Management of hypoxaemia in the critically ill patient

Luke Flower, Anaesthetics Department, University College Hospital, London, UK; Daniel Martin, Intensive Care Unit, Royal Free Hospital, London, UK, Correspondence to: Luke Flower (luke.flower@doctors.org.uk)

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Abstract

Hypoxaemia is a common presentation in critically ill patients, with the potential for severe harm if not addressed appropriately. This review provides a framework to guide the management of any hypoxaemic patient, regardless of the clinical setting. Key steps in managing such patients include ascertaining the severity of hypoxaemia, the underlying diagnosis and implementing the most appropriate treatment. Oxygen therapy can be delivered by variable or fixed rate devices, and non-invasive ventilation; if patients deteriorate they may require tracheal intubation and mechanical ventilation. Early critical care team involvement is a key part of this pathway. Specialist treatments for severe hypoxaemia can only be undertaken on an intensive care unit and this field is developing rapidly as trial results become available. It is important that each new scenario is approached in a structured manner with an open diagnostic mind and a clear escalation plan.

Key words

Acute respiratory distress syndrome, Critical care, Hospital medicine, Hypoxaemia, Hypoxia, Intensive care

Introduction

Hypoxaemia refers to a lower than normal arterial blood oxygen level, measured either as oxygen saturation (SaO_2) or partial pressure of oxygen (PaO_2). It is a common feature of acutely unwell hospitalised patients and can result in substantial morbidity and mortality if not treated rapidly and appropriately. Hypoxaemic patients may require admission to an intensive care unit, with more than 60% of those that do eventually requiring invasive ventilation. The mortality of hypoxaemic critically ill patients is 27%, rising to as high as 50% in patients with severe hypoxaemia (Grimaldi et al, 2018**).**

A structured approach to the management of hypoxaemic patients is essential in order to establish a diagnosis and implement the most appropriate therapy. Knowledge of relevant physiology is important when considering both the diagnosis and treatment. Tailoring therapies to individual patients will be necessary, particularly in terms of oxygenation targets.

This review provides a logical framework that can facilitate the management of all hypoxaemic patients. The evidence base in this field is in a constant state of flux and there have been a number of key publications in the past few years that have made us rethink our approach to this problem.

Definitions and basic physiology

Hypoxaemia

No specific threshold of SaO_2 or PaO_2 defines hypoxaemia. Suggested normal values for PaO_2 are 10.5–13.5 kPa, and for SaO_2 are 94–98% (O'Driscoll et al, 2017). This information can be obtained via arterial blood gas (providing PaO_2 and SaO_2) and pulse oximetry (providing peripheral capillary oxygen saturation). It should be noted that normal values decline with age and are influenced by the presence of comorbidities such as chronic lung disease.

Describing the magnitude of hypoxaemia in a patient receiving oxygen can be challenging; from a physiological perspective. Knowledge of the alveolar–arterial partial pressure difference ($PA-aO_2$) or Aa gradient can be useful when determining the cause of hypoxaemia. It requires the patient's arterial partial pressure of carbon dioxide ($PaCO_2$) to calculate it. Alternatively, the PaO_2 to fraction of inspired oxygen (FiO_2) ratio (PF ratio) may be a helpful guide to quantifying the degree of hypoxaemia and is frequently used in the intensive care unit (*Figure 1*).

Figure 1. Partial pressure of oxygen to fraction of inspired oxygen ratio association with severity of hypoxaemia.

