Oxygen Therapy, Respiratory Care, and Monitoring

VITTORIA COMELLINI, LARA PISANI, and STEFANO NAVA

INTRODUCTION

Supplemental oxygen is one of the most widely used therapies for people admitted to the hospital and it is used across the whole range of specialties. Although oxygen therapy is used as a medical treatment in both acute and chronic setting, it is often administered improperly. The major problems consist in the fact that about this topic there are strongly held beliefs, but very few randomized controlled trials and frequently health care professionals receive conflicting advice about oxygen use from different “experts” during their clinical training and during their careers, and many are confused about the oxygen’s prescription and use. This chapter will give a comprehensive and practical overview of oxygen pathophysiologic effects, current modalities for its delivery, and monitoring in the critical care setting. In order to give a more complete view about the whole range of specialties. Although oxygen therapy is used

OXYGEN THERAPY

Oxygen makes up 21% of the atmosphere we breathe; in the air it exists in a diatomic molecular form (O₂, molecular weight [MW] 16 g/mol) that is the state in which we administer oxygen to our patients as a respiratory gas, either pure oxygen or in mixtures with air or helium (Heliox). While the gaseous state is most clinically relevant, oxygen can be found in liquid and solid states as well, under appropriate conditions. Oxygen was not discovered as a separate gas until the late 18th century, when the Swedish apothecary, Karl W. Scheele in 1772, made a series of experiments with mercuric oxide and potassium nitrate and, heating these two elements, obtained a gas that caused candles to burn more brightly; he did not, however, rush to publication. In the same years, the English amateur chemist Joseph Priestley liberated oxygen by intensely heating mercurius calcinatus (mercuric oxide) placed over liquid mercury in a closed vessel; he called this new gas “dephlogisticated air” (1).

The first notice about the use of oxygen as a remedy in disease dates back to 1870 (2). Although oxygen life-supporting role was understood, it took about 150 years for the gas to be used in a proper way: during the first 150 years after this discovery, the therapeutic use of oxygen was sporadic, erratic, and controversial.

Currently, oxygen is administered for three main indications, but only one is evidence-based. First, oxygen is given to correct hypoxemia as there is good evidence that severe hypoxemia is harmful. Second, oxygen is administered to ill patients in case they might become hypoxemic. Recent evidence suggests that this practice may actually place patients at increased risk of developing the toxic effects mediated by reactive oxygen species (ROS) (3), leading to tissue damage and absorption atelectasis. Third, a very high proportion of medical oxygen is administered because most clinicians believe that oxygen can alleviate breathlessness. However, there is no evidence that oxygen holds this beneficial effect in nonhypoxemic patients and there is evidence of lack of effectiveness in nonhypoxemic breathless patients with chronic obstructive pulmonary disease (COPD) and advanced cancer (4,5).

PATHOPHYSIOLOGY

Respiration is the process that involves the exchange of oxygen and carbon dioxide (CO₂) between the environment and a living organism. Oxygen is indispensable for the aerobic metabolism of cells, so it is essential for humans to maintain a safe level of this gas in the bloodstream. Several mechanisms exist to regulate breathing in such a way that it is maintained within quite a narrow range. Inside the lungs, oxygen passes from inspired air into the bloodstream, and its diffusion depends on alveolar oxygen pressure. Most of the oxygen in the blood is bound to a carrying protein contained in red blood cells and called hemoglobin, whereas, normally, only a small amount is dissolved in the blood itself. Under normal conditions, almost all of the oxygen-carrying capacity of hemoglobin in the blood is used when the oxygen saturation (SaO₂) is in the normal range, 95% to 98%. Therefore, giving supplementary oxygen to a healthy young person will increase the saturation level only slightly from about 97% to 99% or a maximum of 100%, producing only a very small increase in amount of oxygen made available to the tissues.

Hypoxemia is the result of respiratory failure, a condition that leads to inadequate oxygen delivery (DO₂) to the tissues (partial respiratory failure) and/or to inadequate removal of carbon dioxide (global respiratory failure). The most common form of hypoxemia occurs when there is sufficient oxygen-carrying capacity—in patients with a normal level of hemoglobin—but insufficient oxygen uptake in the lungs. This can be the result of poor ventilation of areas of lung or abnormalities of gas exchange during illnesses such as pneumonia. This form of hypoxemia is the easiest to treat with oxygen therapy; on the contrary oxygen therapy is less effective in other situations, including anemia where there is a low carrying capacity or intoxications where the carrying capacity of hemoglobin has been reduced by a toxic substance. For example, carbon monoxide (CO), by combining with hemoglobin
to form carboxyhemoglobin (HbCO), blocks oxygen binding to hemoglobin despite having a normal level of oxygen in the lungs and in the blood.

