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Review Article

Oxygen therapy: a panacea for the critically ill

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Abstract

'Oxygen is so toxic that if it was discovered today FDA would not have approved its use'. We started using oxygen for resuscitation because it seemed like a good idea. Now we use it because we always have. Majority of healthcare professionals including doctors use oxygen like freely available water without understanding the science behind its use. While nature always knew that living things do not require more than 21% oxygen, scientist are just figuring out that to resuscitate a full term asphyxiated baby we need only 21% oxygen and that anything more than that can actually be harmful particularly in premature babies. The following article describes oxygen as a drug with all the advantages and pitfalls of using oxygen.

Introduction:

Nature has provided us with an abundance of oxygen around us, 21% of the atmospheric gases, to be precise, but what has always been puzzling the philosophical mind is that our body does not contain any storage of oxygen. Ever since this element was discovered in 1774, by Joseph Priestly, the use of oxygen in illnesses has been taken for granted. We started using oxygen for resuscitation because it seemed like a good idea. Now we use it because we always have.

Oxygen therapy is not simply an act of attaching a mask to the patient's face, turning on the oxygen cylinder and attaching the pulse oximeter probe. Two common case scenarios will illustrate this point.

1. 3 year old child is admitted in PICU with an acute illness. Child's oxygenation status: SpO2 100% and PaO2 100 mmHg. 6 hours later, child died of HYPOXIA.
2. 2 year old baby admitted with diarrhea and moderate dehydration. Her oxygenation status seems adequate, SpO2 100%, PaO2 100 mmHg. She is later found to have lactic acidosis suggesting tissue hypoxia, despite a normal oxygenation value!

Oxygen Therapy- Physiology:

The above cited cases illustrate the need to shift our focus from just giving oxygen to a patient to ensuring proper delivery of oxygen to the tissues for optimum benefit. Two terminologies need to be understood before discussing oxygen therapy viz hypoxemia and hypoxia. Hypoxemia is defined as inadequate oxygenation of blood and is indicated by SaO2 <94% and PaO2 <60 mmHg. Hypoxia is inadequate delivery of oxygen to the tissues (DO2) (1).

Delivery of oxygen (DO2) to the tissues is determined by the cardiac output and the content of oxygen (CO2) in the blood.

Do2 = CO (cardiac output) x CO2 (content of oxygen).

Content of Oxygen is calculated by the following formula:

CO2 = [1.36 x Hb x SaO2] + .003 x PaO2

In a normal individual with hemoglobin of 15gm/dl and 100% saturation with oxygen [SaO2 100%], with normal PaO2 of 100, the content of oxygen may be calculated as follows:

[1.36 x 15 x 100] + .003 x 100 = 20.40 mg/dl + 0.3 mg/dl

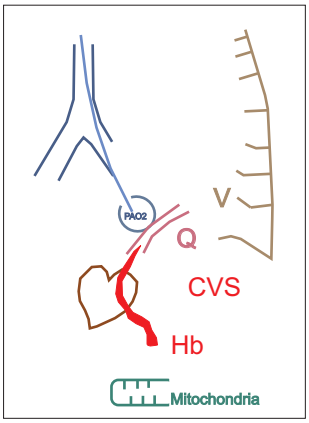


Fig 1: Delivery of Oxygen

It is obvious from the above that the major amount of oxygen in blood is carried by hemoglobin (Fig. 1) and only a small quantity (0.003 x PaO2) is carried dissolved in plasma. It is also clear from the above formula that, in terms of delivery of oxygen to the tissues, SaO2 i.e. saturation of hemoglobin with oxygen plays a greater role than PaO2. Considering the very small amount of oxygen dissolved in plasma (0.003 x PaO2), one is inclined to ignore the dissolved oxygen. This is not true as dissolved oxygen can occasionally play a significant role. Consider the following example:

A child with severe anemia has:

Hb 3 gm%, FiO2 21% (i.e. she is breathing room air), SpO2 100 and PaO2 100.

Her Content of O2 (CO2) is:

[1.36 x 3 x 100] + [.003 x 100]= 4.08 mg/dl + 0.3 mg/dl

If this child is given increased oxygen (despite having normal SpO2), up to FiO2 100 then her PaO2 becomes 500 (21 x 5 is ≈100) hence PaO2 will increase 5 times i.e. from 100 to 500) and the formula will now read as:

[1.36 x 3 x 100] + [.003 x 500] = 4.08 mg/dl + 1.5 mg/dl

There is a 40% net increase in total oxygen carried by blood. This increase in DO2 is often sufficient to stabilize the patient, before cross matched blood is available.