Arterial partial pressure of oxygen (PaO2)	Fractional inspired oxygen concentraion (FIO2)																
	0.21	0.25	0.30	0.35	0.40	0.45	0.50	0.55	0.60	0.65	0.70	0.75	0.80	0.85	0.90	0.95	1.00
4.0	19.0	16.0	13.3	11.4	10.0	8.9	8.0	7.3	6.7	6.2	5.7	5.3	5.0	4.7	4.4	4.2	4.0
4.5	21.4	18.0	15.0	12.9	11.3	10.0	9.0	8.2	7.5	6.9	6.4	6.0	5.6	5.3	5.0	4.7	4.5
5.0	23.8	20.0	16.7	14.3	12.5	11.1	10.0	9.1	8.3	7.7	7.1	6.7	6.3	5.9	5.6	5.3	5.0
5.5	26.2	22.0	18.3	15.7	13.8	12.2	11.0	10.0	9.2	8.5	7.9	7.3	6.9	6.5	6.1	5.8	5.5
6.0	28.6	24.0	20.0	17.1	15.0	13.3	12.0	10.9	10.0	9.2	8.6	8.0	7.5	7.1	6.7	6.3	6.0
6.5	31.0	26.0	21.7	18.6	16.3	14.4	13.0	11.8	10.8	10.0	9.3	8.7	8.1	7.6	7.2	6.8	6.5
7.0	33.3	28.0	23.3	20.0	17.5	15.6	14.0	12.7	11.7	10.8	10.0	9.3	8.8	8.2	7.8	7.4	7.0
7.5	35.7	30.0	25.0	21.4	18.8	16.7	15.0	13.6	12.5	11.5	10.7	10.0	9.4	8.8	8.3	7.9	7.5
8.0	38.1	32.0	26.7	22.9	20.0	17.8	16.0	14.5	13.3	12.3	11.4	10.7	10.0	9.4	8.9	8.4	8.0
8.5	40.5	34.0	28.3	24.3	21.3	18.9	17.0	15.5	14.2	13.1	12.1	11.3	10.6	10.0	9.4	8.9	8.5
9.0	42.9	36.0	30.0	25.7	22.5	20.0	18.0	16.4	15.0	13.8	12.9	12.0	11.3	10.6	10.0	9.5	9.0
9.5	45.2	38.0	31.7	27.1	23.8	21.1	19.0	17.3	15.8	14.6	13.6	12.7	11.9	11.2	10.6	10.0	9.5
10.0	47.6	40.0	33.3	28.6	25.0	22.2	20.0	18.2	16.7	15.4	14.3	13.3	12.5	11.8	11.1	10.5	10.0
10.5	50.0	42.0	35.0	30.0	26.3	23.3	21.0	19.1	17.5	16.2	15.0	14.0	13.1	12.4	11.7	11.1	10.5
11.0	52.4	44.0	36.7	31.4	27.5	24.4	22.0	20.0	18.3	16.9	15.7	14.7	13.8	12.9	12.2	11.6	11.0
11.5	54.8	46.0	38.3	32.9	28.8	25.6	23.0	20.9	19.2	17.7	16.4	15.3	14.4	13.5	12.8	12.1	11.5
12.0	57.1	48.0	40.0	34.3	30.0	26.7	24.0	21.8	20.0	18.5	17.1	16.0	15.0	14.1	13.3	12.6	12.0
12.5	59.5	50.0	41.7	35.7	31.3	27.8	25.0	22.7	20.8	19.2	17.9	16.7	15.6	14.7	13.9	13.2	12.5
13.0	61.9	52.0	43.3	37.1	32.5	28.9	26.0	23.6	21.7	20.0	18.6	17.3	16.3	15.3	14.4	13.7	13.0
13.5	64.3	54.0	45.0	38.6	33.8	30.0	27.0	24.5	22.5	20.8	19.3	18.0	16.9	15.9	15.0	14.2	13.5
14.0	66.7	56.0	46.7	40.0	35.0	31.1	28.0	25.5	23.3	21.5	20.0	18.7	17.5	16.5	15.6	14.7	14.0
14.5	69.0	58.0	48.3	41.4	36.3	32.2	29.0	26.4	24.2	22.3	20.7	19.3	18.1	17.1	16.1	15.3	14.5
15.0	71.4	60.0	50.0	42.9	37.5	33.3	30.0	27.3	25.0	23.1	21.4	20.0	18.8	17.6	16.7	15.8	15.0

SEVERITY OF HYPOXAEMIA According to P:F Ratio
Severe
Moderate
Mild
Nil

Hypoxaemia may result from a multitude of pathologies; however, the basic physiology underlying these can be split into:

- Hypoventilation
- Ventilation–perfusion (VQ) mismatch (either an increased or decreased VQ ratio)
- Right to left circulatory shunting of blood
- Impaired diffusion of oxygen across the alveolar membrane
- Reduced FiO_2 (Sarkar et al, 2017).

