Oxygen Requirements for Acutely and Critically Ill Patients

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Oxygen administration is often assumed to be required for all patients who are acutely or critically ill. However, in many situations, this assumption is not based on evidence. Injured body tissues and cells throughout the body respond both beneficially and adversely to delivery of supplemental oxygen. Available evidence indicates that oxygen administration is not warranted for patients who are not hypoxemic, and hyperoxia may contribute to increased tissue damage and mortality. Nurses must be aware of implications related to oxygen administration for all types of acutely and critically ill patients. These implications include having knowledge of oxygenation processes and pathophysiology; assessing global, tissue, and organ oxygenation status; avoiding either hypoxia or hyperoxia; and creating partnerships with respiratory therapists. Nurses can contribute to patients' oxygen status well-being by being proficient in determining each patient's specific oxygen needs and appropriate oxygen administration. (*Critical Care Nurse*. 2017;37[4]:58-70)

Supplemental oxygen is often assumed to be required for all patients who are acutely or critically ill. However, in many situations, this assumption is not based on evidence. In this article, we review oxygenation processes in the body, different types of oxygen administration, latest evidence on oxygen administration in acute and critical illnesses, and nursing implications for appropriate oxygen administration to acutely and critically ill patients.

Cellular Respiration, Normoxia, Hypoxia, Hyperoxia, and Reactive Oxygen Species

Cellular respiration occurs through either anaerobic or aerobic processes. Cellular anaerobic respiration does not use oxygen to produce adenosine-5-triphosphate (ATP), but this anaerobic process is inefficient in converting glucose to pyruvate because it produces only 2 ATP molecules and lactate.[1,2] Cellular aerobic respiration involves conversion of glucose into pyruvate, which goes through oxidative phosphorylation (the Kreb cycle) in the mitochondria, and yields 28 ATP molecules.[1,2] Thus, oxygen is required for efficient cellular energy production.

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Active respiring cells in tissues set a concentration gradient of molecular oxygen across several cellular interfaces.[3] When the oxygen levels decrease in the cells, oxygen diffuses from the blood into the cells because of the concentration gradient.[1-3] If cellular respiration is slowed or stopped, oxygen diffusion into cells slows down or ceases regardless of the availability of oxygen in the blood. If the oxygen supply to an actively respiring cell is interrupted by a reduction in blood flow, ischemia results.[1,4]

Normoxia is the level of oxygen required or the optimal level needed for normal physiological aerobic processes in the cell.[1] Hypoxia is defined as lack of adequate oxygen supply in body tissues or cells.[1] Hyperoxia occurs when the oxygen level is higher than the normoxic level.[1] Hypoxia can cause cell injury, and, if prolonged, can cause cell death. Hyperoxia can cause cell injury or cell death due to production of reactive oxygen species (ROS) in vital organs and the central nervous system.

Reactive oxygen species are by-products of ATP synthesis that produces molecular oxygen.[3] ROS are created by enzymatic and nonenzymatic catalysis, resulting in radical or nonradical forms. A free oxygen radical is an oxygen molecule with a free electron.[1,4,5] ROS can react with almost every available molecule in the body. Generation of ROS by mitochondria increases with oxygen levels and depends on the clinical balance between metabolism and oxygen supply. ROS can be helpful and important in regulating normal physiological processes such as immunity. However, ROS reactions can damage lipids, carbohydrates, proteins, and DNA, especially when levels of ROS are excessive.

Both hyperoxia and hypoxia can lead to production of damaging ROS from available molecular oxygen in cells. Natural, enzymatic, and nonenzymatic antioxidants are available to slow or inhibit reactions with free oxygen radicals.[1] Natural antioxidants often become depleted if overwhelmed by ROS, thus necessitating exogenous antioxidants. Exogenous enzymatic antioxidants include superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, and thioredoxin.[1] Examples of nonenzymatic antioxidants are vitamins A, B_6, B_{12}, C, and E; selenium; folic acid; and β-carotenoids.[1]

Excess ROS cause oxidative stress. Oxidative stress arises when the antioxidant and oxidant balance becomes unbalanced, allowing unrestricted activity of free radicals.[1] Oxidative stress may damage the body systems at the molecular, cellular, and organ levels. Therefore, in order to reduce oxidative stress, administration of antioxidants or prevention of either hypoxia or hyperoxia may be necessary. Each organ and tissue system is affected differently by different oxygenation levels and resultant oxidative stress.[1] Some tissues and organs can tolerate lack of oxygen and can generate a high percentage of energy needed through anaerobic glycolysis.[6]

