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REVIEW ARTICLE

Oxygen Therapy in Children - An Update

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Abstract

In 1774, Joseph Priestley of England discovered the colorless, odorless, tasteless gas that Antoine Lavoisier named oxygen.Oxygen is a lifesaving drug has safe dose ranges, adverse physiologic effects, and toxic manifestations that are associated with higher doses and prolonged use. So, the administration of oxygen should be done with as much care and attention as any other drugs. Oxygen is transported in the blood in two ways: dissolved in the serum and in combination with hemoglobin.Children with any of the following signs are likely to have hypoxemia: central cyanosis, nasal flaring, inability to drink or feed due to respiratory distress, grunting with every breath and depressed mental state, severe lower chest wall indrawing, tachypnea or head nodding. The sources of oxygen and its delivery depend on the facility and the availability of resources. Most commonly use devices for oxygen delivery are nasal cannula, nasal prongs, simple face mask. An FiO_2 of >0.5 is considered toxic. After only a few hours of breathing 100% O_2, mucociliary function is depressed and clearance of mucous is impaired followed by nonproductive cough, substernal pain and nasal stuffiness may develop. More prolonged exposure to high O_2 tention may lead to changes in the lung that mimic adult respiratory distress syndrome. In premature neonates, lower SpO2 may be targeted to reduce the toxic effects of oxygen therapy, such as retinopathy of prematurity or bronchopulmonary dysplasia.

Introduction

Oxygen is the most frequently used "drug" in the management of sick children.[1] Oxygen is a drug, like most drugs, has safe dose ranges, adverse physiologic effects, and toxic manifestations that are associated with higher doses and prolonged use. So, the administration of oxygen should be done with as much care and attention as any other drugs.[2] Oxygen therapy is the process of increasing the concentration of oxygen in inspired air to treat hypoxia.[3] The goal of oxygen therapy is to give just enough oxygen to return the arterial oxygen saturation to the appropriate amount for the patient. The usual target is 90% in the infant, child and adult. Oxygen should be administered to saturate the hemoglobin 92% or better and this will safely achieve a PaO_2 of about 60-70 mm Hg.

History of oxygen as a drug

In 1774, Joseph Priestley of England discovered the colorless, odorless, tasteless gas that Antoine Lavoisiernamed oxygen.[2] It is not flammable but does support combustion. Oxygen is a highly reactive, non-metallicchemical element of atomic number 8 that readily forms compounds, particularly oxides, with most elements. Oxygen normally exists in the atmosphere as a diatomic gas, O_2, and makes up 0.209 the earth's atmosphere by volume and 0.232 by weight.[4] In 1907, Budin recommended oxygen "supplied through a funnel, the large opening of which is placed beside the infant's face" for the treatment of

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cyanotic episodes in newborns. Nearly 150 years afterits discovery, Finnish pediatrician Arvo Ylppo¨ recommended the intragastric administration of this gas to infants.[4] It was not until 1934 that Dr Julius Hess, Chief of Pediatrics at the Michael Reese Hospital in Chicago, createdthe first inhaled oxygen delivery device for infants and young children.[5] His "oxygen box," which consisted of a metal hood with a small window, was the first oxygen chamber used within an incubator.[5] The device was criticized both for making it difficult to view the infant and for its inability to provide high oxygen concentrations, but it paved the way for the development of oxygen administration devices in pediatrics. By the 1940s, a commercially available incubator capable of providing and facilitating oxygen therapy for the treatment of cyanosis, apnea, andperiodic breathing in newborns was the standard of care.[3,6] Further development and use of these delivery devices has resulted in significant health-care benefits, including a reductionin mortality. Today the administration of oxygen by inhalation continues to play an essential role in the survival of infants and children.[4,7] Before the 1960s and 1970s, oxygen administration was guided by the clinical observation of skin color, as well as the breathing frequency, regularity, and work of breathing. It was not until the 1960s and 1970s that technology (micro sampling of blood gases, transcutaneous oxygen monitoring, and later pulse oximetry) became available formore precise monitoring of the physiologic effect.[8]

Oxygen transport in the blood

Oxygen is transported in the blood in two ways: dissolved in the serum and in combination with hemoglobin. The oxygen dissolved in the serum is measured as the PaO_2 that constitutes only 2% to 3% of the total O_2 transported in the body. There is 0.0031 ml of O_2 dissolved in each 100 ml blood for each 1 mm Hg partial pressure of O_2. Thus, at a PaO_2 of 100 mm Hg, only 0.3 ml O_2 would be carried per 100 ml of plasma. Most O_2 in the body (97% to 98%) is transported to the cells in combination with hemoglobin and is measured as the percentage of O_2 saturation SpO_2. The percentage of saturation of blood is that portion of the total hemoglobin saturated with O_2. It is a relationship between the amount of O_2 that is carried and the amount that can be carried. Each gram of hemoglobin can transport 1.34 ml of O_2 per 100 ml of blood.[9]