Oxygen therapy increases alveolar oxygen (PAO₂) and is, therefore, effective only when alveolar capillary units have some functional ventilation. In turn, it is ineffective if there is a pure shunt, such as pulmonary arteriovenous malformations, where mixed venous blood does not pass through an alveolar capillary unit. There will be, in this situation, a small overall increase in PaO₂ due to an increase in dissolved oxygen in the pulmonary venous blood from ventilated alveolar capillary units, which is minor compared with the oxygen carried by hemoglobin. Despite this, there is good evidence that breath-hold times can be increased by breathing oxygen (6,7). The same principles are used to preoxygenate, actually denitrogenate, patients before intubation during anesthesia; it is thought that the additional breath-hold time is produced not by the marginal increase in blood oxygen levels but by the increased reservoir of oxygen in the lungs after breathing oxygen-enriched air. In poorly ventilated alveoli (i.e., low ventilation/perfusion ratio [V/Q]), PAO₂ will be low and increasing FiO₂ will increase PAO₂ and therefore PaO₂ (7). When there is a diffusion barrier due to increased alveolar capillary membrane thickness, such as in fibrotic lung disease (6), increasing PAO₂ will augment the rate of diffusion across the alveolar capillary membrane by increasing the concentration gradient.

**TREATMENT**

Oxygen represents the first line of treatment for hypoxemia in those patients who are not breathless, aiming to achieve normal or near-normal oxygen saturation. For critically ill patients with an oxygen saturation below the target, after having ascertained that the airway is clear, oxygen should be administered as soon as possible and the flow rates should be adjusted to keep the oxygen saturation (SpO₂) in the target range, or at least above 90% (8,9). Indeed when prescribing oxygen therapy, the health care professional should indicate the target SpO₂ range rather than prescribing a fixed dose of oxygen or FiO₂. The clinician may indicate a starting dose, the device and the flow rate, but there needs to be an agreed-on system for adjusting the oxygen dose upward or downward according to the patient’s needs. It is important to consider that every requirement for an increased dose of oxygen is an indication for urgent clinical reassessment of the patient, repeating arterial blood gas (ABG) measurements in most instances. The SpO₂ should be monitored continuously until the patient is stable and, as soon as ABG measurements are available, the patient’s further treatment should be guided by the results of this test.

Some subjects, especially those older than 70 years, may have SpO₂ measurements below 94% and yet do not require oxygen therapy if clinically stable. Despite this, a reduction of more than 3% in a patient’s usual SpO₂, even if it remains within the target range, may be the first evidence of an acute illness. It is known that oxygenation is reduced in the supine position, so fully conscious hypoxemic patients should ideally be allowed to maintain the most upright posture possible, or the most comfortable posture for the patient, unless there are contraindications (e.g., skeletal or spinal trauma, severe hypotension). A wide variation in SpO₂ characterizes sleep: all healthy subjects in all age groups routinely have transient dips overnight with a mean saturation nadir of 90.4% (10). These decrements should be interpreted with caution, monitoring the subject for few minutes in order to determine whether the hypoxemia is sustained or just a transient, normal nocturnal dip.

There are several medical emergencies in which patients are likely to suffer from hypoxemia, including cardiac arrest, major trauma, shock, major sepsis, anaphylaxis, major pulmonary hemorrhage, massive hemoptysis, major head injury, and near-drowning. In all these conditions initial treatment should involve high-concentration oxygen, aiming at an SpO₂ of 94% to 98% pending availability of satisfactory ABG measurements or until the airway is secured by endotracheal intubation. High-concentration oxygen is additionally recommended during resuscitation and in case of CO poisoning, taking into account that in this condition patients have a normal level of PaO₂ but a greatly reduced level of oxygen bound to hemoglobin because this has been displaced by the CO (11). Pulse oximetry cannot screen for CO exposure, as it does not differentiate carboxyhemoglobin from oxyhemoglobin and ABG analysis will show an apparently normal SaO₂. The blood carboxyhemoglobin level must be measured to assess the degree of CO poisoning. The half-life of carboxyhemoglobin in a patient breathing room air is approximately 30 minutes; this decreases to 90 minutes with high-concentration oxygen via a reservoir mask. The most important treatment for a patient with CO poisoning is, therefore, to give high-dose oxygen via a reservoir mask. Comatose patients or those with severe mental impairment should be endotracheally intubated and ventilated with 100% oxygen. The role of hyperbaric oxygen remains controversial (12,13).

Patients who present serious illness but are not critical or greatly hypoxic—pneumonia, acute asthma, lung cancer, interstitial lung disease, pneumothorax, pleural effusion, pulmonary embolism, acute heart failure with hypoxemia, stroke with hypoxemia, labor with hypoxemia, postoperative breathlessness or hypoxemia, or severe anemia with breathlessness—can be treated with medium-dose oxygen therapy with a target SpO₂ range of 94% to 98%. Generally, breathless and hypoxic patients do not have a firm diagnosis at the time of presentation to the hospital. For most acutely hypoxemic patients whose medical problem is not yet diagnosed, an SpO₂ range of 94% to 98% will avoid the potential risks associated with hypoxemia or hyperoxia. Aiming for an SpO₂ in the normal range will also have the effect of using the lowest effective FiO₂, avoiding risks such as absorption atelectasis and V/Q mismatch. The priority for such patients is to make a specific diagnosis as early as possible and to institute specific treatment for the underlying condition. Early ABG measurement is mandatory in the management of patients with sudden unexplained hypoxemia.