Assessment of Whole-Body, Regional, and Tissue- and Organ-Specific Oxygenation

Assessment of oxygenation parameters varies depending on body location, including the circulation. Most oxygenation assessments are whole-body tissue measurements from the macrocirculation and do not directly reflect tissue oxygenation. The macrocirculation includes large arteries and veins, whereas the microcirculation includes the arterioles, capillaries, and venules at the tissue level.[3] Measurements of oxygenation supply in the macrocirculation include those made upstream from the tissue level. The parameters measured are arterial partial pressure of oxygen (PaO_2), arterial oxygen content (CaO_2), arterial oxygen saturation (SaO_2) determined on the basis of arterial blood gas (ABG) analysis and pulse oximetry (SpO_2), and ratio of PaO_2 to fraction of inspired oxygen (FIO_2) or the PF ratio (Table 1). Measurements of oxygenation or oxygen extraction or consumption in the macrocirculation made downstream from tissues include tissue oxygen consumption, mixed venous oxygen saturation ($S\bar{v}O_2$) or central venous oxygen saturation ($ScvO_2$), and blood levels of lactate (Table 1). Monitoring for $S\bar{v}O_2$ greater than 70% gives a broad perspective of adequate tissue oxygen extraction and indicates the difference between tissue delivery

The choice of oxygen system or device depends on the desired performance in delivery of FIO_2 or oxygen concentration.

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Table 1 Global oxygenation parameters

	Reference range
Global oxygen supply	
Partial pressure arterial oxygen (Pao_2), mm Hg	80-100
Arterial oxygen content (Cao_2), mL/dL	19-20
Arterial oxygen saturation (Sao_2 and Spo_2), %	>94
PF ratio (Pao_2/Fio_2 ratio)	>300
Global oxygen demand (extraction and consumption)	
Tissue oxygen consumption ($\dot{V}o_2$), mL/min	200-250
Mixed venous oxygen saturation ($S\bar{v}o_2$ and $Scvo_2$), %	60-80 ($S\bar{v}o_2$ slightly higher)
Global oxygen supply or demand	
Lactate, mmol/L	Venous: <2 Arterial: <1.6
Contributing factors to oxygen supply	
Cardiac output, L/min	4-8
Hemoglobin, g/dL	
Female	12-16
Male	14-18

and consumption.[7] $S\bar{v}o_2$ will decrease when more oxygen is extracted, less oxygen is delivered, or tissue oxygen demand is increased. $S\bar{v}o_2$ will increase when less oxygen is extracted because of an increase in oxygen delivery or reduction in oxygen demand or during severe systemic inflammation or sepsis.

Measuring regional or tissue oxygenation or both rather than just global oxygenation is important.[2,7] Brain oxygenation can be measured directly via intracerebral sensors for tissue partial pressure of oxygen (Po_2) and indirectly via the jugular bulb or with near-infrared spectroscopy with sensors placed on the forehead to quantify hemoglobin oxygenation in cerebral tissue. Direct monitoring of regional or tissue oxygenation in other organs will eventually be preferred and may be available soon.[2] Markers of hypoxic effects in various other organs and body systems can be monitored, such as gut pH, renal tubular function, cardiac ischemic markers, and liver function.[2,3,7]

Devices and Systems for Oxygen Administration

Devices for administering oxygen come in several designs, including low-flow, reservoir, and high-flow systems. With low-flow, reservoir, and high-flow systems, oxygen is delivered to spontaneously breathing patients through cannulas and masks and through endotracheal and tracheostomy tubes with T-tubes and tracheostomy collars. Systems that blend oxygen are used with mechanical ventilators to allow an Fio_2 of room air (21%-100%) to be delivered through ventilator circuits into endotracheal tubes or tracheostomy tubes[8] (Table 2).

The choice of oxygen system or device depends on the desired performance in delivery of Fio_2 or oxygen concentration. Heuer[8] suggests that answers to 2 questions help determine the appropriate system or device for oxygen delivery to the lungs. The first question is How much oxygen can the system deliver (Fio_2 or Fio_2 range)? The second is Does the delivered Fio_2 remain fixed or does it vary according to changes in a patient's oxygen demands?

Oxygen systems can be classified as a low (<35%), moderate (35%-60%), or high (>60%) oxygen concentration or Fio_2.[7] Some systems deliver oxygen across the full range of Fio_2, from 21% to 100%. Oxygen devices deliver either a fixed or a variable Fio_2, depending on whether the oxygen device supplies the total gas volume inhaled on each inspiration by the patient.[8] If the oxygen device supplies the total amount of a patient's inspired gas volume, the Fio_2 remains fixed. If the device supplies only part of a patient's total inspired gas volume, the patient must inhale additional air, thus diluting or lowering the amount of the delivered Fio_2. In addition, if a patient breathes faster or deeper, inspired oxygen is diluted with even more air, thereby decreasing the Fio_2. Thus, Fio_2 is variable when not all of a patient's inspired gas volume is delivered with the oxygen, particularly with mask devices. High-flow oxygen nasal cannulas may deliver enough total flow of air with oxygen to satisfy the inspiratory volume needs of patients as well as the patients' oxygen needs.

