DRUG PROFILE

OXYGEN AS A PRESCRIPTION

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Abstract: *Oxygen is one of the most common life saving drugs widely used all over the world. It is often needed in many of the acute respiratory emergencies such as pneumonia and asthma where there is a risk of hypoxia. Long term oxygen therapy may be indicated in chronic respiratory conditions such as bronchopulmonary dysplasia (BPD), cystic fibrosis (CF), sleep disordered breathing, interstitial lung disease and pulmonary hypertension. Since medical grade oxygen is classified as a drug with specific biochemical and physiologic actions, with a distinct range of effective doses and well-defined adverse effects at high doses, oxygen needs to be prescribed like any other medication with specifications regarding dose, duration and method of delivery.*

Keywords: *Oxygen, Prescription, Delivery devices.*

In 1774, Joseph Priestley of England discovered the colorless, odorless, tasteless gas that Antoine Lavoisier later named oxygen.[1] It was not until 1934 that Dr Julius Hess, from Chicago, created the first inhaled oxygen delivery device for infants and young children which was an "oxygen box," that can be used within an incubator.[2] Further development and use of these delivery devices has resulted in significant health-care benefits, including a reduction in mortality. Today the administration of oxygen by inhalation continues to play an essential role in the survival of infants and children. However, it is one of the most misused drugs forgetting its toxic effects on lungs and neonatal retina.[3]

Oxygen is a drug and therefore must be prescribed only in life-threatening emergencies when it must be started immediately. Doctors should prescribe oxygen using target saturation range and sign the drug chart. Pulse oximetry should be available in all areas where oxygen is used and the oxygen saturation should be noted and documented prior to commencing oxygen. Suggested target saturation for most patients is 94-98%. However, patients at risk of hypercapnic respiratory failure have a lower target saturation range of 88-92%. Based on the clinical assessment of the patient, an appropriate delivery device and flow rate should be chosen and it should be adjusted to ensure that the patient's saturation is maintained within the target range using the lowest possible oxygen flow rate.[4]

All patients on oxygen therapy should have regular pulse oximetry measurements and the therapy should be decreased in stable patients with satisfactory oxygen saturations. Any changes to FiO_2 or flow rate must be documented, with corresponding respiratory assessment. When the oxygen is decreased, saturation should be monitored after 5-10 minutes, 30 minutes and 60 minutes or more to ensure that oxygen saturation remains within the desired range. When the amount of oxygen administered is changed and/or when oxygen saturation is recorded, the amount of oxygen the patient is receiving and the delivery device should be recorded in the clinical record. At each drug round the oxygen therapy being delivered to the patient must to be checked against the prescription. The current saturation, the delivery device and flow rate should be recorded in the case sheet.[5] In addition to the duration of use and oxygen flow, the prescription completed by the physician should define the delivery device (nasal cannula, mask, transtracheal catheter, etc.) and oxygen source (concentrator, liquid, compressed oxygen tanks, etc.)

Uses of oxygen in pediatrics

Oxygen, being the most common drug used in medical emergencies should be prescribed initially to achieve normal or near-normal oxygen saturation. In most acutely ill children with an expected or known normal or low arterial carbon dioxide ($PaCO_2$), oxygen saturation should be maintained above 92%; some clinicians may aim for a target of 94-98%. Hypercapnic respiratory failure is rare in children; in those children at risk, a lower oxygen saturation target of 88-92% is indicated.[6] In some clinical situations, such as carbon monoxide poisoning, hyperbaric oxygen therapy may be needed until the child is stable.[7]

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In certain conditions like pneumonia, pulmonary thromboembolism, pulmonary fibrosis, shock, severe trauma, sepsis, or anaphylaxis low arterial oxygen (PaO_2) is usually associated with low or normal arterial carbon dioxide ($PaCO_2$). Therefore there is little risk of hypoventilation and carbon dioxide retention, making high concentration oxygen therapy safe. In severe acute asthma, the $PaCO_2$ is usually subnormal but as asthma deteriorates it may rise steeply especially in children. These patients usually require high concentrations of oxygen and if the $PaCO_2$ remains high despite other treatment, intermittent positive-pressure ventilation needs to be considered urgently. Low concentration oxygen therapy is reserved for children at risk of hypercapnic respiratory failure, which is more likely in children with advanced cystic fibrosis or non-cystic fibrosis bronchiectasis, severe kyphoscoliosis or ankylosing spondylitis, severe lung scarring caused by tuberculosis, musculoskeletal disorders with respiratory weakness, an overdose of opioids, benzodiazepines or other drugs causing respiratory depression.[8] Oxygen therapy in neonates is a double edged sword and should be under expert supervision due to the risk of developing reactive oxygen species. Particular care is required in preterm neonates because of the risk of hyperoxia.[9]

Domiciliary oxygen therapy may be indicated in selected cases. It should be done only after careful evaluation by a respiratory care specialist. Special care should be taken to avoid smoking near the premises as there is always a risk of fire.[10] Long-term oxygen therapy may be necessary to maintain a target oxygen saturation of at least 92% in some children with bronchopulmonary dysplasia, primary or secondary pulmonary hypertension, sickle-cell disease with persistent nocturnal hypoxia, interstitial lung disease, cystic fibrosis, obstructive sleep apnoea syndrome, neuromuscular or skeletal disease requiring non-invasive ventilation.[11]