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Respiratory failure is a broad term that describes inadequate gas exchange that either consists of hypoxaemia alone (type 1) or in combination with hypercapnia (type 2).

Hypoxia

The term hypoxia generally refers to a lack of oxygen at a cellular level. Severe hypoxia can affect the production of ATP by mitochondrial oxidative phosphorylation, threatening cellular integrity. Non-oxygen dependent bioenergetic pathways are referred to as anaerobic metabolism; they are short-term inefficient systems that are unable to sustain life for prolonged periods of time in humans. A brief summary of the causes of hypoxia can be seen in *Table 1*.

Table 1. Causes of hypoxia (a lack of oxygen at the cellular level)

Cause of hypoxia	PaO_2	Common causes	Treatment strategies
Hypoxic	Low	Altitude	Supplementary oxygen
Anaemic	Normal	Bleeding and anaemia	Blood transfusion and address underlying cause of anaemia*
Ischaemic	Normal	Embolism, thrombus	Treat underlying cause by increasing blood flow to target organ*
Histotoxic	Normal	Cyanide poisoning	Reverse or address causal agent*
*increasing FiO_2 is not beneficial			

One of the challenges in critically ill patients is that cellular oxygen levels cannot be measured. Anaerobic metabolism produces lactate as a byproduct, but this generally indicates poor organ perfusion (ischaemic hypoxia) rather than a lack of oxygen.

Acute respiratory distress syndrome

Acute respiratory distress syndrome is defined as: ‘The presence of new or worsening respiratory symptoms within 1 week of onset of symptoms; bilateral opacities on chest imaging not fully explained by effusions, atelectasis or nodules; respiratory failure from lung oedema not fully explained by cardiac failure or fluid overload; and oxygenation impairment. The degree of oxygenation impairment is defined by the following PF ratios: mild 40.0–26.8 kPa; moderate 26.7–13.4 kPa; severe ≤13.3 kPa.’ (ARDS Definition Task Force et al, 2012).

Acute respiratory distress syndrome can present in a broad range of patients and have a multitude of causes. The incidence in UK intensive care units was estimated to be 12.5% (Summers et al, 2016) and data from a worldwide multicentre study suggested an in-hospital mortality of up to 40% (Bellani et al, 2016). The pathophysiology that underlies acute respiratory distress syndrome is likely secondary to acute lung inflammation, resulting in increased vascular permeability, pulmonary oedema and worsening surfactant function. The culmination of this results in worsening gas exchange, shunt formation and worsening VQ mismatch (Pham and Rubenfeld, 2016). When severe this leads to extreme hypoxaemia. The complex pathophysiology behind acute respiratory distress syndrome means multiple treatment strategies have been suggested and trialled, often with little effect on mortality.

Initial approach to the hypoxaemic patient

Clinical assessment

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As with any acutely unwell patient, it is important to adopt the airway, breathing, circulation, disability, exposure approach to assessment and management. During this it is essential to look for any life-threatening causes of hypoxaemia (e.g. pneumothorax) so these can be treated swiftly. The degree of hypoxaemia and nature of respiratory failure should be determined early, and appropriate monitoring implemented to evaluate deterioration and effectiveness of treatment. On the intensive care unit this usually consists of continuous SpO_2, intermittent arterial blood gases and careful documentation of FiO_2. It is also important to ascertain any past medical history suggestive of chronic cardiopulmonary disease as this will help differentiate between worsening of chronic disease or acute pathology.

Investigations

It is important to try and identify the underlying cause of hypoxaemia so that an appropriate treatment may be initiated. *Table 2* summarises the common causes of hypoxaemia by pathology. A routine panel of blood tests is indicated in most cases, with more specific tests (e.g. D-dimer and cardiac enzymes) to be performed as clinically indicated. If infection is suspected then blood cultures, an atypical pneumonia screen, sputum samples and HIV tests may also be relevant. Depending on the clinical presentation it may also be appropriate to consider diagnoses such as *Mycobacterium tuberculosis* infection, pneumocystis pneumonia and vasculitis. Intubated patients may benefit from a bronchoscopy with or without bronchoalveolar lavage, as this can be both a beneficial diagnostic and therapeutic tool.

