulmonary capillaries, but is due to ventilation perfusion(V/Q) mismatch within the lungs. Ventilation exceeds 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_AO_2) from the partial pressure of inspired oxygen (P_iO_2) and the respiratory exchange ratio (R) which is usually 0.8.

$$P_AO_2 = P_iO_2 - \frac{P_ACO_2}{R} + P_ACO_2 F_iO_2 . \frac{1-R}{R}$$
(Alveolar Air Equation)

where P_A is the partial pressure of a gas in the alveoli, and F_iO_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:

$$P_AO_2 = P_iO_2 - P_ACO_2 / R$$
(Simplified Alveolar Air Equation)

or even more simply:

$$P_AO_2 = P_iO_2 - (P_aCO_2 \times 1.2)$$

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 $P_aCO_2 = P_ACO_2$.

The partial pressure of inspired oxygen (P_iO_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_iO_2 approximates to the fraction of inspired O_2 at sea level. So breathing 28% oxygen (F_iO_2 = 28%) gives a P_iO_2 of 28kPa at sea level.

For a normal young adult with a P_aO_2 13KPa, P_aCO_2 5kPa breathing air, the A-a gradient is:

$$= P_AO_2 - P_aO_2$$
$$= P_iO_2 - (P_aCO_2 \times 1.2) - P_aO_2$$
$$= 21 - (5 \times 1.2) - 13$$
$$= 2kPa$$

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.

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_iO_2 is above 28%.

Going back to the example of the 25 year old girl in A&E with a P_aO_2 12.5 and P_aCO_2 3.5 breathing room air, from the above equations:

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

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_iO_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_2 dissociation curve flattens after haemoglobin reaches 90% saturation (equivalent to a P_aO_2 of approximately 7.5kPa). (Fig 1)

Each gm/dl of haemoglobin carries 1.34mls of O_2 when fully saturated (i.e. SaO_2 = 100%). If the haemoglobin is only 95% saturated, then it carries 0.95 x 1.34 mlO_2/gm. The oxygen content of one decilitre of blood can be calculated thus:

$$Hb \times SaO_2 \times 1.34 + O_2\ dissolved\ in$$
$$plasma$$

With a normal haemoglobin of 14g/dl which is 100% saturated, the amount of oxygen attached to haemoglobin is 18.76 mlO_2/dl. There is only 0.3ml of O_2 dissolved in 100ml of plasma at a P_aO_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 PaO_2 of 8kPa (= SaO_2 of 92%), one litre of blood contains:
12 x 0.92 x 1.34 x10 (to convert to litres)
= **148 mlO$_2$/l**

The delivery of O_2 (DO_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 x 4 = **592 mlO$_2$/min**

Increasing the P_aO_2 to12 and thus the SaO_2 to 97% with supplemental oxygen will increase the oxygen content of blood to:

12 x 0.97 x 1.34 x 10 = **156 mlO$_2$/l**
and thus, the oxygen delivery with the same cardiac output of 4l/min to:
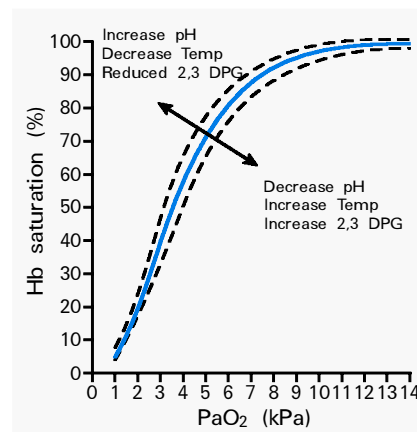
156 x 4 = **624 mlO$_2$/min**

Fig 1. Haemoglobin – oxygen dissociation curve

This is an increase of only 32 mlO_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_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 x 5 = **740 ml/O$_2$/min**

This is an increase of 148 mlO_2/min (a useful 25% improvement). Giving both oxygen and fluids increases the delivery of oxygen by 188 mlO_2/min (32%). Thus the proportion of oxygen delivery contributed to by increasing the P_aO_2 or the SaO_2 once it is already above the shoulder of the Hb-O_2 dissociation curve (about 8kPa and 92% SaO_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:

1   Raine JM, Bishop JM. A- a difference in O_2 tension and physiological dead space in normal man. *J Appl Physiol* 1963;**18**: 284–288.

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Table 1. Change in predicted P_aO_2 and A-a gradient with age. A-a gradient calculated using I/R = 1.2. Predicted P_aO_2 = 0.133 (104 – 0.24 age)[1]

Age	P_aO_2 (kPa)	A-a Gradient (kPa)
20	13.2	1.8
40	12.5	2.5
60	11.9	3.1
80	11.3	3.7