Patients with chronic lung disease may tolerate a low SpO₂ chronically when clinically stable; however, these resting oxygen levels may not be adequate for tissue oxygenation during acute illness or in those conditions where oxygen demand increases. For those patients with COPD (14–22) or other known risk factors that can predispose to hypercapnic respiratory failure with acidosis—obesity, chest wall deformities, or neuromuscular disorders, cystic fibrosis, severe lung scarring from old tuberculosis, overdose of respiratory depressant drugs—a target SpO₂ range of 88% to 92% is suggested pending the availability of ABG results. For this
subgroup of patients, it is recommended that treatment is carefully titrated with ABG measurements in order to prevent episodes of hypercapnic respiratory failure, using, if necessary, noninvasive or invasive mechanical ventilation. Noninvasive ventilation is recommended for patients with COPD with hypercapnia and a pH less than 7.35 despite 1 hour of standard medical treatment (23,24).

On the contrary, there are no published trials supporting the use of oxygen to relieve breathlessness in nonhypoxemic patients, and there is evidence from randomized studies that oxygen does not relieve breathlessness compared with air in nonhypoxemic patients with COPD who are breathless following exertion (25).

**Oxygen Delivery Devices**

Oxygen can be delivered to spontaneously breathing patients through a very wide range of devices that are described in the following. But first we note the main method of storage and provision of oxygen. Compressed gas can be contained at a very high pressure into cylinders that come in an array of sizes and, hence, capacity ranging from small portable cylinders for individual use to large ones suitable for hospital use. Additionally, oxygen exists in a liquid form, which is obtained from atmospheric oxygen by fractional distillation and is stored in pressure tanks; it has to be evaporated into gas before use. Finally, oxygen can be obtained from the concentrators.

Returning to delivery devices for oxygen therapy, they are typically classified into two groups: variable flow or fixed-flow equipment. The term variable flow relates to the fact that as the patient’s respiratory pattern changes, delivered oxygen is diluted with room air. This results in a widely inconsistent and fluctuating FiO₂. In fact, despite some commonly published figures for delivered FiO₂ at given flow rates, the actual FiO₂ delivered to the patient by various devices is neither precise nor predictable. Variable flow devices include nasal catheter, nasal cannulae, transtracheal oxygen catheter, and various oxygen masks. Fixed-flow equipment, on the other hand, provides the entire patient’s inspired gas with a precisely controlled FiO₂; when applied appropriately, the FiO₂ delivered to the patient is therefore constant, regardless of ventilatory pattern. Fixed-flow devices include air-entrainment masks, large-volume aerosol systems, and large-volume humidifier systems.

The choice of a specific system will depend upon the clinical status of the patients, the dose of oxygen required, and the tolerance of the patient for the device. Oxygen should be humidified, whenever possible, in order to prevent dried secretions to obstructing smaller airways. A nasal cannula provides oxygen through oxygen supply tubing with two soft prongs that are inserted into the nares. It can deliver low and medium-dose oxygen concentrations—respectively with low- and high-flow devices—that, flowing into the nasopharynx, mixes with room air; consequently, the FiO₂ varies depending upon factors such as respiratory rate, tidal volume, oxygen flow rate, and extent of mouth breathing. Although one might expect mouth breathing to reduce the efficiency of nasal cannulae, the majority of studies have shown that mouth breathing results in either the same inspired oxygen concentration or a higher concentration, especially when the respiratory rate is increased. This is important because patients with acute breathlessness are likely to breathe quickly and via the mouth rather than the nose. As there is marked individual variation in breathing pattern, the flow rate must be adjusted based on SpO₂ and, where necessary, ABG measurements. The formula to calculate the FiO₂ delivered with nasal cannula is:

\[ \text{FiO}_2 = 20\% + (4 \times \text{oxygen liter flow}) \]

Low-flow nasal cannulae typically deliver rates between 1 and 4 L/min with an FiO₂ that varies from 25% to 40% (26). Generally, low-flow nasal cannulae are used to deliver oxygen to an adult with a low oxygen requirement; this system is lightweight and inexpensive. In addition, the patient can talk and feed without interruption of oxygen delivery. On the other hand, they are of limited use during the stabilization of acutely ill patients, since they cannot reliably deliver high concentrations of oxygen. Moreover, some patients may experience discomfort, nasal dryness, and epistaxis at flows above 4 L/min, especially if it is maintained for many hours, even when a bubble humidifier is used. Therefore, if higher oxygen flow rates and FiO₂ are needed, it is better to use a mask.