Going back to the equation for DO2 [DO2 = CO (cardiac output) x CO2 (content of oxygen), it is important to note that cardiac output occupies a prime place in DO2 and is often neglected during oxygen therapy. While a low content of oxygen in blood is often compensated by an increase in the cardiac output (CO), if the CO is low, content of oxygen cannot increase resulting in significant hypoxia. Consider a patient with parenchymal lung disease. Some of the deoxygenated blood coursing through non ventilated alveolar tissue will return to the heart in a deoxygenated state resulting in a low mixed venous saturation at the pulmonary artery. An increase in cardiac output in such a case would result in decreased oxygen extraction at the tissue level thereby increasing the mixed venous saturation (the amount of oxygen taken up at the tissue level depends on the cardiac output, low cardiac output results in near complete extraction of oxygen by the tissues (Fig 2)

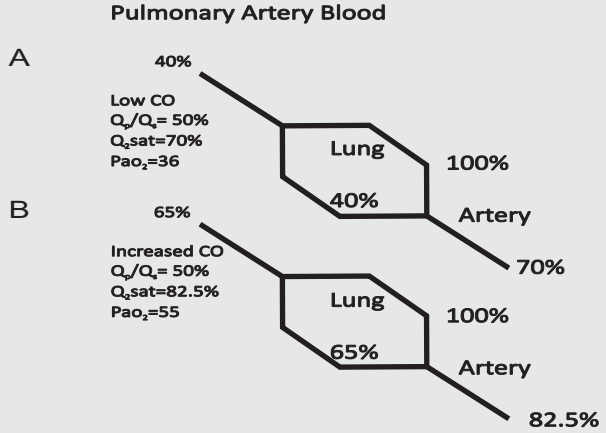


Fig 2:
Showing a diseased side of lung tissue (lower -40% & 65%) and a side where ventilation is carried out normally (upper-100%). On the diseased side the saturation of the mixed venous blood remains unchanged, but with increase in cardiac output (B), increase in the venous saturation (65%) results in a higher average saturation after ventilation (average of 100 & 65) causing a rise in PaO2 from 36 to 55 mmHg. (Picture from PALS Provider Manual, American Heart Association).

From the foregoing it is clear that hypoxia is decreased delivery of O2 to the tissues and can be classified into three types and the treatment accordingly determined (Table I).

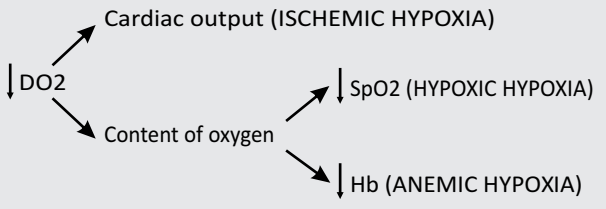


Table I: Classification of hypoxia and the treatment priorities

Type of Hypoxia	Treatment Priorities	
	Primary	Secondary
Hypoxemic (↓SpO2)	O2	↑cardiac output (CO), ↑Hb
Anemic (↓Hb)	↑Hb	↑PaO2, ↑CO
Ischemic (↓CO)	↑CO	↑PaO2, ↑Hb

Oxygen Therapy – Monitoring Oxygen Therapy

Once a patient has been put on oxygen, there are several ways by which we can judge the adequacy of oxygen therapy:

1. Pulse oximeter
2. A-aO2 gradient
3. PaO2/FiO2
4. SpO2/FiO2

Pulse Oximeter has become an indispensable part of any clinic or hospital. It is very important to understand that the SpO2 obtained by the pulse oximeter does not have a linear relationship with the PaO2 (see fig 3)

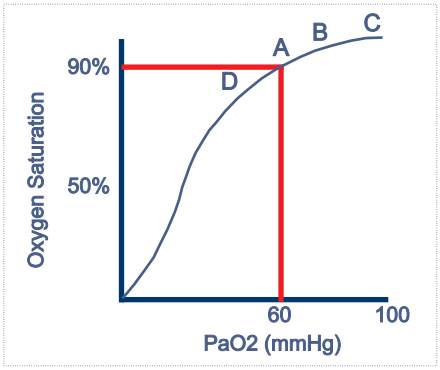


Fig 3: Relationship between SpO2 and PaO2

The pulse oximeter is in fact now considered the fifth vital sign not only because it is a noninvasive simple estimate of PaO2 but because we know that SpO2 contributes maximally to content of Oxygen (CO2). SpO2 below 93-94% is considered hypoxemia. This golden figure of 93-94% can be understood if one looks at the 'S' slide in figure 2.when the PaO2 falls from 100 to 60, there is very little fall in SpO2. Beyond a PaO2 of 60 mmHg, there is a steep fall in SpO2, suggesting significant hypoxemia, hence SpO2 below 93-94% is considered unsafe.