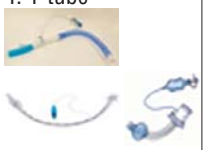
Patients with severe hypoxemia sometimes require invasive mechanical ventilation because of the inability to increase blood oxygen levels with low- or high-flow oxygen administration with spontaneous breathing alone.[8] If hypoxemia is caused by decreased alveolar ventilation, oxygen administration through invasive mechanical ventilation should correct the hypoxemia. However, increased oxygen alone will not correct the alveolar hypoventilation; only increasing the volume of ventilation will do so. If a shunt from damage to the alveolar capillary membrane is causing the hypoxemia, increased oxygen and ventilation via mechanical ventilation most likely will not increase blood oxygen levels. Adding positive end-expiratory pressure (PEEP) to the ventilator settings for an

Table 2 Oxygen delivery devices

Device	Device category	Flow	FIO_2/Stability	Use
Low-flow (nasal) cannula 	Low-flow oxygen	250 mL/min to 6 L/min <2 L/min (infants)	22%-40%/variable Depends on air dilution and rate and depth of breathing	Patient in stable condition who requires low FIO_2 Home care patient for long-term oxygen
Low-flow reservoir systems, cannula 	Low-flow oxygen Contains a reservoir mechanism for gathering and storing oxygen	250 mL to 4 L/min	22%-35%/variable	Home care or ambulatory patients who need mobility
Low-flow reservoir systems, mask 		Minimum of 10 L/min	60%-80%/variable	Emergencies Short-term therapy requiring high FIO_2
High-flow nasal cannula 	High-flow oxygen	Up to 60 L/min	35%-90%/variable or fixed	Patients with high minute ventilation who require high FIO_2 and high flow
High-flow air-entrainment masks (AEMs) AEM 1  AEM 2 	AEM Venturi/Venti type High-pressure oxygen is directed through a small jet surrounded by ports for air entrainment; the larger the jet, the more oxygen or higher FIO_2	Varies	24%-50%/fixed See FIO_2 options on green adapter next to oxygen tubing in picture AEM 1 and different FIO_2 color coded air entrainment Inserts in picture AEM 2	Patients in unstable condition who need precise low FIO_2
AEM 	AEM (used for the devices 1 to 4) As for AEM high-flow oxygen except with humidification and temperature control	Varies up to 60 L/min	28%-100%/fixed FIO_2 options on orange entrainment adaptor on nebulizer	Patients who require high-flow aerosolized oxygen
1. Aerosol mask 	High-flow air entrainment	Varies up to 60 L/min	28%-100%/fixed FIO_2 options on orange entrainment adaptor on nebulizer	Over mouth and nose
2. Face tent 	High-flow air entrainment	Varies up to 60 L/min	28%-100%/fixed FIO_2 options on orange entrainment adaptor on nebulizer	Covers lower half of face and is open at top

Continued

Table 2 *Continued*

Device	Device category	Flow	FIO_2/Stability	Use
AEM *(continued)*				
3. Tracheostomy collar 	High-flow entrainment	Varies up to 60 L/min	28%-100%/fixed FIO_2 options on orange entrainment adaptor on nebulizer	Covers tracheostomy tube for patients who require high-flow aerosolized oxygen
4. T-tube 	High-flow entrainment	Varies up to 60 L/min	28%-100%/fixed FIO_2 options on orange entrainment adaptor on nebulizer	Connects to endotracheal tubes or tracheostomy tubes that require high-flow aerosolized oxygen for spontaneously breathing patients
Oxygen-blending system  Invasive mechanical ventilator 	Oxygen blending Used for ventilators and other oxygen devices as above, used when air-entrainment devices cannot provide a high enough oxygen concentration or flow; most critical care and noninvasive ventilators have their own internal oxygen-blending system	Provides more than 60 L/min output flow	21%-100%/fixed	Spontaneously breathing or intubated patients with high or variable minute ventilation who need supplemental oxygen that is not adequately provided by air-entrainment devices Invasive mechanical ventilation occurs when a patient is intubated with an endotracheal or tracheostomy tube and mechanical ventilation is initiated to support and maintain adequate alveolar ventilation, oxygen delivery, and acid-base balance and reduce the work of breathing
Positive end-expiratory pressure (PEEP)  Continuous positive airway pressure (CPAP) nasal mask 	Positive pressure greater than atmospheric pressure is applied at the end of expiration for PEEP with a mechanical ventilator; CPAP is the application of continuous airway pressure greater than atmospheric pressure incorporating oxygen with a mechanical ventilator			PEEP recruits atelectatic alveoli and increases functional residual capacity with a resultant increase in blood oxygenation CPAP through an endotracheal tube or tracheostomy tube is continuous airway pressure applied by a ventilator with patients initiating their own breathing. Used primarily to improve oxygen gas exchange in patients with severe hypoxemia CPAP by mask is continuous airway pressure applied by a ventilator used for spontaneously breathing patients with severe hypoxemia
Noninvasive ventilation (NIV) oronasal/full face mask  NIV ventilator 	NIV Uses an internal oxygen blending system, has no exhalation valve, has a continuous air leak, an inspiratory pressure of about 30 cm H_2O, an expiratory PEEP up to 15 cm H_2O, and up to 30 breaths/min (BiPAP)	Provides more than 60 L/min oxygen flow	21%-100%/fixed	BiPAP uses 2 different pressures applied during inspiration (IPAP) and expiration (EPAP or PEEP); BiPAP is used for poorly breathing patients in respiratory distress with abnormal gas exchange causing hypoxemia

Continued

Table 2 *Continued*

Device	Device category	Flow	FIO_2/Stability	Use
Enclosure Oxyhood 	Air-entrainment nebulizer provides oxygen or an oxygen-blending system is used to obtain precise oxygen levels	7 L/min	21%-100%	Spontaneously breathing neonates and infants who need supplemental oxygen

intubated patient with shunt hypoxemia will be necessary to induce an increase in blood oxygen.