Assessment of Inadequate Oxygen Delivery

To identify a patient's, need for oxygen, several physical signs and laboratory values can be assessed. Hypoxemia is often diagnosed by a lower than normal PaO_2, most often considered <80 mm Hg. A routinely sited indication for providing oxygen is when $PaO_2$is <60 mm Hg in children, yet PaO_2 alone is inadequate to determine oxygen delivery. Oxygen delivery is determined by the concentration ofhemoglobin in the blood; its oxygen saturation; the rate of blood circulation; and, last, the efficiency with which oxygenis unloaded from the hemoglobin to the tissues. Oxygen delivery is often expressed in the following equation:

$$DO_2 = CO\ [(Hb \times SaO_2 \times 1.34) + (PaO_2 \times 0.0031)]$$

where DO_2 is the rate of oxygen delivery, Hb is the hemoglobin concentration, and SaO_2 is the percentage of saturatedhemoglobin with oxygen.[16] The 1.34 represents theoxygen carrying capacity of the hemoglobin. The PaO_2 is the PO_2 in the arterial blood. The 0.003 is the solubility coefficient for oxygen in blood. CO is cardiac output. Therefore, you can see within this equation that PaO_2 is based on a relatively insignificant amount dissolved within the blood. In a patient who is anemic or hypovolemic, hasan abnormal hemoglobin with increased affinity for oxygen, or has a low CO, his/her oxygen delivery may be inadequate even in the presence of a normal PaO_2. Inadequate oxygen delivery in this case is often referred to ashypoxia.[9,10]

Table I

Signs and symptoms of hypoxemia

System	Mild to moderate	Severe
Central nervous system	Confusion, agitation, combativeness	Lethargy, obtunded mental status
Cardiac	Tachycardia, ectopy, hypertension	Bradycardia, hypotension
Respiratory	Dyspnea, tachypnea, shallow respirations, labored breathing	Increasing dyspnea and tachypnea, possible bradypnea or agonal respirations
Skin	Cool, clammy	Cyanosis
Arterial blood gas	PaO_2: 60-80 mm Hg	PaO_2 : <60 mm Hg

Since a PaO_2 of 60 and 80 corresponds with a noninvasive SpO_2 value of approximately 90 and 95%, respectively, in the patient with a normal pH, PCO_2, temperature, and diphosphoglycerate. Oximetry is often used to help identify hypoxemia, has its limitations and is known to be inaccurate in carbon monoxide poisoning. The patient condition needs to be considered during the assessment of adequate oxygen delivery. Underlying pathophysiologic mechanisms of hypoxemiaare: pulmonary disease, hypoventilation, uneven matchingof ventilation to perfusion, diffusion defects, intrapulmonary shunts or "right to left" cardiac shunts, or reduced oxygen-carrying capacity due to anemia or abnormal blood hemoglobin. Physical signs, such as cyanosis, confusion, tachycardia, retractions, nasal flaring, and expiratory grunting (infants) can be indications of an oxygen need.[11] Hypoxiais more serious and is defined as a deficit of oxygen at the cellular level. It is commonly caused by hypoxemia or hypoxia due to inadequate oxygen delivery due to high metabolic demand, such as sepsis, or abnormal cardiac function like heart failure or localized decreases in perfusion, such asstroke.[12] It is often a proper assumption that if left untreated, severe hypoxia can lead to serious and permanent brain injury and death.[7,8,13-15] It must be emphasized that hypoxia is determined not by PaO_2 or SpO_2/SaO_2 alone but also by hemoglobin, oxygen extraction, and metabolic demand of the body as described previously.