Table 2. Common causes of hypoxaemia

Pathology	Speed of onset and symptoms	Examination findings	Diagnosis	Treatment
Pneumonia	Days to weeks, infective symptoms, check travel history	Pleuritic chest pain, systemic signs of infection, possible crackles/bronchial breathing on auscultation	Chest X-ray, sputum samples, computed tomography may be required if complex	As per local sepsis and antimicrobial guidelines, supplementary oxygen often required
Pulmonary oedema	Acute if new event. If inpatient, check fluid balance and preceding history	Peripheral signs of heart failure if cardiogenic, bi-basal crackles, peripheral oedema	Chest X-ray, echocardiogram, ultrasound	If acute event – as per acute coronary syndrome treatment, diuresis, continuous positive airway pressure to be considered
Pneumothorax	Commonly acute	Pleuritic chest pain, reduced air entry, increased resonance on percussion	Chest X-ray, ultrasound, computed tomography may be required if complex	If tension pneumothorax – needle decompression and chest drain insertion, otherwise as per the British Thoracic Society guidelines (Havelock et al, 2010) dependent on size and past medical history

Pulmonary embolism	Commonly acute, can present as chronic – history often reduced mobility or pro-coagulant state	Pleuritic chest pain, tachycardia, tachypnoea, possible circulatory collapse	Computed tomography pulmonary angiogram as gold standard, echocardiogram for right heart strain, ventilation-perfusion scan if computed tomography pulmonary angiogram not possible	If circulatory collapse and nil contraindications – thrombolysis as per guidelines. Otherwise anticoagulation as per British Thoracic Society guidelines
Pleural effusion	Acute or chronic	Reduced air entry at site of effusion, stony dull to percuss	Chest X-ray, ultrasound, computed tomography scan if complex	As per British Thoracic Society management (Havelock et al, 2010), if significant or possibly infective then pleural tap +/ - drain insertion
Haemothorax	Commonly acute, often associated with trauma	Reduced air entry, dull to percuss, may have signs of trauma	Chest X-ray, ultrasound, computed tomography scan	If indicated – surgical chest drain insertion

Imaging

Chest X-rays and ultrasound scans can be performed quickly and easily at the bedside and maintain a high level of sensitivity and specificity across a broad range of pathologies. More complex cases may require cross-sectional imaging in the form of computed tomography with or without pulmonary angiography. Echocardiography is also a useful and quick bedside diagnostic tool; particular attention should be paid to right ventricular function and pulmonary artery pressure, as this may aid diagnosis of acute or chronic pathologies (e.g. pulmonary emboli or pulmonary hypertension) and help guide treatments thereafter.

Non-invasive treatment strategies

Some general strategies can be used when approaching almost all ward-based hypoxaemic patients. It is important that all such patients are managed in high-acuity wards, with constant pulse oximetry, regular clinical reviews and, if appropriate, blood–gas analysis.

Management of type 1 respiratory failure

This is defined as hypoxaemia without hypercapnia. First, simple strategies such as optimising patient positioning by sitting the patient upright, physiotherapy and upper airway suctioning in patients with abundant or thick secretions may aid ventilation. Variable performance

oxygen masks and nasal cannula may be appropriate initially; however, their design prevents accurate or high concentration oxygen delivery. Patients with severe hypoxaemia may require high-flow oxygen, delivered via fixed performance masks with a precise FiO_2. Venturi masks fit these criteria and are available for 24–60% oxygen. Anaesthetic breathing systems such as the Water's circuit also use high-flow oxygen and can deliver up to 100% oxygen. A non-rebreathe mask requires 15 litres/min of oxygen and can deliver up to 80% oxygen (Wagstaff and Soni, 2007).