Continuous positive airway pressure (CPAP) is a setting on mechanical ventilators that maintains a constant positive pressure during inspiration and expiration that does not provide ventilation. CPAP assists in maintaining open alveoli for better gas exchange. Therefore, a patient must be spontaneously breathing in order for CPAP to be used. CPAP is administered through endotracheal tubes, tracheostomy tubes, and per mask.

The primary indication for noninvasive mechanical ventilation in acute care is hypercapnic respiratory failure, although this type of ventilation is also used for hypoxemic respiratory failure such as pneumonia and cardiogenic pulmonary edema. Noninvasive mechanical ventilation includes bilevel positive airway pressure (BiPAP). With BiPAP, different pressures are used for inspiration and expiration, and the device performs like the invasive mechanical ventilator modes of pressure-support mode on inspiration and like PEEP on expiration. Nasal and face masks are used for BiPAP and are connected to a noninvasive mechanical ventilator that delivers pressurized gases. The effectiveness of BiPAP for hypoxemia usually depends on its ability to improve alveolar ventilation.

Oxygen Administration for Acutely and Critically Ill Patients

Acute Myocardial Infarction and Acute Coronary Syndrome

High-concentration oxygen is known to cause vasoconstriction in systemic arteries at high levels or during hyperoxia states.[9-13] Evidence[10-12,14] suggests that oxygen increases vascular resistance in coronary arteries. Oxygen administration in acute critical illness increases blood pressure and lowers cardiac index, heart rate, and cardiac oxygen consumption.[10-13] Coronary blood flow decreases in response to vasoconstriction caused by hyperoxia regardless of an initial normal oxygen saturation.[10,11] Oxygen-induced vasoconstriction also lowers cerebral and renal blood flow.[9]

High oxygen levels in vascular beds reduce vessel arteriole diameter, leading to a reduction in oxygen transport into muscle.[9,10] When this change in diameter occurs in the coronary circulation, myocardial oxygen consumption decreases because of the reduction in oxygen transport into myocardial muscle.[9,10] High-flow administration of oxygen may disturb blood distribution in the microcirculation, leading to functional oxygen shunting and lowered total-body oxygen consumption, perhaps to protect tissues from toxic effects of high oxygen tension.[10]

Moradkhan and Sinoway[14] reviewed the use of oxygen for patients with acute coronary artery disease or acute coronary syndrome. According to the authors,[14] evidence supporting oxygen use in acute coronary syndrome is limited; no studies indicate that normoxic patients undergoing percutaneous coronary intervention derive any benefit from supplemental oxygen. As a result Moradkhan and Sinoway suggested that the use of oxygen in cardiac disease most likely has adverse physiological effects, such as coronary artery vasoconstriction.

No data support or refute routine use of oxygen in the acute phase of STEMI.

The 2013 guidelines of the American College of Cardiology Foundation/American Heart Association for management of ST-elevation myocardial infarction (STEMI) note that no data support or refute routine use of oxygen in the acute phase of STEMI.[15] A Cochrane analysis indicated that the risk for death for myocardial infarction patients treated with oxygen is 3 times higher than the risk for patients receiving room air. These guidelines[15] recommend that supplemental oxygen be used

only if a patient has clinically significant hypoxemia with oxygen saturation less than 90%, heart failure, or dyspnea.

In a presentation at the American Heart Association annual meeting in 2014, Stub[16] described the AVOID study (air vs oxygen in STEMI), a randomized trial of oxygen therapy in acute myocardial infarction in Australia. Nonhypoxic patients with paramedic-assessed symptoms of STEMI were randomized into 2 groups; one group (n = 318) received supplemental oxygen and the other group (n = 320) did not. Once in the emergency center, patients whose diagnosis of STEMI was confirmed had percutaneous catheter intervention: 218 patients who had received supplemental oxygen and 223 who had not. Baseline characteristics between the 2 groups were similar in demographics, vital signs, location of infarct, and details of the percutaneous catheter intervention. Supplemental oxygen therapy in patients who had STEMI but no hypoxia increased myocardial injury, recurrent myocardial infarction, and major cardiac dysrhythmia and was associated with larger sized myocardial infarct at 6 months.

Burls et al[17] conducted a meta-analysis of 3 randomized controlled trials of oxygen therapy for acute myocardial infarction. They concluded that treatment with supplemental oxygen during acute myocardial infarction may be harmful. In a Cochrane review published in 2013, the same group of researchers[18] considered the 3 previous randomized trials covered in the 2011 article and an additional randomized controlled trial with a total of 403 people with acute myocardial infarction with or without ST-segment elevation less than 24 hours after onset of the infarction. The intervention was oxygen compared with room air regardless of the similar cotherapies provided to these patients. Among the 17 deaths, the mortality rate of patients treated with supplemental oxygen was 2-fold higher than the rate of patients who received just room air. Cabello et al[18] concluded that routine supplemental oxygen may cause harm in patients with acute myocardial infarction and that a large randomized trial is needed to determine if that conclusion is correct.