Where there is no pulse oximetry, clinical signs may be used to guide use of oxygen. Children with any of the following signs are likely to have hypoxemia:

- Central cyanosis
- Nasal flaring
- Inability to drink or feed (when this is due to respiratory distress)
- Grunting with every breath
- Depressed mental state (i.e., drowsy, lethargic)

In some situations, and depending on their overall clinical condition, children with the following less specific respiratory signs may also have hypoxemia:

- Severe lower chest wall indrawing,
- Respiratory rate of >70/min, or,
- Head nodding (i.e., a nodding movement of the head, synchronous with the respiration and indicating severe respiratory distress).[9]

Indications

The need for supplemental oxygen should be determined through evaluation of the patient's arterial blood gas and clinical assessment findings. In general, indications for oxygen therapy include the following:

- Correction of hypoxemia, thereby decreasing the work of breathing and the myocardial workload it imposes, and promotion of adequate oxygen delivery to the tissues. The correction of hypoxemia, in and itself, will not ensure the sufficient delivery of oxygenated blood to the tissues. A competent cardiovascular system is also necessary for carrying the adequately oxygenated blood to the tissues.
- Improvement of oxygenation in patients with decreased O_2 carrying capacity (i.e., those with anemia, sickle cell anemia).
- Promotion of the reabsorption of air in body cavities (e.g., pneumo-cephalus, small pneumothorax).[10]

Contraindications

Although there are very few contraindications to oxygentherapy, in congenital heart disease patients who have ductal-dependent lesions oxygen therapy may cause over circulation within the pulmonary system as a potent pulmonary vasodilator. In premature neonates, lower SpO2 may be targeted to reduce the toxic effects of oxygen therapy, such as retinopathy of prematurity or bronchopulmonary dysplasia.[16]

Complications associated with oxygen use

Administering supplemental oxygen, once hemoglobin is fully saturated (99% to 100%), places the patient at risk of having toxic effects of this drug.[17] The detrimental effects of oxygen therapy were first recognized in the late 19th century by Paul Bert, usinghyperbaric oxygen systems. It has been known for years that breathing an FiO_2 of 1.0 for as little as 3 h can start tocause chest pain, with longer periods leading to signs similar to broncho-pneumonia. Exposure to high concentrations of oxygen first damages the capillary endothelium, followed by interstitial edema (0-12 h), worsening complianceand vital capacity (12–30 h), followed by thickeningof the alveolar-capillary membrane (30-72 h).[18] If theprocess continues, type I alveolar cells are destroyed, andtype II cells proliferate. An exudative phase follows, resultingin a low ventilation/perfusion ratio, physiologic shunting, and worsening hypoxemia.[18]

Generally, an FiO_2 of >0.5 is considered toxic. The first sign of oxygen toxicity is due to the irritant effect of oxygen and reflect an acute tracheobronchitis. After only a few hours of breathing 100% O_2, mucociliary function is depressed and clearance of mucous is impaired followed by nonproductive cough, substernal pain and nasal stuffiness may develop. More prolonged exposure to high O_2 tention may lead to changes in the lung that mimic adult respiratory distress syndrome. Disruption of the endothelial lining of the pulmonary microcirculation results in leakage of proteinaceous fluid. An exudate consisting of edema, hemorrhage, and white blood cells forms in the lung. The damage to the lung may progress to cell death. The function of the pulmonary macrophage is also depressed, rendering the patient more susceptible to infection. The tissue injury in the lung caused by hyperoxia is generally agreed to be due to the production of biochemically reactive, oxygen derived free radicals that overwhelm the body's antioxidant defense.[9,19] FiO2>0.50 presents a significant risk of absorption atelectasis. Breathing high levels of oxygen quickly depletes body nitrogen levels. As blood nitrogen, a relatively insoluble gas decrease, the total pressure of venous gases rapidly decreases. Under these conditions, gases that exist at atmospheric pressure within the alveoli rapidly diffuse into the venous blood, and collapse occurs. The risk of absorption atelectasis may be greatest in children breathing at low tidalvolumes.[20] Oxygen-induced hypoventilation may occur because of suppression of the hypoxic respiratory drive. Normally, CO_2 is the primary stimulant driving the respiratory system. However, in patients with chronic hypercapnia ($PaCO_2$ >45mmHg), the CNS response to an elevated CO_2 level becomes blunted and hypoxemia becomes the major ventilatory stimulus. Administration of oxygen-enriched gas to these individuals may result in hypoventilation, hypercapnia, and possibly apnea.[21]

Sources and delivery of oxygen

The sources of oxygen and its delivery depend on the facility and the availability of resources. The most common sources of oxygen are cylinders, concentrators and pipelines or central piped oxygen. Many devices for administering supplemental oxygen are available. These devices are classified into two general categories; low-flow and high-flow systems. Whether a system is low or high flow does not determine its capability of delivering low versus high concentrations of oxygen. When choosing the appropriate technique for delivering supplemental oxygen, one must consider the device's advantages, the FiO_2 limits of the device and its appropriateness for a particular patient.[9,10]

