Austin Journal of Emergency and Critical Care Medicine

Open Access

Austin Publishing Group

Review Article

Acute Hypoxia: An Overview

Weledji EP[1]*, Ngomba MN[2] and Njie KT[3]

[1]Department of Surgery, Faculty of Health Sciences, University of Buea, Cameroon

[2]Intensive Care Unit, Regional Hospital limbe, S.W. Region, Cameroon

[3]Infectious Disease & Community Health, Director, Regional Hospital Limbe, S.W. Region, Cameroon

***Corresponding author:** Weledji EP, Pemset House, Lumpsum Qrts, Limbe, S.W. Region, Cameroon

Received: February 15, 2020; **Accepted:** April 13, 2020; **Published:** April 20, 2020

Abstract

Hypoxia kills and kills quickly. In the healthy individual total oxygen delivery far exceeds total oxygen consumption. An acute hypoxic patient would therefore be critically ill and need oxygen. The assessment of the suitability of a patient to withstand surgery and anaesthesia is closely related to their ability to increase oxygen delivery to vital tissues. Optimizing these factors would maximize the patient's reserves. Oxygen is only one aspect of treatment and the underlying cause of the respiratory failure must be treated. This article reviewed acute hypoxia, respiratory failure and the indications for oxygen therapy.

Keywords: Hypoxia; Acute; Respiratory failure; Monitoring; Oxygen therapy

Introduction

Respiratory failure occurs when pulmonary gas exchange is sufficiently impaired to cause hypoxaemia with or without hypercarbia. In practical terms, respiratory failure is present when the partial pressure of arterial oxygen (PaO_2) is <8KPa (60mmHg) i.e. an arterial saturation of oxygen ($Sa0_2$) of <90% or the partial pressure of arterial carbon dioxide ($PaCO_2$) is >7kPa (55mmHg). The normal PaO_2 is 75-100mmHg (10-13.3KPa). It is the oxygen content of the arterial blood that matters and this is determined by the percentage saturation of haemoglobin (Hb) with oxygen. The measure of the oxygen saturation of Hb-oxyhaemoglobin gives an estimate +/-2% of the percentage of oxygen carrying sites which are occupied in Hb. The maximum number of sites which could be occupied is obviously 100%. Thus the normal oxygen saturation for arterial blood (SaO_2) is 95-100% (Figure 1). In health SaO_2 is normally near maximal i.e. around 97%. Oxygen supplementation should ideally be given when oxygen saturation is <95%. Pulmonary distribution of blood flow is improved by hypoxia as a result of hypoxic pulmonary vasoconstriction to favour ventilation-perfusion matching. The persistence of chronic alveolar hypoxia and hypercapnoea leads to constriction of the pulmonary arterioles and subsequent pulmonary arterial hypertension [1,2]. It is also important to appreciate that the lungs normally never empty completely. At the end of each breath an 'average' man with a total lung capacity (TLC) of 6 litres will still have around 2.5 litres of gas in the lungs (functional residual capacity, FRC) and even if he expires as much as he can the expiratory reserve volume, (ERV) he will only reduce this to 1.2 litres (residual volume, RV) (Figure 2) [3]. In addition, the signs of hypoxia are generally non-specific and often difficult to assess. The primary aim of the management of respiratory failure is to improve the PaO_2 by continuous controlled oxygen therapy. This nearly always leads to a rise in the $PaCO_2$. A small increase in $PaCO_2$ can be tolerated but not if the pH falls dramatically or below 7.25. Under such circumstances, increased ventilation must be achieved either by the use of a respiratory stimulant or artificial ventilation [4]. However, oxygen is only one aspect of treatment and the underlying cause of the respiratory failure must be treated.

Types and Causes of Respiratory Failure

There are two types of respiratory failure (type 1 and type II). Type I or acute hypoxaemic respiratory failure occurs in diseases which damage lung tissue with hypoxaemia due to R to L shunting or ventilation/perfusion mismatch. The PaO_2 is low but $PaCO_2$ is normal or low i.e. there is some compensation by spontaneous hyperventilation. Hyperventilation results from a decreased arterial PO_2 but the response is non linear. There is little effect until arterial PO_2 is reduced to about 7kPa (52mmHg) and maximal response is at 4kPa (30mmHg). The common causes are pneumonia, pulmonary oedema, acute respiratory distress syndrome (ARDS) and the chronic situation such as pulmonary fibrosing alveolitis. Type II or ventilatory failure occurs when alveolar ventilation is insufficient to excrete the volume of carbon dioxide (CO_2) being produced by tissue metabolism. Thus, CO_2 retention is the hallmark. Inadequate ventilation is due to reduced ventilatory effort, inability to overcome an increased resistance to ventilation and failure to compensate for an increase in dead space and/or CO_2 production, or a combination of these. The most common cause is chronic bronchitis. Others include chest wall deformities, respiratory muscle weakness e.g. Guillaine-Barre syndrome, and depression of the respiratory centre by sedative morphine-type drugs [5,6].