Masks are the most frequently used oxygen delivery system; they are indicated in patients who breathe spontaneously, especially if they are strictly mouth breathers, and who require FiO₂ that cannot be delivered using nasal cannulae. The device should be placed over the patient’s nose and mouth and secured with an elastic strap fitted around the head. There exist several different types of masks, characterized by the range of oxygen concentration that can be delivered and the possibility to avoid carbon dioxide rebreathing. However, the masks have some disadvantages, such as the risk for aspiration if the patient vomits, and limitations in communication, coughing, and eating. Moreover, masks are not suitable for patients with hypercapnic respiratory failure, because of the risk of rebreathing associated with their use.

The simple face mask delivers moderate amounts of oxygen with a higher concentration than nasal cannula; it receives the oxygen through a tube connected at the base of the mask, delivering oxygen flows between 6 and 10 L/min. The mask itself, with its volume of 100 to 300 mL, serves as a reservoir. Room air enters through the holes on each side of the mask and mixes with pure oxygen, thereby decreasing the percentage of oxygen inspired by the patient; the final concentration generally varies between 35% and 30%, depending on the patient’s respiratory rate and the mask fit (27–29). Thus, precise concentration of oxygen cannot be reliably delivered. Using this mask, an oxygen flow rate greater than 5 L/min is recommended to prevent rebreathing of carbon dioxide (28,30).

A specific type of simple mask is the Venturi mask, the operation of which is based upon the Venturi principle: pure oxygen flows into the mask and is diluted with air entrained via ports on the Venturi valve. The amount of air entrained into the mask is related to the thickness of the ports and to the flow of oxygen into the system. The proportion of air entrained remains essentially the same through a range of oxygen flow rates and, therefore, the Venturi mask delivers the same oxygen concentration as the flow rate is increased (the minimum suggested flow rate is written on each Venturi device). Because this high-flow mask provides an accurate concentration of oxygen to the patient, regardless of the flow rate, it is suitable for patients needing a known concentration of oxygen. For patients with a high respiratory rate, the flow rate is set above the minimum indicated on the valve so as to exceed the inspiratory flow rate of the patient.
A simple mask connected to a reservoir is defined as a partial rebreathing mask. This kind of mask needs oxygen flow rates of between 10 and 12 L/min and delivers an oxygen concentration ranging between 50% and 60% (28,31). During inspiration, air is drawn predominantly from the fresh oxygen contained in the reservoir. Despite the fact that this compartment contains some exhaled gases as well, gases in the reservoir are oxygen rich because the early exhaled air that flows into the reservoir from respiratory dead space is oxygen rich and contains little carbon dioxide (31,32). To avoid this commingling of pure oxygen flow with exhaled gas, and to avoid the risk of rebreathing, it can be used a nonrebreathing face mask with reservoir and one-way valves. This system is composed of one-way valves over the exhalation ports that allow the egress of expired gases during exhalation and prevent room air from entering the mask during inspiration (33). Another one-way valve is located between the mask and the reservoir in order to prevent flow of exhaled gases into the reservoir. With this mask, oxygen should flow into the reservoir at 8 to 15 L/min and, in any case, the flow should be adjusted to prevent the collapse of reservoir. Notwithstanding the fact that, with this aid, an FiO 2 of up to 95% can be achieved to prevent the collapse of reservoir. Notwithstanding the fact that, with this aid, an FiO 2 of up to 95% can be achieved.

Another one-way valve is located between the mask and the reservoir in order to prevent flow of exhaled gases into the reservoir. With this mask, oxygen should flow into the reservoir at 8 to 15 L/min and, in any case, the flow should be adjusted to prevent the collapse of reservoir. Notwithstanding the fact that, with this aid, an FiO 2 of up to 95% can be achieved.

High-flow Nasal Cannulae (HFNC)

All the conventional high-flow oxygen delivery systems discussed above are not well tolerated by the patients due to discomfort, obtrusiveness, and insufficient heating and humidification of the inspired gases (35–37). To obviate these disadvantages, effort has been spent over the past two decades to develop and validate an alternative oxygen delivery system: the high-flow nasal cannulae (HFNC). This device provides a gas mixture, with an FiO 2 ranging from 0.21 to nearly 1.0 to nares via nasal prolongs. The presence of an oxygen blender allows the desired FiO 2 to be set and delivered, adjusting it independently from the flow rate, which can reach a maximum of 60 L/min. In addition, the gas mixture can be warmed to body temperature and saturated with water via an inline humidifier. Several studies showed that the use of HFNC was associated with a greater comfort and tolerance, lower dyspnea, lower dryness of upper airways, and lower desiccation of secretions, compared to conventional face masks (38–40). One of the consequences of inhaling a warmed and fully humidified gas mixture is the maintenance of the integrity of mucociliary function, consequently rendering secretions easier to mobilize. This produces a decrease in the work imposed on muscles for expectoration. Another beneficial effect of this device consists in its ability to generate a flow rate that exceeds the patient’s peak inspiratory flow rate, in most cases, guaranteeing that there is less room air mixed with the inspired gas, and the desired FiO 2 is more reliably delivered to the patient (41,42). This is particularly useful for patients in respiratory distress, who often have inspiratory flow rates that exceed those that can be delivered by standard systems (33). Patients with respiratory distress can also benefit from the continuous wash out of carbon dioxide from the anatomic dead space (43,44), occurring with HFNC, especially at higher flow rates (45). Over the last 10 years, multiple studies have shown that HFNC generate a positive pressure inside the nasopharynx and esophagus during both inspiration and expiration (46,47). Perhaps as a consequence, HFNC may reduce the work of breathing by providing inspiratory assistance, which increases the tidal volume, reduces respiratory rate, and counterbalances autoPEEP, especially in COPD patients (48–50). Although HFNC has been proposed as a management tool for various conditions, including hypoxic respiratory failure, cardiogenic pulmonary edema, as well as to prevent respiratory failure in postoperative and postextubation patients, the data available for adult applications of HFNC are limited (51).