The methods used to deliver oxygen should be safe, simple, effective, inexpensive. There are different delivery methods. The noninvasive methods are face mask, head box, incubator or tent or holding tubing close to infant's face and semi-invasive methods are insertion of prongs or catheters into the upper airway. Semi-invasive delivery methods require a low oxygen flow and are cheaper than non-invasive methods, which require high oxygen flow. Nasal and nasopharyngeal catheters have a beneficial effect on lung function, as they produce a positive end expiratory pressure (PEEP) of up to 5 cm of H_2O to improve oxygenation. PEEP production may also be effective in the management of apnea associated with prematurity or bronchiolitis. The recommended methods for neonates, infants and children are nasal prongs, nasal catheters and nasopharyngeal catheters.[22]

Table II

Oxygen delivery systems

Low-flow Systems	High-flow Systems
Nasal cannula	Venturi mask
Nasal prongs	Large-volume aerosol system
Simple face mask	• High-humidity face mask
Partial rebreathing mask	• High-humidity face tent
Nonrebreathing mask	• High-humidity tracheostomy mask/collar
	• High-humidity T piece or blow-by

Nasal Prongs

Nasal prongs are the preferred oxygen delivery method in most circumstances for an optimal balance between safety, efficacy and efficiency. Prongs are a device that ends in two short tapered tubes (about 1cm in length)designed to lie just within the nostrils. They are also called nasal cannula. Standard flow rates through nasal prongs are 0.5-1L/min for neonates, 1-2 L/min for infants, 1-4 L/min preschool children and 6 L/min in school children. Humidification is not required with standard flow rates, as the natural nasal mechanisms heat and humidify the inspired oxygen. There is slight risk of obstruction by mucus if a high flow with no humidification is used, but there is no risk of gastric distention. The fraction of inspired oxygen (FiO_2) depends on the oxygen flow rate, the relation between prong and nasal diameters and the patients body weight, which partly determines the volume delivered per minute. PEEP production with nasal prongs is unpredictable. In infants up to 10 kg, oxygen flows of 0.5 L/min, 1 L/min and 2 L/min result in FiO_2 values of about 35%, 45% and 55% respectively.

Nasal Catheter

A nasal catheter is a thin, flexible tube that is passed into the nose and ends with its tip in the nasal cavity. Nasal catheters are usually well tolerated, and they are unlikely to be dislodged. In neonates and infants, 8 (F) size catheters should be used and passed for a distance from the side of the nostril to the inner margin of the eyebrow (about 2.5 cm). The tip usually reaches the posterior part of the nasal cavity and should not be visible below the uvula. Nasal catheters are usually well tolerated, and they are unlikely to be dislodged. The oxygen does not have to be humidified because the tip of the catheter lies in the nasal cavity. The maximum flow rate should be set at 0.5-1 L/min for neonates and 1-2 L/min for infants and children. A nasogastric tube should be in place at the same time, in the same nostril so as not to be obstruct both nostrils. Higher flow rates without effective humidification may cause drying of the nasal mucosa with associated bleeding and airway obstruction.Actual FiO_2 values or PEEP achieved with nasal catheters have not been established.

Nasopharyngeal Catheters

Oxygen delivery through a nasopharyngeal catheter is the most economical of all the methods. Better oxygenation is achieved with a lower oxygen flow than the nasal prongs, because of the relatively high FiO_2 in the trachea and significant PEEP production of about 2.8 cm of H_2O with 1L/min. These catheters are inserted through the nose to a depth 1 cm less than the distance from the side of the nose to the front of the ear (tragus) and passed into the pharynx just below the level of the uvula (about 7 cm in infants). In neonates and infants, (8F) catheters should be used. The maximum flow rate should be set at 0.5 L/min for neonates and 1L/min for infants. Higher flow rates without effective humidification may cause drying of the nasal mucosa, with associated bleeding and airway obstruction. Nasopharyngeal catheters can be displaced downwards into the esophagus and caused gagging, vomiting and gastric distention, a nasogastric tube should also always be in place, in the same nostril to permit rapid decompression of the stomach. Their use should therefore be limited to situations in which nasal prongs are unavailable, staff are familiar with the insertion technique and with supervision, the oxygen supply is limited and in the case of children in whom cyanosis or oxygen desaturation is not relieved by oxygen given via nasal prongs or a nasal catheter. The catheter should be removed and cleaned at least twice a day.[23]