There are clinical conditions where SpO2 may be normal yet patient may have hypoxia (one of the case scenarios mentioned at the beginning of this article). Two common situations where this may occur are:

1. Anemia
2. Shock

These are conditions where even if SpO2 is normal, 100% oxygen must be given. As discussed earlier, the dissolved oxygen increases by almost 40% resulting in improved delivery of oxygen to the tissues (DO2).

Remember 0.003 x 500 (FiO2 100%) is better than 0.003 x 100 (FiO2 21%)!

The pulse oximeter has some limitations in its uses (2). The most important is its use in a patient in shock. As the reading is based on pulsatile flow of blood in the extremities, it may be unreliable in shock. In such situations, the probe should be kept over the tongue or ears. Another condition where pulse oximeter is unreliable is Methhemoglobinemia or Carboxyhemoglobinemia. Pulse oximetry only reads the percentage of bound hemoglobin. It can be bound to other gasses such as carbon monoxide and still read high even though the patient is hypoxemic. The only noninvasive methodology that allows for the continuous and noninvasive measurement of the dyshemoglobins is a pulseco-oximeter. Pulse oximeter has a major limitation in neonates where hyperoxia is as deleterious as hypoxia and pulse oximeter cannot detect hyperoxia. The plateau at the top of the 'S' shaped curve means that the PaO2 may rise from 100 to 500 but the SpO2 will remain 100!

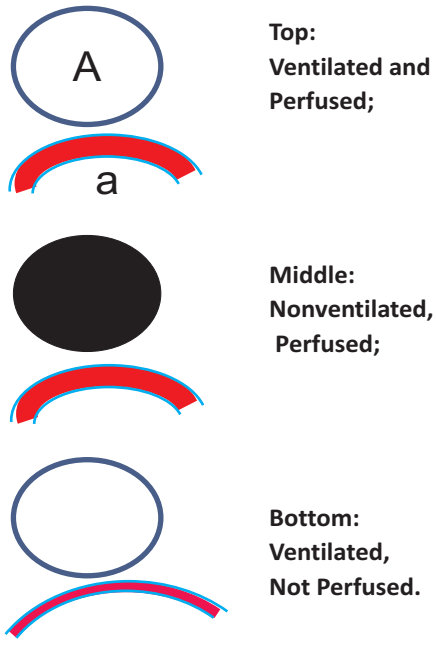
Pulse oximeter measures only oxygenation, not ventilation. There is a case report of a patient who had a normal SpO2 (100%) but had a PaCO2 650! Hence pulse oximeter can never be a substitute for blood gas analysis.

A-a O2 gradient: Normally the oxygen present in the alveoli (AO2) should be taken up entirely by the blood (aO2) and hence there should be no A-aO2 gradient. But even in normal individuals there exist some alveoli which do not participate in ventilation despite being well perfused (see fig 3) and some alveoli are not perfused despite being filled with O2, resulting in V/Q (ventilation/perfusion) mismatch, thereby creating a PAO2-PaO2 gradient, albeit very small. When this V/Q mismatch increases it results in increased PAO2-PaO2 gradient indicating hypoxemia.

PAO2= FiO2 x 713 – PaCO2/0.8, and PaO2 is calculated from the ABG.

Serial measurement of A-a gradient provides excellent information on oxygenation. For those who cannot face the 'wrath of math', a simpler way to monitor adequacy of oxygen therapy is the PaO2: FiO2 ratio. Normally the ratio is

Fig 4: A-aO2 gradient.

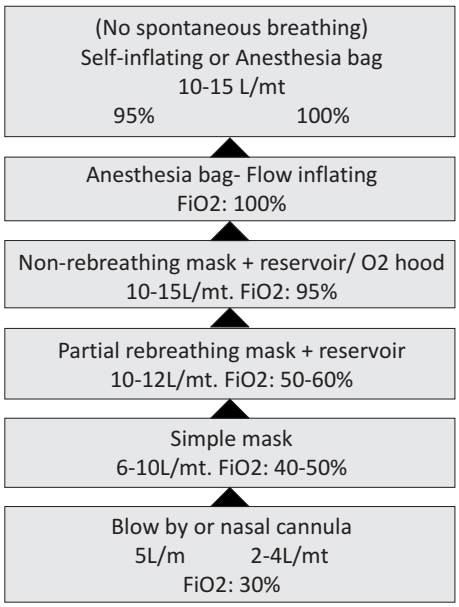


100: 0.21 or 500. A value < 300 suggests abnormal gas exchange and < 200 indicates severe hypoxemia.