For patients who have a tracheostomy or a transtracheal fistula, oxygen can be delivered through a tracheostomy mask or a transtracheal catheter. These devices deliver high-flow oxygen directly into trachea, promoting gas exchange; indeed they can reduce the work of breathing and augment carbon dioxide removal. When oxygen is given in this way for a prolonged period, humidification and suctions to remove the mucus from the airways are indicated.

RESPIRATORY CARE AND MONITORING IN THE ICU

Respiratory monitoring in critically ill patients is mandatory to detect inadequate oxygenation, acid–base imbalance and tissue hypoperfusion at an early stage. The correct use and interpretation of data from bedside assessment can improve patient outcomes. We describe here the potential clinical value of advanced respiratory monitoring technologies, according with a recent published consensus (52).

Monitoring Systems

Gas Exchange

The diagnosis of hypoxemia is essentially based on two parameters: oxygen saturation and arterial oxygen tension. The amount of oxygen carried in the blood is often expressed in terms of oxygen saturation of circulating hemoglobin. This is what is meant by “oxygen saturation level” (SpO 2, SaO 2), defined as one of the five vital signs. If the measurement is obtained using pulse oximeter, rather than via an ABG measurement (SaO 2), it is called the SpO 2: for adults aged less than 70 years, the normal range is approximately 95% to 98% at sea level, and it declines gradually within this age range (53).

The mean SpO 2 may be lower in older people; however, it is difficult to dissociate the effects of advancing age from the effects of the disease which are common in old age (54,55). If the oxygen saturation is measured directly from an arterial blood sample, it is called the SaO 2 (56–58).

Alternatively, it is possible to measure the oxygen tension of the blood (PaO 2), known as the “partial pressure of oxygen.” This measurement can be expressed in kilopascals (kPa, normal range 12.0 to 14.6 kPa) or in millimeters of mercury (normal range 90 to 110 mmHg for young adults) and it is usually obtained from an arterial specimen. More rarely, it is obtained from arterialized earlobe blood. In both cases, it is preferable to use local anesthesia to obtain these specimens, except in emergencies or if the patient is unconscious or anesthetized.

The presence of a normal saturation measured by SpO 2 does not exclude the need for performing ABG analysis, especially among critically ill patients. Indeed SpO 2 can be normal in...
a patient with an alteration of pH or arterial carbon dioxide tension (PaCO₂) or with anemia. Therefore, ABG analysis should be evaluated early in all critically ill patients, in all subjects having an unexpected or inappropriate SpO₂, in any case of increasing breathlessness in a patient with previously stable hypoxemia, in a stable patient who deteriorates and requires a significantly increased FiO₂ to maintain a constant SpO₂, in any patient with risk factors for hypercapnic respiratory failure who develops acute breathlessness, deteriorating oxygen saturation or drowsiness, or other symptoms of CO₂ retention. Additionally, ABG analysis should be performed in breathless patients who are thought to be at risk of metabolic conditions such as diabetic ketoacidosis or metabolic acidosis due to renal failure, in acutely breathless or critically ill patients with poor peripheral circulation in whom a reliable oximetry signal cannot be obtained, or in the presence of any other evidence that would indicate that ABG blood gas results would be useful in the patient’s management, for example, an unexpected change in “track and trigger” systems such as a sudden rise of several units in the medical early warning score (MEWS) or an unexpected fall in SpO₂ of 3% or more, even if within the target range (59).

Before evaluating the oxygenation of a patient, it’s important to record the FiO₂ and the PaO₂/FiO₂ ratio; the latter is a quick and simple parameter that refers to the ratio of arterial oxygen partial pressure to fractional inspired oxygen. According to the Berlin definition of acute respiratory distress syndrome (ARDS; see Chapter 109), patients are categorized into three different categories (mild, moderate, or severe), based on the PaO₂/FiO₂ ratio (60). Although it has limitations, the PaO₂/FiO₂ ratio is a very useful clinical parameter used for predicting outcome and response to therapy in patients with ARDS (61).