Monitoring

Clinical assessment

The clinical signs of respiratory distress would include the use of accessory muscles of respiration, tachypnoea, tachycardia, sweating, pulsus paradoxus, inability to speak from exhaustion and signs of carbon dioxide retention. With regard to tachypnoea, the minute ventilation rises initially in acute respiratory failure and falls precipitously only at a late stage when the patient is exhausted. In Guillain- Barre syndrome the vital capacity decreases as the respiratory muscle weakness increases. Tachycardia is the most sensitive clinical indication of increasing respiratory difficulty. The signs of CO_2 retention include a bounding pulse, peripheral vasodilatation and later a coarse flapping tremor of the outstretched hands. More severe hypercapnoea leads to confusion, progressive drowsiness and coma with papilloedema [7].

Blood gas analysis

Blood gas analysis from an arterial puncture provides the modern automated objective assessment of respiratory function and a guide

Citation: Weledji EP, Ngomba MN and Njie KT. Acute Hypoxia: An Overview. Austin J Emergency & Crit Care Med. 2020; 6(1): 1069.

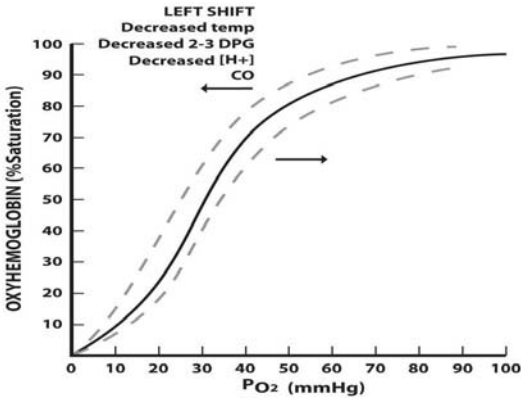

Figure 1: Oxygen haemoglobin dissociation curve. Keep the saturation >94%!

to oxygen therapy. First, it demonstrates the disturbances of acid-base balance such as respiratory acidosis caused by retention of carbon dioxide (type II respiratory failure), respiratory alkalosis seen with hypoxaemic (type 1) respiratory failure and in those living at high altitudes, metabolic acidosis and metabolic alkalosis. Second, it demonstrates the alterations in oxygenation (the percentage saturation of haemoglobin with oxygen) which is important with regard to the oxygen haemoglobin dissociation curve (Figure 1). According to the sigmoid shape of the oxygen haemoglobin dissociation curve, if the percentage oxygen saturation is >90% oxygenation can be considered adequate i.e. PaO_2 is within the normal (75-100mmHg). After this a small fall in PaO_2 will cause significant reduction in oxygen content. A SaO_2 of 60% is associated with a PaO_2 of only about 35mmHg. No oxygen is available below SaO_2 of 30% (Figure 1). It is important to note that PaO_2 complements SaO_2 and is a better indicator of the pressure driving oxygen into the tissues. Normal PaO_2 depends on the fraction of inspired oxygen (FiO_2) As the FiO_2 increases towards 1, so should the PaO_2 increases-a PaO_2 of 100mmHg (13.3kPa) indicates good oxygenating ability for an individual breathing air (FiO_2 0.21) but not for a patient on high flow oxygen. Errors in blood gas analysis can result from malfunction of the analyser or incorrect sampling techniques [8]. Table 1 illustrates the normal values when blood gas analysis is used.

Pulse oximetry

Pulse oximetry has revolutionized the detection and management of hypoxaemia. It is a non-invasive technique that allows continuous or intermittent determination of arterial oxygen saturation in almost all patients. It uses the signal of pulsatile flow (plethysmography) and changes in light absorbency (spectophotometry) between oxygenated and reduced haemoglobin to determine arterial oxygen saturation of Hb. Signal processing produces a display of heart rate and arterial oxygen saturation (SaO_2) [9]. A limitation of pulse oximetry is that it does not measure CO_2 but blood gases do, and, acute hypercapnia needs increased ventilation. Nonetheless, it is less expensive than arterial blood gas analysis and invaluable in low resourced settings. It is more sensitive and simple to use than the measure of the PaO_2 of blood using the gold standard arterial blood gas analysis (ABG). However, pulse oximetry may be unreliable under certain circumstances [10]. These include movement, poor application of the probe, dirty probe, low output states, peripheral vasoconstriction such as in a cold patient, abnormal haemoglobins e.g. carboxyhaemoglobin in smokers [11,12], jaundice and excessive ambient light.