If traditional oxygen delivery systems fail to adequately oxygenate a patient, continuous positive airway pressure ventilation may be beneficial (British Thoracic Society Standards of Care Committee, 2012). Continuous positive airway pressure improves oxygenation by preventing the collapse of alveoli and small airways at the end of expiration and lessening VQ inequality via redistribution of fluid within the lungs (Mas and Masip, 2014). Low levels of end-expiratory pressure can also improve cardiac function in the presence of left ventricular failure (by reducing the afterload) or right ventricular failure (by reducing the preload) (Sin et al, 2000; Agarwal et al, 2005). Administering continuous positive airway pressure requires specialist skills and frequent patient observations and review.

An alternative is high-flow nasal oxygen, which provides flow rates of up to 60 litres/minute and delivers precise humidified oxygen concentrations up to 100%. It has been associated with significant improvement in acutely hypoxaemic patients in the intensive care unit (Sztrymf et al, 2012). Proposed mechanisms of action include positive airway pressure generation, flushing of dead space gas and benefits from humidification and heating of the oxygen delivered through the circuit (Ashraf-Kashani and Kumar, 2017).

Management of type 2 respiratory failure

Type 2 respiratory failure is hypoxaemia with associated hypercapnia and is common in patients with chronic obstructive pulmonary disease. The approach to managing a patient with hypercapnic respiratory failure is similar to type 1 respiratory failure, with the avoidance of severe hypoxaemia remaining key.

The first step in treating these patients is initiation of oxygen via a fixed performance device. A sub-group of patients with chronic obstructive pulmonary disease is at increased risk of hypercapnic respiratory failure because of a combination of worsening VQ mismatch (following the loss of hypoxic pulmonary vasoconstriction), the Haldane effect and decreased minute ventilation (Hanson et al, 1996). In such patients supplemental oxygen must be carefully titrated using fixed performance, with acid–base balance, neurological status and carbon dioxide levels closely monitored. It is important to emphasise that the risk of severe hypoxaemia in these patients outweighs that of hypercapnia.

If hypoxaemia and/or hypercapnia persists, non-invasive ventilation should be considered. Bi-level positive airway pressure is the appropriate intervention; its benefit over continuous positive airway pressure for these patients is the addition of an inspiratory pressure to augment their tidal volume. The rise in minute ventilation that results from this should reduce $PaCO_2$. It is important that these patients are reviewed regularly and their bi-level positive airway pressure settings adjusted according to their response. The British Thoracic Society/Intensive Care Society joint guidelines currently advise starting at an inspiratory pressure of 15 cmH_2O and positive end expiratory pressure of 3 cmH_2O, with the view to up-titrate the inspiratory pressure, positive end expiratory pressure or both over 10–30 minutes until adequate ventilation and oxygenation is reached (targeting an SpO_2 of 88–92%). If inspiratory pressure reaches >30 cmH_2O or positive end expiratory pressure >8 cmH_2O then expert review is advised. Contraindications to bi-level positive airway pressure include airway

obstruction, recent upper gastrointestinal or craniofacial surgery, facial or airway burns, high risk of aspiration and untreated pneumothoraces (Davidson et al, 2015).

Management of mechanically ventilated patients

Failure to respond to high-flow oxygen and/or non-invasive ventilation may require a patient to be transferred to an intensive care unit for consideration for invasive ventilation. Early referral to the intensive care unit team will help them to assess the situation and determine the need for transfer. Indications for intubation and critical care referral for hypoxaemic patients include an inability to maintain their airway, protect their airway from aspiration (e.g. low Glasgow Coma Scale score), ventilate sufficiently, oxygenate sufficiently despite optimisation of non-invasive techniques, or anticipation of a deteriorating clinical picture. Mechanical ventilation in the acutely unwell patient requires sedation and usually neuromuscular blockade to facilitate tracheal intubation.

Not all patients will be suitable for this level of treatment as it comes at risk of multiple organ failure, prolonged ventilation and the possibility of the need for a tracheostomy. The intensive care unit team, in discussion with the primary team, patient and patient's relatives, should clarify the patient's suitability for this level of treatment as soon as possible. While mechanical ventilation should improve oxygenation and CO_2 clearance, it will not treat the underlying pathology; this will also need to be addressed to promote recovery.