Reperfusion injury due to the introduction of oxygen into an ischemic area can occur via generation of ROS that damage the previously ischemic area. The influx of oxygen into the ischemic area with the area's high levels of substrates most likely causes the formation of ROS, which can cause extensive tissue damage. Antioxidants may help prevent reperfusion injury. Other options include reperfusion of the heart with blood that has regulated oxygen levels to minimize oxidative stress.[1,19]

Heart Failure

Patients with heart failure often experience dyspnea and hypoxia. High-concentration oxygen is often given to these patients, despite previous studies indicating that an F_{IO_2} of 100% in healthy subjects decreases cardiac output and increases systemic vascular resistance. Little is known about the hemodynamic effects of oxygen administration in these patients. Evidence for use of oxygen in patients with heart failure is scarce. The few available studies had small samples and were too underpowered to make a determination about oxygen administration. The available literature suggests that inducing hyperoxemia in patients with heart failure may be harmful. Oxygen use should be limited to patients who have hypoxemia and should be titrated to achieve normoxia. Large random controlled trials are needed to confirm these findings.[20] However, extracorporeal membrane oxygenation may be considered for patients with severe heart failure who need a heart transplant to survive or in whom conventional therapy is unsuccessful.[21]

After Resuscitation

The high mortality rate attributed to postcardiac arrest syndrome involves global ischemia-reperfusion injury, myocardial stunning, and anoxic brain injury.[5,14] The role of supplemental oxygen, which is often administered in high concentrations to patients after cardiac arrest, is no longer a standard intervention. Problems are associated with delivery of oxygen to the injured brain. Too much oxygen may increase production of oxygen free radicals, possibly triggering cellular injury and apoptosis.[22]

In a large multicenter cohort of adult patients admitted to the intensive care unit after resuscitation from cardiac arrest, Kilgannon et al[23] found that hyperoxia was a common occurrence and an independent predictor of in-hospital mortality. Data were from the Project Impact database of 6236 adults admitted to 120 intensive care units with nontraumatic cardiac arrest after resuscitation. Findings revealed hyperoxia in 18%, hypoxia in 63%, and normoxia in 19% of the patients after resuscitation. These data support the hypothesis that hyperoxia after resuscitation could be harmful and provide scientific rationale for clinical trials of controlled reoxygenation during the period after resuscitation.[23] Blakeman[20] found that compared with normoxia or hypoxia, hyperoxia was associated with increased in-hospital mortality. The increase was dose dependent: the higher the Pa_{O_2}, the higher was

the mortality. Oxygen saturation may be 100% according to pulse oximetry, but Pao_2 values in hyperoxia may range from 100 to 450 mm Hg with an oxygen saturation of 100%.[20] ABG analysis is needed to measure the Pao_2.

Acute Respiratory Failure

Alveolar Flooding and ARDS. The 2012 Berlin definition of ARDS no longer includes a definition of acute lung injury[24] (see Sidebar Definition of Acute Respiratory Distress Syndrome). ARDS is a difficult condition to manage; treatment requires a balance between mechanical ventilation with low tidal volumes and the right level of PEEP to support oxygenation and minimize the harmful effects of exposure to high levels of oxygen.[4] The most important factor to consider is balancing the risk of pressure injury to the lung due to excessive PEEP and tidal volume and the risk for oxygen poisoning.[25]

Many guidelines for management of patients with acute respiratory failure define an Sao_2 of 88% as the lowest acceptable level.[7] In individual patients, this target might be adjusted on the basis of global measures of perfusion, including $S\bar{v}o_2$ and arterial levels of lactate.[7] For example, the ARDS Network guidelines for the management of oxygen therapy in patients with ARDS recommend the use of FIO_2 greater than 70% only in patients who require PEEP greater than 12 cm H_2O to maintain an Sao_2 greater than 88% to less than 95% or a Pao_2 greater than 55 mm Hg.[26]

The results of a meta-analysis[27] published in 2010 suggested a survival benefit from higher PEEP in patients with ARDS, whereas lower PEEP was more appropriate for acute lung injury In this meta-analysis, acute lung injury was still considered a separate definition from ARDS. In the same meta-analysis,[27] differences between treatment with high PEEP and low PEEP differed significantly; Pao_2 was significantly higher with high PEEP on day 1 and day 3. In addition, the FIO_2 was significantly lower with the higher PEEP for day 1, day 3, and day 7 and with the higher Pao_2 for day 1 and day 3. Thus, oxygenation is improved with higher PEEP in both acute lung injury and ARDS. No significant differences in mortality occurred between patients who had high PEEP and those who had low PEEP.[27] However, differences in the FIO_2 were significant; less FIO_2 was used with higher PEEP than with lower PEEP to achieve mean Pao_2 between 78 and 85 mm Hg on days 1, 3, and 7.