As mentioned above, when assessing the level of oxygenation of critically ill patients with respiratory failure, PaO₂ and SaO₂ (or SpO₂) are the main determinants and are most frequently used; however, there are many conditions where they may not provide sufficient information about the adequacy of oxygen delivery (DO₂). Indeed this parameter relies on many determinants, such as passive oxygen diffusion into the arterial blood, but also on oxygen-carrying capacity of blood, adequate cardiac output, and local control of blood flow to the organs. Global DO₂ is the product of cardiac output (CO) and arterial oxygen content (CaO₂); CaO₂ is, in turn, the product of SaO₂, hemoglobin concentration and a constant reflecting hemoglobin–oxygen binding capacity (6). In the case of V/Q abnormalities, anemia, or low CO, the PA–aO₂ gradient or the PaO₂/FiO₂ ratio may be more sensitive indicators and correlate better with the adequacy of DO₂.

Devices for Titration of Oxygen Flow

Over the past several years, devices have been developed that automatically adjust—in a closed-loop manner—oxygen flow to spontaneously breathing patients, maintaining a set oxygenation target, such as the O₂ flow regulator (62) and the free O₂ (63). It is recognized that the oxygen flow administered to the patient is not always optimal; patient’s needs vary during the day, and even in healthy people, episodes of oxygen desaturation may occur during daily activities or during sleep. These drops in saturation occur more frequently in the critically ill patient and in those affected by COPD (64), inducing complications such as reduction in exercise tolerance (65), pulmonary hypertension, right heart failure, polycythemia, and increased mortality (66). Some studies have found that oxygen therapy is not optimally prescribed in COPD patients; that the commonly prescribed, fixed dose, usually titrated at rest, may not meet the patient’s needs during an exacerbation, inducing both hypoxemia and hyperoxia, with their attendant complications (67–70). It would be preferable, therefore, to tailor the oxygen flow to the actual changing need of the patient, and to titrate the flow rate based upon an SpO₂ signal to maintain a target saturation, for example, a target of 93% or more (71). This adjustment in oxygen flow minimizes episodes of desaturation, avoids excessive administration that may produce respiratory acidosis, and maintains stable SpO₂ at all activity levels.

Transcutaneous Arterial Carbon Dioxide Pressure

Transcutaneous carbon dioxide monitoring (PtCO₂) is a noninvasive method used to estimate the PaCO₂. It is able to give an electrochemical measurement of PaCO₂ by warming the skin and inducing hyperperfusion (72). Although there is a good concordance between arterial and transcutaneous PaCO₂ values (73), the role of PtCO₂ in the adult intensive care setting remains unclear. Major issues include the need for frequent recalibration and the mismatch in presence of hyperoxia, hyperperfusion, improper electrode placement, and tissue edema. Additionally, skin breakdown and tissue loss can occur, especially if the probe is left in place for long time (74).

Volumetric Capnography

Volumetric capnography is a noninvasive technique that examines the CO₂ concentration in exhaled air as a function of expired volume by using infrared light. As described for the first time by Aitken and Clarke–Kennedy (75), the capnogram curve represents one respiratory cycle and has several components: the first part of the waveform (phase I) represents the CO₂ from the airway (dead space), the second part (phase II) is a sharp rise (beginning of exhalation) that coincides with the transition between airway and alveolar gas. The highest portion of this segment is called the end-tidal CO₂ and represents the maximum pressure of CO₂ at the end of breath; normally it is between 35 and 40 mmHg. The phase III corresponds to the CO₂ eliminated from the alveoli (plateau line). The homogeneity of the gas distribution and alveolar ventilation are the major determinants of the capnogram’s shape.

In addition, dead space can be deduced noninvasively using volumetric capnography (76–78). It has, thus, been useful in the monitoring of various diseases, particularly when V/Q mismatch is present, such as in pulmonary thromboembolism (79), interstitial lung disease, and acute lung injury, as well as in patients undergoing mechanical ventilation (52,80). However, this technique needs a complex equipment which represents a limitation of its use in clinical practice (52).

Respiratory System Mechanics

The respiratory system includes both passive (lung and the chest wall) and active structures (respiratory muscles); these components have both elastic and resistive properties. The elasticity is defined as a driving pressure variation (ΔP) over a change in volume (ΔV). Resistance is expressed as the
ratio between the pressure change and the gas flow (V) variation (ΔP/ΔV). It is not possible to separate the chest wall and the lung from the respiratory muscles, and so the respiratory mechanics properties can be evaluated only when the respiratory muscle activity is quiescent (patient deeply sedated or paralyzed). During passive mechanical ventilation, compliance is calculated as the ratio between Vt and plateau pressure (Pplat) minus positive end-expiratory pressure (PEEP). On the other hand, the difference between peak or maximal pressure (Pmax) and plateau pressure (Pplat) over a constant V define the resistance (81,82).