Table 1: Normal values for measurements obtained when blood gas analysis is performed.

H^+	35-45 nmol.l^{-1}	(pH 7.35-7.45)
PO_2	10-13.3 kPa	(75-100 mmHg)
PCO_2	4.8-6.1 kPa	(36-46 mmHg)
Plasma HCO_3	22-26 mmol.l^{-1}	
O_2 saturation		95-100%

Factors Influencing Oxygen Delivery

It is important to note that the arterial partial pressure of oxygen is also influenced by oxygen delivery. According to Fick's principle, the total oxygen delivery (oxygen flux) to the tissues depends upon the cardiac output (CO) and the amount of oxygen contained in that blood, i.e. Oxygen delivery (DO_2) = CO x (constant x [Hb] x SaO_2] + dissolved oxygen. With the normal CO of 5l/min, constant 1.34ml/g, [Hb} 150g/l, SaO_2 0.97 the oxygen delivery is 1000ml/min at rest. The resting oxygen consumption (VO_2) is about 250mls/min, and thus there is a four- fold reserve of oxygen utilization [13]. Hypoxia presents a serious threat to the body as it only occurs when this four-fold reserve has been utilized. Oxygen delivery is increased during exercise by increase in the cardiac output which could reach 30l/min via increase in heart rate and stroke volume by the sympathetic nervous system [14]. The sympathetic system is concerned in many of the responses to hypoxia, particularly the increase in organ perfusion [15]. The immediate response is reflex and is initiated by chemoreceptor stimulation occurring before there is any measurable increase in circulating catecholamines [16]. Cardiac output is increased by hypoxia, together with the regional blood flow to almost every major organ, particularly the brain [17]. Reduction of cerebral and probably myocardial vascular resistance is not dependent on the autonomic system but on local microcirculatory responses via paracrine-dependent vasorelaxation by endothelium- derived production of the gaseous mediator nitric oxide (NO) [18,19]. With the exception of pulmonary vessels which cause vasoconstriction and shunting for V/Q match [2], hypoxia causes vasodilatation of blood vessels mainly from a direct effect of adenosine and other metabolites generated by hypoxia [19]. Certain organs, notably the gut, are more prone to covert hypovolaemia and the consequent hypoxia may continue to drive the inflammatory process (including multiple organ failure) probably via bacterial translocation even when the initial causal factors are dealt with. One approach to overcome this has been to ensure that the critically ill patient with MOF has a circulation which provides an oxygen delivery greater than normal, thus minimizing the chance of occult hypoxia [20,21].

Types of Hypoxia

Hypoxia is classified in four types. Hypoxic hypoxia (hypoxaemia) occurs from factors affecting the saturation of oxygen; anaemic hypoxia occurs from factors affecting haemoglobin; stagnant hypoxia (ischaemia) occurs from factors affecting cardiac output or the local circulation, and histotoxic hypoxia occurs from factors affecting tissue utilization such as cyanide poisoning which directly affects the cellular (mitochondria and cytochrome) respiratory processes. Causes of