Simple face mask

The simple face mask has vent holes on the sides for the entrainment of room air and the release of exhaled gases. It has no valve or reservoir bag. It should be securely placed over the patient's mouth, nose and chin, then press the flexible metal pieces over the bridge of the nose to create a seal for prevention of gas loss. Finally adjust the strap around the patient's head. The placing of mask over the patient's face increases the size of the oxygen reservoir beyond the limit of anatomic reservoir; therefore, a higher FiO_2 can be delivered up to 0.60. The oxygen flow must be run at a sufficient rate, usually 5L/min or greater, to prevent collection, and thus rebreathing of exhaled gases high in carbon dioxide.[24]

Head boxes, incubators and tents

Non-invasive methods of oxygen administration have some advantages like oxygen piped into the head box, incubator or tent, the actual FiO_2 can be determined precisely with an oxygen analyzer placed near the infant's mouth. There is no increased risk of airway obstruction by mucus or of gastric distention, and

humidification is not necessary.[25] The disadvantage of these methods is however carbon dioxide toxicity if the flow of oxygen is inadequate, setting the oxygen flow too low or from kinking or disconnection of the oxygen tubing. When a head box is used with an inappropriately tight seal around the infant's neck, carbon dioxide can be retained. A gas flow of 2-3 L/Kg per minute is necessary to avoid rebreathing of carbon dioxide in a head box. Head boxes, face masks, incubators and tents all require high oxygen flows to achieve adequate concentrations of oxygen and avoid carbon dioxide accumulation, and they are therefore expensive and wasteful. Head boxes and face masks also interfere with feeding. Therefore, these methods are not recommended for oxygen administration, especially in settings where oxygen supplies are inadequate.[26]

Mechanical Ventilation

Mechanical ventilation is often used to deliver oxygen therapy and treat moderate to severe hypoxemia. Current clinical teaching emphasizes the avoidance of hypoxemia during mechanical ventilation. Continuous Positive Airway Pressure (CPAP) is a form of noninvasive ventilation delivers PEEP with a variable amount of oxygen to the airway of a spontaneously breathing patient to maintain lung volume during expiration. CPAP decreases atelectasis, respiratory fatigue and improves oxygenation. It is indicated for infants with severe respiratory distress, hypoxemia or apnea despite receiving oxygen.[9,10]

Table III

Estimated FiO_2 with low-flow oxygen delivery devices

100% O_2, Flow rate (L/min)	FiO_2
Nasal canula	
1	0.24
2	0.28
3	0.32
4	0.36
5	0.40
6	0.44
Simple oxygen mask	
5-6	0.40
6-7	0.50
7-8	0.60

Monitoring of oxygen therapy

After introduction of oxygen therapy, a planned desired physiologic outcome and the adequacy of the patient's response to therapy should be monitored. Assessment frequency should be based on the severity of hypoxemia (e.g., level of FiO_2 required), overall severity of illness, or variability of oxygen delivery device. Oxygen administration by any method must be supervised by trained personnel to detect and manage complications appropriately. A nurse should check every 3 hours that the prongs or catheter are in the correct position and not blocked with mucus, that all connections are secure, that the oxygen flow rate is correct, that the airways are not obstructed by mucus and that there is no gastric distension. Prongs or catheters should be removed and cleaned at least twice a day.[27] Most use a noninvasive monitoring strategy like pulse oximetry or arterial blood gases for the acid/base balance (indicator of hypoxia leading to a metabolic acidosis) or a PaO_2 to assist with their clinical assessment. Venous or capillary blood gases are not used to evaluate oxygenation. Pulse oximetry, the most appropriate way to monitor children to determine whether they need oxygen and to determine how long children should receive oxygen. Children receiving oxygen should be monitored clinically at least twice a day by pulse oximetry. For children in a stable condition, and with SpO_2 >90%, oxygen should be interrupted once a day for 10-15 minutes and carefully examined for changes in clinical signs and SpO_2 to assess whether supplemental O_2 is still required.[28] Where oxygen supplies are ample, children should receive supplemental oxygen until their SpO_2 on room air is ≥90%. If the SpO_2 is ≥90% after a trial on room air, they should remain off oxygen, and the SpO_2 should be rechecked after 1hr, as late desaturation can sometimes occur.[29]

Conclusions

Oxygen therapy is important, universally accepted as a life-saving therapy and has saved many lives. Oxygen administration should be considered in the same way as other drugs and titrated to ameasured end point to avoid excessive or inadequate dosing. Withholding oxygen can have detrimental effects; however, continuing to provide oxygen therapy when it is no longer indicated can prolong hospitalization and increase the cost of care. One must ensure that oxygen content and cardiacoutput are adequate when assessing the effectiveness of oxygen therapy. Device selection is vitally important in pediatrics because not

only is the size of our patients avariable, but what they will wear is an additional consideration.

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