During volume-controlled ventilation, with a constant flow, it is possible to calculate both the resistive forces and the compliance of the respiratory system by performing easily bedside end-inspiratory and end-expiratory occlusion maneuvers. Briefly, after the end-inspiratory occlusion technique, the rapid pressure drop from Pmax to Pplat represents the pressure required to move the flow through the airways and the endotracheal tube (ETT). The following slow drop until a plateau depends mainly on the elastic properties of the system. With the end-expiratory occlusion, clinicians can evaluate the values for intrinsic (auto) PEEP and total PEEP. Thus, compliance and resistance measurements provided by ventilators performing end-inspiratory and end-expiratory pauses, as well as the interpretation of PV curves with the identification of the lower (LIP) and upper (UIP) inflection points, furnish useful information to optimize mechanical ventilation management according with the underlying diseases.

**Esophageal and Transpulmonary Pressure**

The esophageal pressure (Pes) is an acceptable surrogate of pleural pressure and can be measured by using an esophageal balloon catheter. Thanks to this correlation, it is possible to estimate the transpulmonary pressure (Ptp), the pressure needed to distend the lungs, as the difference between the airway pressure (Paw) and the pleural pressure (Ppl); it is also possible to measure the gastric pressure (Pga) and, consequently, the transdiaphragmatic pressure (Pdi), which results from the difference between Pes and Paw, by adding a gastric balloon.

Recently, a Pleural Pressure Working Group (PLUG) reviewed the newest information on esophageal pressure monitoring in patients with respiratory failure (83). Currently, the measurement of Pes in mechanically ventilated patients is often performed in an attempt to detect and treat patient/ventilator asynchrony, to measure work of breathing and to guide weaning. Thus, the Pes has been proposed to calculate the end-expiratory Ptp and to set PEEP so as to prevent the cyclic lung recruitment and derecruitment that are present when Paw is greater than Pes at the end of expiration (88). As shown by the EPVent study (89), the strategy that uses Pes to adjust PEEP in order to achieve end-expiratory PEEP between 0 and 10 cm H2O (the esophageal pressure-guided group) significantly improves oxygenation and compliance compared with the control group in which PEEP was set according to the patient’s PaO2 and FiO2 (gas exchange–based PEEP group). Based upon these considerations, the use of the Pes to optimize ventilator setting in ARDS patients seems more useful to avoid both under- and over-lung distension compared to the use of airway pressure as guide.

**The Procedure**

Although advances in electronic and computer technology over the last decades have generated several ventilators with additional pressure transducers that provide Pes measurement at the patient’s bedside, the most commonly used procedure is performed via esophageal and gastric balloons that are now commercially available. The passage of the catheters through the nasal cavity may cause pain, irritation, cough, and sometimes vomiting. Thus, initial preparation of the awake patient includes the local nebulization of lidocaine and a mild dose of sedative, if the patient is particularly anxious. Placing the patient into the semi-recumbent position is the best approach to the insertion of the balloon (90). Usually two operators are required for the operation, the first one dedicated to extend the neck of the patient, with the second one very slowly introducing the catheter into the nares, preferably the one appearing to be unoccluded or less occluded.

The esophageal balloon should be first pushed into the stomach and moved backward step by step until it passes through the esophageal sphincter where the waveform during inspiration will begin to become negative. The balloon is then positioned roughly in the middle third of the esophagus where the “occlusion test” is performed (91). The gastric catheter’s position is checked by pushing over the patient’s abdomen to see a clear positive pressure swing. Once the catheter is in place, it needs to be fixed with tape at the nostril, and 1 mL of air is then inserted with a syringe and then slowly removed until about 0.3 to 0.4 mL remain (92–96).

Despite being relatively well standardized, the technique for measuring respiratory mechanics requires special attention to avoid errors and complications. Patient should be fasting to reduce the risk of vomiting. Additionally, disorders of the mouth, pharynx—tumors, cervical spine disease, or pharyngo-esophageal diverticulum—and esophageal pathologies—tumor, strictures secondary to radiation or chemical burns, medications or ulcers, Schatzki’s ring, or foreign bodies—may represent relative and absolute contraindications to the examination (92). Clinicians must pay careful attention to patients with pre-existing cardiac dysrhythmias, as catheter placement may increase the risk of complication, as well as of a vagal reflex syndrome. Finally, neuromuscular problems—stroke, Parkinson’s disease, Huntington’s disease, multiple sclerosis, myasthenia gravis, muscular dystrophy, polymyositis, amyotrophic lateral sclerosis or scleroderma—may also make balloon passage difficult (92).
Lungs Volumes

Direct Measurement of End-Expiratory Lung Volume

The lung volume at the end of passive expiration is defined functional residual capacity (FRC). The term end-expiratory lung volume (EELV) is the more precise term to describe the lung volume when PEEP is applied during mechanical ventilation. The measurement of FRC and EELV is useful for the management of patients with ARDS that present a reduction in lung volume. To calculate the EELV we can use several methods. The closed dilution technique requires the calculation of a known soluble gas volume (helium or methane) in expired breath. Recently, bedside EELV measurement using nitrogen or O₂ and CO₂ sensors in ICU ventilators—so-called washout/wash-in techniques—have been proposed in clinical practice (52). EELV estimation may help to set PEEP and monitor alveolar recruitment maneuver responses in patients with ARDS when combined with compliance measures (97).