SpO2/ FiO2 also gives a rough estimate of whether the given oxygen therapy is resulting in adequate tissue oxygenation. A SpO2 <94% on simple face mask at 6-10L/mt (roughly FiO2 50%) suggests severe hypoxemia. A SpO2 of 94% corresponds to PaO2 100, and hence the PaO2/FiO2 ratio would be 100/50, this may suggest the need for ventilator support.

Oxygen Therapy – Oxygen Delivery Devices

The choice of the oxygen delivery device depends on the desired FiO2 for optimum delivery of oxygen, as well as the age of the child. As is seen in the figure above, the inspired oxygen concentration depends on the type of device and the flow rate. If a child is very irritable and has hypoxemia due to a reversible cause, for e.g. Asthma, then oxygen should be given as 'blow by' where the oxygen tube is kept on the chest with the jet directed towards the nose. This will ensure delivery of oxygen at a concentration higher than 21%. Nasal cannula should be used in infants at a rate of not more than 2L/mt. Flow rates specified with each delivery device must be maintained not only to achieve the desired oxygen delivery but also to prevent carbon dioxide retention especially in the rebreathing devices. Self-inflating resuscitating bags should not be used as an oxygen delivery device in spontaneously breathing patients. Ideally humidification of oxygen is a must especially when given at > 4L/mt (3).



Oxygen Toxicity:

Oxygen is so toxic that if it was discovered today, FDA will not approve its use! The toxic effects of oxygen are not restricted to neonates.

— Related to high PaO2 – ROP
— Related to high FiO2 –
    1. BPD
    2. Absorption atelectasis
    3. Hypercapnia

The toxic effects of oxygen occur through generation of reactive oxygen species such as O_2, H_2O_2, or OH^- which are highly reactive and cause oxidative damage to the lipid and proteins on the cell wall. Antioxidants like superoxide dismutase, vitamin C, etc are reducing agents, and limit oxidative damage (4). Neonates are especially deficient in antioxidants and are more vulnerable to the toxic effects of oxygen. Hyperoxia in neonates results in conditions such as Retinopathy of prematurity, Broncho pulmonary dysplasia, Patent ductus arteriosus, Necrotising enterocolitis, and Periventricular leucomalacia.

Oxygen and Resuscitation:

Why do we use 100% in resuscitation? This has been a matter of intense debate, and the current consensus, according to the NRP guidelines (2006), is that there is no apparent clinical disadvantage of using room air (21%) for resuscitation of asphyxiated neonates. It has been found that room air resuscitated infants recover more quickly and that neonates resuscitated with 100% O2 had prolonged oxidative stress persisting even after 4 weeks of life (5).

Key Points:

- Oxygen is a drug that saves lives, and like all drugs its administration deserves careful consideration.
- Continuous pulse oximeter monitoring is a must to judge the efficiency of oxygen delivery
- In extremely agitated patient with reversible cause of hypoxia, e.g. Croup, Asthma, oxygen is preferably given as 'blow by'.
- NEVER use self-inflating bag to provide increased FiO2 in spontaneously breathing patients.
- If nasal cannula is used, the oxygen flow rate must not be below 2l/mt.
- Humidification oxygen is must when it is given in a concentration of >4L/mt.
- Low flow oxygen delivery system versus high flow system is not a question of inferior or superior type of delivery device; it just indicates a variable performance (low flow) as compared to a fixed oxygen concentration delivered (high flow).
- Oxygen is a part of the fire triangle and hence must be accompanied by ready availability of fire hazard safety.
- Specified flow rates must be maintained especially in rebreathing systems to decrease CO2 retention.
- A collapsed reservoir bag in a nonrebreathing system suggests inadequate flow rates.
- Optimal oxygen for preterm infants is still debated. More studies are needed for a final say.
- NRP still recommends resuscitation with 100%. Role of 100% O2 during resuscitation should be reassessed.
- Even a brief period of hyperoxia immediately after birth may have long term consequences.
- New strategies to reduce oxidative stress in neonates e.g. Antioxidant, may play a big role in making oxygen therapy safer.

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