hypoxic hypoxia include airway obstruction, inadequate ventilation, low inspired partial pressure of oxygen, reduced alveolar gas transfer and low mixed venous PO_2 shunt. Causes of anaemic hypoxia include low normal Hb (anaemia) seen in surgical conditions or other medical conditions with consequent decreased capacity of blood to carry oxygen; decreased functional Hb such as carboxyhaemoglobin (COHB) in smokers and in the trauma patient with smoke inhalation, and methaemoglobin from large local anaesthetic (prilocaine) use [2,22,23]. Carbon monoxide from cigarette smoke has 240 times greater affinity for haemoglobin than oxygen. It therefore prevents Hb binding oxygen and only slowly dissociate. Heavy cigarette smokers may have up to 15% of their Hb as COHB. Abstinence, even for 24 hrs, will reverse most of this (1). Certain dysfunctional haemoglobins may be relevant to the surgical patient as they cause a relative reduction in haemoglobin. Stagnant hypoxia is caused by decreased preload and/or contractility and/or increased afterload against which the heart must pump [24]. In all these situations the remaining normal Hb may well have a normal saturation of oxygen but the overall oxygen content is reduced. Certain compensatory mechanisms will come into play whatever the reason for the hypoxia, although their effectiveness will depend to a large extent on the cause [20]. For example, hyperventilation will be largely ineffective in stagnant or anaemic hypoxia because hyperventilation while breathing air can do little to increase the oxygen content of arterial blood, and usually nothing to increase perfusion. Nevertheless, oxygen therapy is useful as up to 75% of red blood cells have to be lost in anaemic hypoxia for significant hypoxaemia to manifest [1,19]. The oxygen haemoglobin dissociation curve is displaced to the right by an increase in 2,3-diphosphoglyserate (2,3-DPG) in red blood cells by hypoxia and by the Bohr effect of acidosis (a lower pH) which may also be present. This tends to increase the tissue delivery (PO_2) of oxygen. On the contrary, alkalaemia shifts the curve to the left, increasing the oxygen affinity to Hb and oxygen delivery is impaired (Figure 1). Anaerobic metabolism is increased in severe hypoxia in an attempt to maintain the level of the energy currency-adenosine triphosphate (ATP) (2). However, unless the cause and the consequences of the inbalance between oxygen delivery (DO_2) and oxygen consumption (VO_2) are treated anaerobic cellular metabolism will be initiated with serious consequences from cellular oxygen debt [20,21]. The basis of resuscitation is regaining this balance [20].

Hypoxia in Early Trauma and Critical Care

Hypoxia is one of the main causes of preventable death in serious trauma [25]. Patients with significant traumatic event require oxygen. The trimodal distribution of death in civilian trauma categorized deaths into one of three distinct time periods. In the first peak death occurs within seconds to minutes due to massive injuries to the major vessels, heart, brain and high spinal cord. Deaths in the second peak i.e. within the golden hour occur from injuries that are potentially treatable. Deaths in the third peak arise from sepsis and multiple organ failure [26]. The Advanced trauma life support (ATLS) focuses on providing rapid assessment and resuscitation which mostly entails management of hypoxia and hypovolaemia. The sequence of a primary survey, resuscitation, secondary survey and definitive treatment had a direct effect on outcome by reducing both the second and third peaks of death. The primary survey follows a system of attending to life-threatening problems in a sequence of what may kill the patient first. It begins with A (Airway and care of the cervical spine) as death from airway obstruction occurs within seconds, B, (breathing with provision of adequate ventilation and oxygenation). Breathing problems such as tension pneumothorax, cardiac tamponade, a large flail chest etc, may cause death within minutes; C (Circulation including haemorrhage control). Haemorrhage may kill a patient within an hour; D (disability of the central nervous system-CNS; E (Exposure for clinical examination as appropriate without causing hypothermia). Trauma, being a dynamic problem requires continuous re-evaluation and monitoring of the vital signs of the patient. Ongoing resuscitation requires oxygenation and ventilation, and the "C" stage of the ATLS may continue in the operating theatre for haemorrage control. If there is no spontaneous respiration or ventilation is inadequate then ventilator support is provided. Adequate ventilation essentially means the body receives adequate oxygen and there is no carbon dioxide retention and is ensured at all times. The normal respiratory rate (RR) should be between 12 and 18/min. Oxygen supplementation is indicated if the RR is 10-12 or 18-28 in an adult. If the RR is <9 or >28 assisted ventilation is indicated [25-27]. The decision-making priorities of critical care of the trauma patient in the ICU are oxygen delivery, hypothermia, clotting and acid-bas balance and electrolytes. Hypothermia (temp $<34^0$C)-coagulopathy (PT >16secs) –acidosis (pH <7.2) is the lethal triad of death [28]. After major trauma, cellular shock and resultant anaerobic metabolism rapidly leads to a systemic lactic acidosis. The acidosis is compounded by reduced or deficient renal function and a major blood transfusion. The chief method of correcting the metabolic acidosis is by optimizing peripheral and renal perfusion and oxygenation, thereby allowing autocorrection [28,29].