Prone positioning improved Pao_2 in ARDS patients in all clinical studies and in experimental studies dealing with the prone position for 8 to 17 h/d.[28] The most probable mechanism for improvement in oxygenation is that the recruitment of perfused alveoli in the dorsal lung regions exceeds that of derecruitment in the ventral lung regions.[28] The major trials associated with use of the prone position indicated significant survival benefit for patients with PF ratios less than 100.[28] Short-term prone positioning is useful for severe hypoxemia. Long-term prone positioning is highly recommended for patients with severe ARDS but not for those with mild to moderate ARDS with PF ratios greater than 150.[28]

Extracorporeal membrane oxygenation can be used for patients with ARDS with refractory hypoxemia when conventional oxygenation methods do not increase blood oxygen levels.[29-31] Because of the many possible complications associated with its use, extracorporeal membrane oxygenation must be carefully considered for individual patients on the basis of the benefits the treatment may provide.[29-31]

Alveolar Hypoventilation Disorders in Acute Respiratory Failure. A reduction in minute ventilation can occur in patients with drug overdoses, brainstem dysfunction, neuromuscular diseases, and chest wall abnormalities that can result in alveolar hypoventilation. The reduction in minute ventilation causes alveolar Po_2 to decrease and $Paco_2$ to increase. Relative alveolar hypoventilation occurs with obstructive airway disease, interstitial lung disease, and pulmonary vascular diseases.

Definition of Acute Respiratory Distress Syndrome

- New or worsening respiratory signs or symptoms or a known clinical injury
- Bilateral opacities on chest imaging not fully explained by effusions, lobar or lung collapse, or nodules
- Edema in respiratory failure not fully explained by cardiac failure or fluid overload; need objective assessment to exclude hydrostatic edema if no risk factor present
- Oxygenation
  Mild: Pao_2/FIO_2 ratio ≥200-300
  Moderate: Pao_2/FIO_2 ratio ≥100-200
  Severe: Pao_2/FIO_2 ratio <100

This type of hypoventilation is due to ventilation-perfusion mismatching with increased physiological dead space ventilation even when total minute ventilation is normal or increased. When alveolar hypoventilation progresses, alveolar P_{O_2} is nearly the same as $P\bar{v}_{O_2}$. However, when hypoxemia is marked, $P\bar{v}_{O_2}$ will be even lower. However, even small increases in the amount of supplemental oxygen in patients with alveolar hypoventilation can result in marked increases in oxyhemoglobin saturation.[4]

The fact that use of supplemental oxygen therapy in some patients with chronic obstructive pulmonary disease (COPD) can cause an increase in Pa_{CO_2} is well known.[4] In many patients, this increase is relatively small and clinically unimportant, but respiratory acidosis develops in some patients if the oxygen therapy is not carefully used and carbon dioxide levels are not monitored.[4] In some patients with COPD, the increase in oxygen in the pulmonary capillaries associated with supplemental oxygen causes vasodilatation and creates a ventilation-perfusion mismatch and an increase in physiological dead space.[32] When much more oxygen than nitrogen is present within the alveoli, absorption atelectasis may occur and fewer alveoli are available for gas exchange. The increased binding of oxygen and hemoglobin results in an increase in unbound carbon dioxide and perhaps a reduction in pH. For COPD patients at risk for oxygen-induced hypercapnia, maintaining Sa_{O_2} between 90% and 93% may help avoid hypercapnia.[32]

Guidelines for management of acute respiratory failure now define an Sa_{O_2} of 88% as the lowest acceptable level.

Carbon dioxide monitoring is used to detect respiratory depression in patients receiving sedatives and opiates. This monitoring can also be used in patients with alveolar hypoventilation of any cause who are receiving supplemental oxygen.[4] The guidelines of the British Thoracic Society[33] recommend that in patients with documented or suspected COPD, titrating oxygen saturation to an Sp_{O_2} of 88% to 92% reduces the risk of death due to respiratory failure, especially in patients susceptible to hypercapnia.

Traumatic Brain Injury

Brain dysfunction due to ischemia and poor perfusion is an instance in which supplemental oxygen is required to create a hyperoxia state. In a retrospective data analysis of 3420 patients with moderate to severe traumatic brain injury, Davis et al[34] found that mild hyperoxemia might be beneficial. These researchers defined hypoxemia for patients with traumatic brain injury as a Pa_{O_2} less than 110 mm Hg, normoxemia as Pa_{O_2} from 110 to 487 mm Hg, and hyperoxemia as Pa_{O_2} greater than 487 mm Hg. As part of their discussion, Davis et al[34] stated that during prehospital oxygen treatment for traumatic brain injury, only oximetry is available to indicate oxygenation, so although Sp_{O_2} may be 100%, the Sp_{O_2} value does not indicate the true level of Pa_{O_2}. In traumatic brain injury, early barriers exist to oxygen diffusion into injured tissue that may not exist in states of pure ischemia such as stroke or cardiac arrest.[20,34,35] Providing oxygen to the injured brain is crucial to slowing secondary brain injury, but the appropriate level of Pa_{O_2} remains unclear, because adequate arterial oxygenation may not always indicate adequate brain oxygenation.[36] However, some evidence[36] indicates that mild to moderate hyperoxemia may increase survival with patients with traumatic brain injury.