A number of strategies have been used in mechanically ventilated intensive care unit patients with respiratory failure, around 30% of whom will not survive (Esteban et al, 2013). Much of the research to date has focused on patients with acute respiratory distress syndrome but strategies for this syndrome can be considered in all patients with refractory hypoxaemia. What follows is a synopsis of these treatment strategies with the evidence base supporting their use.

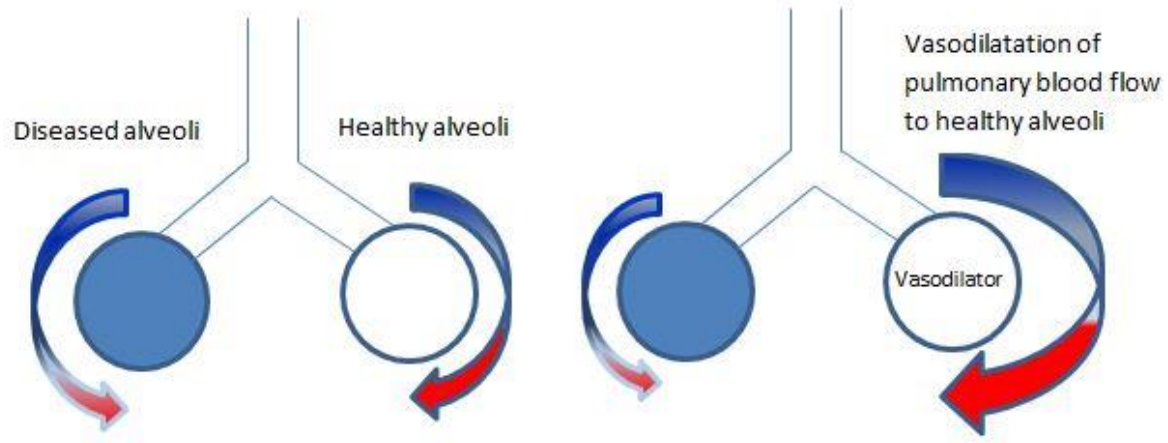
Pharmaceutical approaches

Over recent years various pharmacological strategies have been trialled to aid management in severely hypoxaemic patients.

1. Neuromuscular blocking agents are used to improve synchronisation of ventilation between the patient and ventilator, hopefully improving oxygenation and carbon dioxide clearance. Reduced mortality and number of days requiring mechanical ventilation has been demonstrated when used in patients with moderate to severe acute respiratory distress syndrome (Papazian et al, 2010). Current consensus is in favour of their use in patients suffering from moderate or severe acute respiratory distress syndrome (Griffiths et al, 2019).
2. Corticosteroids may be indicated for specific underlying diagnoses such as asthma or chronic obstructive pulmonary disease, usually in fairly modest doses. In patients suffering from acute respiratory distress syndrome, high-dose steroid strategies (e.g. 1 g intravenous methylprednisolone) have a low level of evidence supporting their use, with a possible associated reduction in mortality (Griffiths et al, 2019). However, the overall evidence pool remains largely equivocal.
3. Inhaled vasodilators (such as epoprostenol and nitric oxide) have also been used, based on the theory that they promote selective vascular dilatation in well-ventilated areas of the lung, thus lessening VQ inequality (*Figure 1*). To date, no mortality benefit has been shown with their use (Griffiths et al, 2019). However, their use as a bridging strategy has been suggested before rescue therapies such as extracorporeal membranous oxygenation (Wright, 2015).

Figure 2. Poorly aerated regions of lung result in ventilation–perfusion mismatch, as blood to these areas is poorly oxygenated. Inhaled vasodilators result in dilatation of vasculature surrounding

healthy lung units, with increased blood flow, oxygenation and thus reduction in ventilation–perfusion mismatch and shunting.



Fluid management

Fluid management in hypoxaemic patients is often complex and dependent on the underlying aetiology of the hypoxaemia. The overwhelming aim is to avoid excess positive fluid balance. This is particularly relevant in patients with cardiogenic pulmonary oedema and acute respiratory distress syndrome. Trials have demonstrated a decreased mortality associated with a conservative (neutral) *vs* liberal fluid approach in such patients and therefore this approach is currently advised (National Heart, Lung and Blood Institute Acute Respiratory Distress Syndrome Clinical Trials Network et al, 2006; Griffiths et al, 2019).