The Critically Ill Patient

The initial recognition, investigation and treatment of a critically ill patient must be performed accurately and rapidly by the experienced clinician. It is important to recognize when the patient requires advanced care in the intensive care unit [29]. Valuable clinical information can be gained from the bedside by following the primary survey of ATLS. Fixed delivery oxygen masks are available up to an inspired oxygen concentration of 60% (FiO_2) of 0.6. All oxygen delivery systems should be humidified; otherwise the dry, cold gas may contribute towards thickening of the patient's secretions and promote sputum retention. Nebulised normal saline (plus bronchodilators if indicated) and regular treatment from a respiratory physiotherapist may prevent worsening of incipient respiratory failure. The response of the patient is assessed according to the improvement of clinical status, oxygen saturation and arterial blood gas analyses. ICU transfer may be indicated by the need for intubation for airway support, with or without ventilation, for respiratory failure requiring ventilation because of either inadequate oxygenation (PaO_2 <9KPa with a FiO_2 1.0) on a non-rebreathing mask or a rising $PaCO_2$ >8Kpa, pH <7.3) and for advanced cardiovascular monitoring. A metabolic acidosis represents a serious derangement indicating the inability of the kidney to excrete hydrogen ion. It is an important signal of anaerobic metabolism and considered as a serious sign of deterioration and cellular oxygen debt. Elevated lactate level representing anaerobic metabolism on admission to the ICU corresponded to higher mortality [20,21)].The beginnings of a metabolic acidosis presents as a PaO_2 remaining low despite an

inspired oxygen of 100%, an elevated hydrogen ion, low base excess and an arterial oxygen saturation that remains low. This is typically seen in major intrapulmonary A-V shunts i.e. pneumonia, major pulmonary embolus and pulmonary oedema [30]. Even if the patient responds to supplemental oxygen therapy and the arterial blood gases improve, it should be remembered that oxygen is only one aspect of treatment as the underlying cause of the respiratory failure must be treated.

Hypoxia in Head Injury

In head injury, primary brain damage has occurred from the impact and the aim is to prevent secondary injury (neuronal hypoxia). The priorities are A (Airway with cervical spine control, B (Breathing, C (circulation/ convulsion control. H (haematoma detection). Avoiding hypoxia including airway obstruction, hypotension, hypercapnia and anaemia is first priority. Oxygen is always given in high concentrations until confirmed as unnecessary by SaO_2 or PaO_2. Intra-abdominal or intrathoracic blood loss is dealt with and the need to insert chest drains in a patient not breathing properly is considered before transfer to a neurosurgical unit. Only once these have been done can attention be turned towards reducing intracranial pressure raised by haematomas or cerebral oedema [26,27]. Factors which reduce cerebral oxygen delivery such as hypertension, hypercapnoea (brain swelling, ICP), hypo-osmolar states (brain swelling, ICP), increased venous pressure (increase ICP) and a missed intracranial haematoma (increase ICP) should be avoided. Factors increasing cerebral oxygen consumption such as hyperpyrexia and convulsions should also be avoided (Table 2). The indications for intubation and ventilation in head injuries are (1) for airway protection (to obtain a secure clear airway and to prevent aspiration of blood or gastric contents), and (2) if intermittent positive pressure ventilation (IPPV) is required. It is important to rapidly assess and record accurately conscious level prior to intubatiion. The respiratory indications for ventilation are clinically inadequate ventilation (PaO_2 less than 10kPa (SaO_2 <90) on 60% O_2 mask or $PaCO_2$ greater than 5.5kPa), hyperventilation ($PaCO_2$ <3.0kPa), and if sedation is required to tolerate endotracheal tube. The neurological indications are uncontrolled convulsions, deteriorating neurological condition (conscious level, pupil signs), severely depressed conscious level (GCS 8 or less), ICP>25. Other indications would be to allow adequate analgesia in presence of multiple injuries, in patients with persistent temperature >38.5 (active cooling required) and to allow safe transport [30].

Post-operative Hypoxia

Perioperative hypoxia is a serious complication resulting in morbidity and mortality. Although there are various causes it is frequently associated with airway management during general anaesthesia, and monitoring of oxygen saturation is a routine. After surgery a wide range of factors may tend to reduce SaO_2. These include inadequate oxygen administration, airway obstruction, hypoventilation secondary to inadequate reversal of muscle relaxation or excessive sedation, lower respiratory complications, e.g. bronchospasm, consolidation, atelectasis, pulmonary oedema or pulmonary embolism [30]. There is no hard and fast rule as to what level of oxygen saturation is safe but one suggestion is that postoperative hypoxaemia be regarded as a PaO_2 less than 8kpa (63mmHg) or SaO2 less than 90%. Others suggest 93% as a 'safe' lower limit [1, 2, 9]. SaO2 of <93% (PaO_2 around 8.5kPa) is a warning and the patient is in severe trouble if SaO_2 is <90% (Figure 1).