Hlatky et al[36] reported that hypoxic traumatically injured brain tissue, which is most likely to benefit from supplemental oxygen, was paradoxically the least likely to receive the extra oxygen because of poor perfusion from noninjured arteries. This notion is in line with the knowledge that oxygen has a vasoconstricting effect, especially in uninjured blood vessels. Hlatky et al[36] concluded that efforts to improve cerebral blood flow would be more likely to improve oxygen delivery than would hyperoxia.

Stroke

Oxygen therapy actually makes intuitive sense in treatment of cerebral ischemia, because tissue oxygen levels are low. However, oxygen levels are low primarily because of poor blood flow to the brain. Oxygen also acts as a vasoconstrictor and can further reduce blood flow. This finding is most likely the reason that evidence does not support oxygen use for nonhypoxemic patients with stroke.[20]

The 2007 guidelines[37] from the American Heart Association and the American Stroke Association recommend use of oxygen for early management of ischemic stroke only if hypoxemia is present. The same recommendation is also in the 2010 guidelines[38] of the American Heart Association for cardiopulmonary resuscitation and emergency cardiovascular care of adults with stroke. Sjöberg and Singer[9] have stated that hyperbaric oxygen

has a greater potential than does normobaric oxygen for oxygen use in stroke. However in 3 randomized control trials, poor outcomes were associated with the use of hyperbaric oxygen for brain ischemia due to stroke or traumatic brain injury.[9,20]

Trauma Before Arrival at a Hospital

Use of oxygen in trauma patients has been assumed to be necessary. McMullan et al[39] conducted a study in which 224 trauma patients received supplemental oxygen before admission to a hospital. More than 60% of trauma patients in the study received oxygen and more than half of these patients had no indication that they required oxygen. McMullan et al[39] concluded that the main indication for supplemental oxygen in trauma is an oximetry reading less than 90%. Concern about hyperoxia complications in trauma patients is warranted.

Blakeman[20] described how often trauma patients with SpO_2 values of 100% receive oxygen through a nonrebreathing mask at a rate of 15 L/min. The standard use of nonrebreathing masks makes it easy for stocking only a single type of oxygen device.[20] Advanced Trauma Life Support guidelines[40] published in 2012 advocate supplementation with high concentrations of oxygen for trauma patients, but little evidence supports use of oxygen, especially in high concentration. The book PHTLS Prehospital Trauma Life Support[41] published in 2011 also advocates a high FIO_2 for trauma patients. On the contrary, the United States Special Operations Command[42] uses a guideline for the battlefield that suggests that oxygen be delivered if SpO_2 is 90% or less or when the patient is unconscious or has traumatic brain injury, hemorrhagic shock, or casualty associated with high altitude. Experts in respiratory care suggest that oxygen be used in trauma patients who have hypoxemia and that the dose should be titrated to a normal oxygen saturation range.[20,43]

Crush injuries are injuries in which skin, bone, muscles, and/or tendons are damaged by a high-pressure force.[44-46] Tissue ischemia can be extremely severe. Once crush injury is diagnosed, treatment with hyperbaric oxygen may promote quicker complete healing than can oxygen treatment at normal atmospheric pressure, so long as arterial blood flow is adequate.[45]

Carbon Monoxide Poisoning

Carbon monoxide poisoning is one condition in which hyperoxemia is desirable. Hemoglobin has an affinity for carbon monoxide that is more than 200 times higher than the affinity for oxygen.[47] Once carbon monoxide levels reach 20%, heart and brain function can be adversely affected.[47] The resulting hypoxemia may be masked, because pulse oximetry cannot differentiate between carbon monoxide and oxygen. In this instance, the half-life of carboxyhemoglobin, normally 4 to 5 hours when a patient is breathing room air, can be reduced to 40 minutes when the patient is breathing 100% oxygen. Although hyperbaric oxygen therapy is used for carbon monoxide poisoning, the efficacy and practicality of this therapy remain controversial.[9] Treatment of patients with carbon monoxide poisoning includes removing the patient from the source of carbon monoxide and supportive care.

Dyspnea

One of the most controversial and misunderstood uses of supplemental oxygen is treatment of patients experiencing breathlessness. Breathlessness is a common symptom of advanced lung, cardiac, and neuromuscular disease, and the intensity of dyspnea increases as death approaches. Even with increased understanding of breathlessness and the pharmacological and nonpharmacological interventions available, dyspnea is still difficult to treat.[48]

Breathlessness makes caregivers and health care providers feel helpless, further complicating treatment.