Ventilation strategies

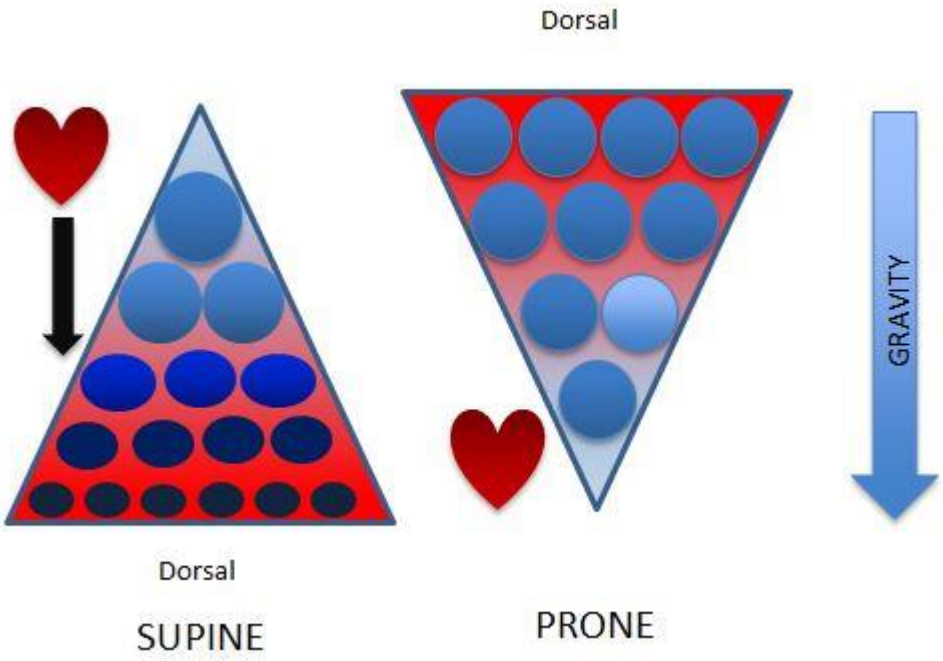
All mechanically ventilated patients should receive lung protective ventilation, defined as a tidal volume of ≤6 ml/kg and plateau pressure ≤30 cmH_2O (as per ARDSnet protocol). This reduces mortality, and local and systemic inflammation in mechanically ventilated patients (Acute Respiratory Distress Syndrome Network et al, 2000; Wolthuis et al, 2008). Originally recommended for patients with acute respiratory distress syndrome, it is now clear that lung protective ventilation should be the default whenever mechanical ventilation is required to prevent damage to lung parenchyma. Thus, the consensus is that most patients should be ventilated with a tidal volume of ≤6 ml/kg unless there is a specific contraindication.

The use of high positive end expiratory pressure (>10 cmH_2O) in hypoxaemic patients stems from the idea that it may improve alveolar ventilation by reducing atelectasis and splinting small airways open. Trials into the use of high positive end expiratory pressure in patients with acute respiratory distress syndrome demonstrated that patients who improved following its initiation then benefitted from its continued use, with no increase in hyperinflation and barotrauma recorded (Guo et al, 2018). Evidence to date supports the use of high positive end expiratory pressure in patients with severe hypoxaemia or acute respiratory distress syndrome who are initially responsive to high positive end expiratory pressure levels (Griffiths et al, 2019). A degree of positive end expiratory pressure, although not high, is used in the majority of ventilated patients.

Prone positioning

A strong evidence base is forming regarding the benefits of ventilating patients with moderate or severe acute respiratory distress syndrome in the prone position. The prone position improves VQ matching by creating a more homogenous pleural pressure gradient, reducing atelectasis and improving drainage of secretions (*Figure 3*). Meta-analyses have shown a reduction in mortality in patients suffering from acute respiratory distress syndrome, most significantly when patients are in the prone position for at least 12 hours (Hu et al, 2014; Park et al, 2015).