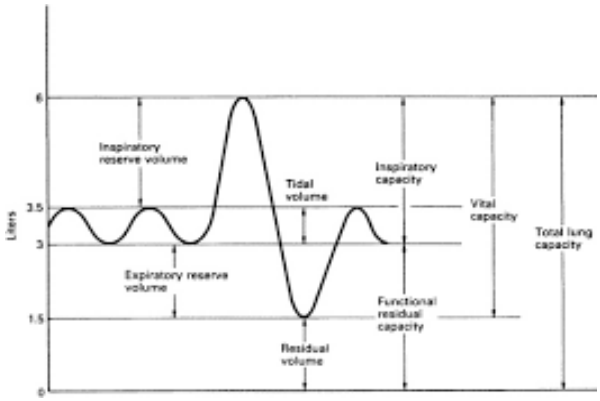

Figure 2: Lung capacity.

Surgical Patients at Risk

It is a principle of surgery that surgical patients at risk of hypoxia are identifiable in the preoperative period for optimization. These would include smokers, patients with chronic pulmonary disease, the elderly (decreased functional residual capacity-FRC, cardiopulmonary disease), diabetes (decreased FRC), preoperative opiates and sedatives (hypoventilation), abdominal surgery especially emergency surgery with splinting of diaphragm from midline laparotomy wounds and orthopaedic surgery from fat emboli [31]. Other operative and preoperative factors, which may lead to a decision for elective post-operative ventilation or re-ventilation are massive blood transfusion intra-operatively, prolonged duration of surgery particularly of one-lung anaesthesia, low preoperative forced expiratory volume in 1 second (FEV1), low preoperative FEV1/ FVC (forced vital capacity) ratio, and extenuating comorbidities [3]. Hypovolaemia and low cardiac output states, will worsen hypoxia during one-lung ventilation in oesophageal surgery because of decrease in mixed venous saturation of blood passing through the shunt to the dependent lung. Thus, haemodynamic optimization with adequate perioperative perfusion of organs and goal-directed therapy (GDT) with fluid and inotropes would improve post-operative surgical outcome. This will require preoperative admission to ICU [32,33].

General Anaesthesia

Hypoxia is a serious complication that continues to be a leading cause of morbidity and mortality, especially in anaesthesia- related deaths [34]. General anaesthesia invariably leads to a reduction in the functional residual capacity of the lungs due to the adoption of the supine position and the development of atelectasis. Prolonged general anaesthesia worsens the situation. With general anaesthesia, desaturation to <90% is common in patients when transferred from theatre to recovery room, and oxygen administration can prevent this. Pulse oximetry identifies desaturation in this situation which would otherwise be undetected but it does not necessarily identify hypoventilation. The use of large volumes (>1500mls) of intra venous fluids intraoperatively is associated with post-operative hypoxia. This may be due to hypothermia from fluids which are not

Table 2: Illustrates a list of paramaters which should be kept within limits at all times in patients with head injury.

PaO_2	>13kPa	Osmolality	>300- <310mosm/kg
SaO_2	>95%	Na^+	>130 - <150mmol/l
$PaCO_2$	4.0kPa	Glucose	>5 - <15mmol/l
BP	>70- <100 mean	Temperature	<38^{0}C
Hb	>12g%	CPP	>70 (MABP-ICP both measured at same reference point)
		ICP	<20

Table 3: Guidelines for initial oxygen dose.

	Fraction of oxygen in inspired air (%)
Cardiac or respiratory arrest	100
Hypoxaemia with $PaCO_2$ < 5.3kPa (type I)	40-60
Hypoxaemia with $PaCO_2$ > 5.3kPa (type II)	24 initially (hypoxic drive in these patients)

warmed or reflect fluid overload with consequent increased lung water (pulmonary oedema) and reduced oxygen uptake. It may also be associated with long abdominal or orthopaedic operations. Myocardial contractility may be adversely affected by hypoxia, hypercapnia, acidosis, drugs or other toxins such as jaundice and inflammatory mediators. Unintentional hypothermia may be associated with hypoxaemia, myocardial infarction (MI) and angina during the early post-operative period. It may also be due to shivering with massive increase in oxygen demand and concurrent hyperventilation. Anaesthetic problems including hypoxaemia are less likely if regional anaesthesia/ local anaesthesia and sedation is used rather than general anaesthesia [34,35].