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In a survey performed by Abernethy et al,[49] the results indicated that 70% of clinicians would prescribe oxygen for breathlessness despite normal oxygen saturation, and 35% would prescribe oxygen if the patient asked for it. Hypoxemia does not appear to be the driving force in chronic breathlessness.[20,50]

However, in patients with hypoxemia, high-flow oxygen reduces the perception of dyspnea. Lenglet et al[51] conducted a study of 17 patients in the emergency department who had acute dyspnea and hypoxemic respiratory failure mainly due to pneumonia. Patients were first treated with low-flow oxygen, but if they required greater than 9 L/min, they were switched to nasal high-flow oxygen. Significant differences were found between low-flow and high-flow oxygen in reduction of dyspnea perceptions, reduction in respiratory rate, and increase in SaO_2. Other researchers[52-55] had similar results

Nursing Implications of Oxygen Administration for Acutely or Critically Ill Patients

- Consider need for oxygen supplementation, depending on disorder, organ, and tissue pathophysiology
- Perform continual assessment of global, tissue, and organ oxygenation status
- Avoid hypoxia or hyperoxia during oxygen administration
- Create a partnership and consult with respiratory therapist for best oxygenation outcomes

with a group of extubated patients who had had endotracheal tubes in place and a group of inpatients with acute respiratory failure.

Thus, high-flow nasal cannula therapy for patients with dyspneic hypoxemia can reduce that breathlessness. This change most likely is due to the higher total flow of gases with oxygen during inspiration, a situation that fulfills the body's inspiratory total flow and volume need. However, for patients with chronic breathlessness with no hypoxemia, oxygen therapy does not affect the sensation of dyspnea. This knowledge can determine appropriate oxygen therapy in patients with dyspnea and prevent hyperoxia. Most studies[33,34] have indicated that oxygen is no better than air for chronic breathlessness in patients without hypoxemia. Larger, adequately powered randomized controlled trials are needed to confirm the results of the smaller studies.

Infants and Neonates

Judicious use of oxygen with neonates is warranted, although the safe FIO_2 and duration of use are still questionable. Published articles[9,20] clearly indicate that administering oxygen despite an oxygen saturation greater than 90% increases the risk of retinopathy of prematurity and bronchopulmonary dysplasia. However, oxygen should be appropriately administered to premature neonates to treat hypoxemia and prevent hyperoxemia.[20,56,57] Full-term neonates at birth may be resuscitated with room air.[58]

Nonoxygen Methods of Increasing Tissue Oxygenation

MacIntyre[7] suggests that tissue oxygenation can be increased via methods other than oxygen administration. These methods include manipulating oxygen consumption through cooling, neuromuscular blockade, pain management, fever control, and agitation control.

New Developments of Oxygen Therapy and Delivery

New oxygenation interventions include intracoronary hyperoxemic therapy (also known as aqueous oxygen therapy), hyperoxemic reperfusion therapy, superoxygenation therapy, and supersaturated oxygen infusion therapy.[59] Aqueous oxygen therapy involves use of a crystalloid solution containing extremely high concentrations of oxygen (1-3 mL of oxygen per milliliter of physiological saline). The aqueous oxygen system mixes the aqueous oxygen solution with a patient's blood from an arterial puncture and delivers the hyperoxemic blood to targeted ischemic myocardium via an infusion catheter for regional correction of hypoxemia and production of hyperoxemia. This treatment can result in a PaO_2 of 760 to 1000 mm Hg.[59] This type of oxygenation can be used instead of hyperbaric chambers for inducing hyperoxygenation and regional oxygenation.

In a study by O'Neill[59] published in 2007, aqueous oxygen was used in randomly assigned patients with acute anterior or inferior myocardial infarction who underwent a percutaneous coronary intervention. Intracoronary hyperoxemic reperfusion was safe and well tolerated after the intervention for acute myocardial infarction but did not improve regional wall motion, ST-segment resolution, or final infarct size. A possible treatment effect was observed in patients with anterior myocardial infarction who had reperfusion within less than 6 hours of the onset of signs and symptoms.[59]

Nursing Implications of Oxygen Administration

See Sidebar Nursing Implications of Oxygen Administration for Acutely or Critically Ill Patients for nursing implications of oxygen administration for acutely or critically ill patients.

Partnership With Respiratory Therapists

A nurse's best friend when patients require oxygen therapy is a respiratory therapist. Oxygen administration to patients requires a team approach to obtain best outcomes. Respiratory therapists have expert knowledge of all of the available oxygen devices. During interprofessional rounds, they can advise the entire health care team of the best method of oxygenation for acutely

and critically ill patients. Nurses should consult with their patient care team respiratory therapist about changes in a patient's oxygenation status that occur during care procedures.

Conclusions

Nurses must understand how oxygen is delivered in the body and which oxygen delivery devices and methods work best to deliver oxygen into the lungs. They must also understand the hazards and complications of the risks of hyperoxia and be aware of implications for oxygen delivery to acutely and critically ill patients. Nurses have a vital role as a member of the health care team in ensuring appropriate oxygenation for patients. CCN

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See also

To learn more about oxygen requirements in critically ill patients, read "Measurement of Oxygen Consumption in Critically Ill Children: Breath-by-Breath Method vs Mass Spectrometry" by Guo et al in the *American Journal of Critical Care,* May 2016;25:243-248. Available at **www.ajcconline.org**.

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