Figure 3. When supine, gravity and the weight of the heart result in compression of dependent dorsal areas of lung and thus hypoventilation. In the prone position, the alveoli become more homogenous and the weight of the heart is instead on the sternum. This leads to increased perfusion of dorsal lung segments with reduced ventilation–perfusion mismatch. Perfusion in the lung remains largely dorsal in both the supine and prone position. Red shading indicates the most perfused lung regions. Adapted from Koulouras et al (2016).



Extracorporeal CO_2 removal

The CO_2 removal provided by this technique allows lung protective and ultra-low tidal volume to be used in acutely hypoxaemic patients, who would otherwise develop severe hypercapnic acidosis (Peperstraete et al, 2017). At this time there is no evidence for or against this treatment strategy so further research is required. Other suggested management strategies include permissive hypercapnia, permissive acidosis (pH >7.2) and the use of sodium bicarbonate, but more research is required.

Extracorporeal membranous oxygenation

A full description of extracorporeal membranous oxygenation is beyond the scope of this article. Veno-venous extracorporeal membranous oxygenation facilitates oxygenation of severely hypoxaemic patients via an extracorporeal circuit and is only available in specialist centres. It requires the insertion of large cannulae into central vessels, anticoagulation of the circulation and specialist intensive care nursing skills. In patients with severe refractory hypoxaemia, referral to a specialist extracorporeal membranous oxygenation centre should be considered early. Criteria for referral to such centres may vary but are generally: severe hypoxaemia (PF ratio <13.3 kPa), severe

hypercapnic acidosis (pH <7.20), inability to achieve lung protective tidal volumes, nil improvement with rescue therapies such as prone position and significant air leak or bronchopleural fistula.

The evidence surrounding the use of extracorporeal membranous oxygenation in patients with acute respiratory distress syndrome is constantly being re-visited, with a small reduction in mortality suggested historically (Peek et al, 2009). However, the 2018 EOLIA trial looking at extracorporeal membranous oxygenation in severe acute respiratory distress syndrome showed no significant improvement in 60-day mortality, and was terminated early for futility (Combes et al, 2018).

Conclusions

Management of a critically ill hypoxaemic patient can be a complex and challenging task. It is important to maintain a structured approach, attempt to identify an underlying cause and pay close attention to any signs of deterioration. The degree and nature of hypoxaemia will direct the chosen treatment route. The clinical picture should constantly be re-reviewed, while asking one's self: Is this patient still severely hypoxaemic? Does this patient require escalation to critical care? Does this patient require referral to a tertiary respiratory centre? If the answer to any of these questions is yes, then immediate advice should be sought. In patients requiring invasive ventilation, lung protective techniques should be used in all cases. Treatment strategies such as the prone position, high positive end expiratory pressure, corticosteroid use, neuromuscular blocking agents and a conservative fluid balance may be beneficial in patients with moderate to severe acute respiratory distress syndrome. While extracorporeal membranous oxygenation, extracorporeal CO_2 removal and inhaled vasodilators may also confer some benefit, more research is indicated to support their ongoing use.

The treatment of severe hypoxaemia is likely to continue to evolve as more research and trials are performed. Nevertheless, as clinicians it is important that we approach each new scenario with a reliable structure, an open diagnostic mind and a clear escalation plan.

Conflicts of interest

D Martin has received consultancy and lecture fees from Siemens Healthineers and Edwards Lifesciences; L Flower: none.

Key points

- Hypoxaemia is defined as a lower than normal arterial blood oxygen level, while hypoxia refers to a lack of oxygen at a cellular level.
- Hypoxaemia is a common presentation in critically ill patients, with the potential for severe harm if not addressed early.
- Determining the nature, cause and severity of hypoxaemia is a key step in enabling effective treatment.
- The treatment strategies required will be dependent on the clinical picture and may involve a combination of non-invasive and invasive modalities.
- Severely hypoxaemic patients, not responding to initial treatment, should be discussed with critical care and specialist respiratory teams early.
- While some specialist centres may use advanced treatment strategies such as extracorporeal membranous oxygenation in this patient group, further research to support and quantify their effectiveness is still required.

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