Clinical assessment

Every post-operative patient is potentially hypoxic in the recovery phase and the diagnostic triad in identification is the history, examination and special investigations. In addition suspect hypoxia if any complication develops. The history would determine the patients at risk [31]. The mortality from acute hypoxic respiratory failure increases with increasing other organ failure (organ failure amplification) [22,36,37]. The examination begins with inspection. Cyanosis is a classical sign which requires at least 5g/dl of reduced haemoglobin, and, therefore there may be significant hypoxaemia before cyanosis can be detected. It is an unreliable sign of mild hypoxaemia. Other signs include an altered mental state, obvious respiratory distress, an unusual respiratory pattern especially any asymmetry, abnormal respiratory rate, the use of accessory muscles of respiration and any patient who is shivering should be assumed to be hypoxaemic. Auscultation may reveal the noisy breathing of airway obstruction and, may also indicate atelectasis or lung collapse, pulmonary oedema, pneumothorax, or pleural effusion. Percussion may demonstrate dullness suggesting consolidation or fluid. Hyper-resonance indicates the presence of pneumorhorax. Any associated distress and tracheal deviation may indicate a tension pneumothorax and if suspected immediate needle thoracocentesis is indicated. Palpation of tracheal deviation away from the side of a suspected pneumothorax indicates a degree of tension which may kill the patient rapidly. Crepitus suggests subcutaneous emphysema which, although rarely a major problem in itself, indicates the need for investigation of the source if not already obvious. It can occur in association with pneumothorax and mediastinal injury. Investigations include a chest X-ray, arterial blood analysis, pulse oximetry and respiratory function 'bedside' tests are appropriate in postoperative patients. Spirometry is probably the simplest and it may be useful to monitor the response to bronchodilators [29,30,38].

Management of Respiratory Failure

Conventional management of patients with respiratory failure includes the administration of supplemental oxygen, the control of secretions, the treatment of pulmonary infection, the control of bronchospasm and measures to limit pulmonary oedema.

Airway

The first line of management is always to ensure a clear airway. The head tilt and chin lift manoeuvres should then be used where appropriate to optimize the airway. If this fails to clear the airway simple adjuncts such as the oropharyngeal airway or a nasopharyngeal airway may be tried. Endotracheal intubation with the application of cricoid pressure will be required where this fail or the risk of aspiration of gastric contents suggest the need to protect the airway. Where endoracheal intubation is indicated but attempts to achieve this orally have failed cricothyroidotomy should be carried out [29,30]. Manoeuvres to improve respiration may include respiratory stimulants such as doxapram given intravenously slowly if there is central depression and the opiate antagonist, naloxone may reverse opiate over dosage. Patients are encouraged to sit up as this would restore FRC and gives the diaphragm and chest wall an added mechanical advantage. If mechanical interference with respiration is due to fluid, blood or air in pleural space aspiration is required. A suspected tension pneumothorax is decompressed by immediate needle thoracocentesis without waiting for an x-ray followed by formal chest drainage. Nebulised bronchodilators e.g. salbutamol 2.5-5mg/4hrly and slow bolus aminophylline infusion may be indicated especially in acute asthma. Adequate analgesia for somatic pain such as non-steroidal anti-inflammatory drugs (NSAIDS) would enable adequate breathing and allow expectoration. Physiotherapy and direct suction via endotracheal tube or cricothyroidotomy helps clear bronchial secretions. Diuretics or vasodilators are indicated in the management of pulmonary oedema and appropriate prompt antibiotic treatment shortens infective exacerbations of chronic bronchitis and emphysema [29,30,39].

Spontaneously Breathing Patients

Once an adequate airway is achieved then oxygen should be administered. If there is adequate spontaneous ventilation then a simple variable performance device e.g. Hudson type face mask (5 l/min oxygen initially) or nasal catheter (2l/min oxygen initially should be used. Nasal cannulas are preferred as they are less claustrophobic and do not interfere with feeding or speaking. However, it can cause ulceration of nasal or pharyngeal mucosa [40]. The concentration of oxygen given is not important and the inspired oxygen concentration ranges between 35-55% (Table 3). Because of the sigmoid shape of the oxygen- haemoglobin dissociation curve a small increase in oxygen given e.g. 24% O_2, which is only slightly greater than the concentration of oxygen in air is invaluable. Gradually, the concentration of inspired oxygen can be increased if there is no dramatic rise in the $PaCO_2$. Oxygen toxicity in humans is less well proven and 50% O_2