Lung Ultrasound

Over the past decade, the use of lung ultrasound (LUS), supported by emerging data, has increased in different clinical settings. The International Consensus Conference provided recommendations and indications for LUS in order to standardize this technique (98). Actually, LUS is considered an accurate tool for bedside respiratory monitoring in the ICUs. In fact, LUS allows detection of pleural effusion, differentiation of consolidation potentially secondary to pulmonary embolism, pneumonia, or atelectasis, and as a tool to rule out pneumothorax and diaphragmatic dysfunction. Moreover, thoracic ultrasound is used as a tool to guide thoracentesis and for placement of thoracostomy tubes or central venous lines. LUS is also able to monitor the effects of therapy in various acute lung diseases, including acute pulmonary edema, ARDS, community-acquired pneumonia, and ventilator-associated pneumonia (98, 99). Thoracic ultrasound has some advantages compared to the chest radiography and CT scan, including portability and the ability to perform real-time imaging. In addition, LUS does not expose the patient to ionizing radiation. The major limitations include the need for staff training and the inability to give precise information in case of deep lesions without consolidation/effusion and/or paravertebral lesions, along with technical challenges in obese or edematous patients (100).

Respiratory Monitoring During Noninvasive Ventilation

NIV is a useful therapeutic modality for many patients and its use in the ICU has increased in the last two decades. As success with NIV depends on several factors, monitoring during NIV should be directed to identify and, if possible, resolving the issues that are associated with failure of this mode of ventilation, in order to improve patient’s outcomes. As noted by Olzyman et al. (101), the possible causes of immediate NIV failure—that is, failure within minutes to less than 1 hour of initiation of NIV—are a weak cough reflex and/or excessive secrections, severe neurologic impairment, patient-ventilator asynchrony, and intolerance and agitation. Thus, an accurate evaluation of vital signs, respiratory muscle function, cough effectiveness, and degree of consciousness is mandatory prior to initiation if NIV. In addition, unstable patients with ARF should be closely monitored with ABG analysis, both to establish the baseline severity and to avoid delay in endotracheal intubation in case of worsening gas exchange.

Patient-ventilator interaction is an important issue that ICU staff should take into account when using NIV. In fact, high inspiratory ventilator pressures and the presence of air leaks are major determinants of NIV asynchronies (52, 102). Although recent technologic advances—for instance, new NIV algorithms and modes such as neurally adjusted ventilator assistance (NAVA)—have been designed to reduce the occurrence of patient-ventilator asynchrony (103–105), bedside methods, including evaluation of spontaneous versus ventilator-delivered breaths and accessory muscle use should be always considered initially. Additionally, air leaks can be identified by following the inspired and expired tidal volume values, and the presence of autoPEEP can be expected when the flow does not reach zero at the end of expiration. These simple measures, in association with flow and pressure waveform observations on the ventilator screen, should be used by physicians to detect “gross” patient-ventilator mismatching. In patients receiving NIV for acute COPD exacerbation, optimization of the ventilator settings by analyzing flow and pressure waveforms on the screen (“optimized ventilation”) is a more efficient manner to set the ventilator than by considering only numerical data (“standard ventilation”) in terms of gas exchange and NIV success (106).

Finally, NIV interface intolerance is another important reason of failure when attempting to utilize NIV for an acute episode. Consequently, sedation should be considered part of the strategy aimed at improving NIV acceptance, mainly related to minimizing interface discomfort (101, 107).

In conclusion, it is advisable for every clinician prescribing NIV to have an experience in clinical, pharmacologic, and technologic competences as well as in monitoring skills in order to improve patient outcomes and to avoid delays in endotracheal intubation, especially in patient with de novo hypoxemic respiratory failure (108).

Key Points

- Oxygen therapy should be handled carefully in critically ill patients according to the underline cause of respiratory failure.
- Oxygen therapy can be delivered via different devices. The choice of the most appropriate system should be made based upon patient’s clinical status, level of required oxygen supply, and patient’s tolerance and comfort. The use of HFNC is associated with a greater comfort and tolerance, lower dyspnea, lower dryness of upper airways, compared to standard oxygen. However, the data available for adult applications of HFNC are limited.
- Critically ill patients should be closely monitored in order to detect the early onset of acute respiratory distress and failure to maintain adequate saturation, to avoid oxygen toxicity and its side effects. On the other hand, respiratory monitoring is essential to identify the causes of the disease involved and the effects of treatment.
References