or less can be given long-term. 100% O_2 can be given for <24hrs [5-7]. Dangerous hypoxia should never be tolerated for fear of oxygen toxicity. Oxygen flow rate ranges from 6-10 l/min. The flow of oxygen should be adjusted according to the measured oxygen saturation by pulse oximetry or arterial blood gas analysis aiming for 95% saturation. If high oxygen flows are required (10-15 l/min) then a Hudson reservoir mask should be used. Failure to achieve adequate oxygenation with this suggests the need for aggressive treatment of the cause or more invasive management of oxygen therapy [41]. This may be with continuous positive airway pressure (CPAP) via tight-fitting face mask or endotracheal intubation, or intermittent positive pressure ventilation (IPPV) via an endotracheal tube. The benefits of CPAP are the recruitment of collapsed alveoli, increase in end-expiratory lung volume, reduced FiO_2 requirement, improved lung compliance and the reduced work of breathing. The disadvantages are the high FiO_2 can conceal severity of the condition; discourages coughing and clearance of secretions, the risk of aspiration and discomfort [41]. IPPV is instituted in acute hypoxaemic respiratory failure if the clinical signs of respiratory distress (e.g. respiratory rate > 40/min, inability to speak) persist despite maximal treatment and the patient appears exhausted, if there is confusion, a decreased conscious level, a rising $PaCO_2$, and extreme hypoxaemia (PaO_2 <8KPa) despite oxygen therapy. The beneficial effects of IPPV are (1) it improves CO_2 elimination, (2) it relieves exhaustion as in some cases exhaustion may culminate in respiratory arrest, (3 As severe pulmonary parenchymal disease stiffens the lung and greatly increase work of breathing, IPPV decreases total oxygen consumption and thus improves PaO_2 (4). it administers high concentration of O_2 (100%) because ventilated patients are connected to a leak-free circuit and (5) it reduces shunting and increase PaO_2. The dangers of IPPV include the complications with endotracheal intubation and tracheostomy required for long-term ventilation, disconnection or mechanical failure and barotrauma from over distension of the lungs causing rupture of the alveoli. Barotrauma is greatest in patients who require high inflation pressures with or without a positive end-expiratory pressure. Other major complications are pneumothorax, pneumomediastinum pneumoperitoneum and subcutaneous emphysema. The risk of pneumothorax is increased in patients with destructive lung disease e.g. staphylococcus pneumonia and emphysema, asthma or fractured ribs. A tension pneumothorax is rapidly fatal in ventilated patients with respiratory failure. Suggestive signs include the development or worsening of hypoxia, fighting the ventilator, an unexplained increase in inflation pressure, and hypotension and tachycardia sometimes accompanied by a rising CVP. Other dangers of IPPV include respiratory complications (secondary pulmonary infection), cardiovascular complications from impeding venous return, gastrointestinal complications (paralytic ileus), and salt and water retention caused by a combination of increased anti-diuretic hormone (ADH) secretion, fall in cardiac output and reduction in renal cortical blood flow [41-43].

Weaning

It is unwise to attempt 'weaning' from the ventilator i.e. returning to spontaneous respiration, until (i) the original cause of respiratory failure has been treated successfully, (ii) sedative drugs have been reduced to a level where they will not depress respiration. (iii) a low inspired oxygen concentration (40%) maintains a normal PaO_2, (iv) CO_2 elimination is no longer a problem, (v) sputum production is minimal, (vi) nutritional status, minerals, trace elements are normal, (vii) neuromuscular function of the diaphragm and intercostals is adequate, and (viii) the patient is reasonably co-operative [30,41].

Conclusions

Oxygen delivery is the product of cardiac output and oxygen content and is fundamental in the management of the critically ill patient. It is four-fold higher than the resting consumption (250mls/min), and therefore a hypoxic patient would be critically ill and need oxygen maintained at greater than 94% saturation. The consideration of factors involved in oxygen delivery is paramount in early trauma, head injury, the critically ill and post-operative hypoxic patient. Appropriate assessment would guide management of the hypoxic patient. The pulse oximeter is a simple, cheap and non-invasive method of measuring and monitoring oxygen saturation which is invaluable particularly in low resource settings. Oxygen is, however, only one aspect of treatment and the underlying cause of the respiratory failure must be treated.

Author Contributions

EPW is the main author and researcher, MNN carried out literature search, KTN provided the facility for research and carried out literature search.

Ethical Statement

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Highlights

- Hypoxia kills and kills quickly.
- Total oxygen delivery far exceeds total oxygen consumption.
- Optimizing oxygen delivery would maximize the patient's reserves.
- A hypoxic patient is critically ill and needs oxygen maintained at >94% saturation.
- Important to recognize when a patient requires advanced respiratory support in ICU.
- Underlying cause of respiratory failure must be treated.

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