Use of oxygen in treatment of asthma: Nebulisations with beta-2 agonists are the drug of choice in the management of acute severe asthma. The nebulisations are to be administered over 5-10 minutes and should be driven by oxygen as these drugs can increase arterial hypoxemia due to ventilation perfusion mismatch. Most jet nebulisers require an optimum flow rate of 6-8 liters/minute and in hospital can be driven by piped air or oxygen. Domiciliary oxygen cylinders do not provide an adequate flow rate and therefore an electrical compressor is required for domiciliary use.[12]

Use of oxygen in management of anaphylaxis: Administering high-flow oxygen is part of the first line management of a child in anaphylactic shock. Angioedema is dangerous if laryngeal edema is present. In this circumstance adrenaline/epinephrine injection, oxygen, antihistamines and corticosteroids should be given as for management of anaphylaxis.[13]

Use of oxygen in treatment of status epilepticus: In all status epilepticus cases, initiation of oxygen is of prime importance to prevent hypoxic brain injury.[14]

Pain in sickle-cell disease: A mixture of nitrous oxide and oxygen may also be used with or without NSAIDS and/or opioids.[15]

Use in anesthesia: Volatile liquid anesthetics are administered using calibrated vaporisers, using air, oxygen, or nitrous oxide-oxygen mixtures as the carrier gas. To prevent hypoxia, the inspired gas mixture should contain a minimum of 25% oxygen at all times. Higher concentrations of oxygen (greater than 30% - up to 50-60%) are usually required during inhalational anesthesia when nitrous oxide is being administered.[16]

Use in poisonings: Oxygen should be administered to children with cyanide poisoning and in carbon monoxide poisoning. The patient should be moved to fresh air, the airway cleared, and high-flow oxygen (100%) administered as soon as available.[17, 7]

Selection of oxygen delivery devices

Oxygen delivery method selected depends on age of the patient, oxygen requirements/therapeutic goals, patient tolerance to selected interface and humidification needs. In general, the delivery devices are classified into low flow systems and high flow systems. Low-flow systems include simple face mask, nasal prongs (low flow) and tracheostomy mask. High flow systems include non-re-breather face mask (mask with oxygen reservoir bag and one-way valves which aims to prevent/reduce room air entrainment), ventilators, CPAP/BiPaP drivers, face mask or tracheostomy mask used in conjunction with an Airvo2 humidifier and High Flow Nasal Cannula therapy (HFNC).[18]

All high flow systems require humidification. The type of humidification device selected will depend on the oxygen delivery system in use, and the patient's requirements. The humidifier should always be placed at a level below the patient's head. Indications for providing humidified oxygen are patients with thick copious secretions, non-invasive and invasive ventilation, high flow rate requirement with nasal prongs (>1L/min in neonates, >2L/min in children under 2 years, >4L/min in children over 2 years), facial mask flow rates of greater than 5 liters/minute and in patients with tracheostomy.[19]

Oxygen sources and flow regulators

Oxygen can be provided either from a wall source or from a cylinder. A wall source should provide at least 50 pounds per square inch **(**psi) of pressure at all times. Cylinders operate at psi of 1800-2400. Such high pressure cannot be directly delivered to the patient; hence a down regulating valve before a flow meter is required. A low flow system provides FiO2 that varies with patient's inspiratory flow rates. A high flow system provides fixed FiO2 at flows that meet or exceed patient's own inspiratory flow requirements. The flow requirement depends on minute ventilation (MV). Normal flow requirements are 3-4 times the MV and [MV= Tidal volume (Vt) x Respiratory rate (RR)]. The average Vt for a child is about 6ml/kg.[20]

Oxygen concentrators are devices that separate oxygen from nitrogen in the air by using adsorption and desorption over a material called zeolite that adsorbs only the nitrogen. No ventilator or CPAP machine can run on this as the outlet pressure is only 5psi. The resultant FiO_2 is about 0.4. This device may be used, if requirements permit, for home oxygen therapy.

Low flow nasal cannula

Oxygen is delivered through two soft prongs in the nostril. The prongs should have some space in the sides for exhalation. Humidification is not necessary. The flow is directed to the nasopharynx where humidification and the heat exchange takes place by natural nasal mechanisms. The maximum accepted flow is 2-4L/min. FiO_2 varies between 24-40% and it increases approximately 4% with each liter of oxygen. This is the preferred method of home oxygen therapy in infants.[21]

Though irritation and nasal obstruction may occur, nasal prongs are generally well tolerated. The indications are minimal oxygen requirements (<30%), weaning off from oxygen and chronic oxygen therapy on low concentrations. The advantages are comfort and conservation of the gas.

Simple face mask

It is useful for acute situations and short term use only (Set at 5-10L/min). O_2 flow must be set to a minimum of 5 Liters/min to facilitate clearance of CO_2. FiO_2 varies between 35-55%. It fits on patient's face without much discomfort and has perforations which are exhalation ports. The most appropriate size should be selected and care must be taken to avoid pressure points or eye damage. They can provide a maximum of 40% oxygen but this can vary with the flow rate. The disadvantage is that it is difficult to feed children requiring face mask and some children feel claustrophobic with its use.[22]

Oxyhood

Usually used for small babies and can deliver FiO_2 precisely. A clear transparent hood that ensures enough room for free neck and head movement is ideal. Every unit should maintain at least 3-4 sizes. Too big a hood will dilute the oxygen and too small a hood will cause discomfort and carbon dioxide accumulation. Oxygen gradients within the hood could vary as much as 20% from top to bottom. Fixed oxygen concentrations from 22 to 80% can be maintained with a minimum of 7-10 L/min oxygen flow. The hood has an outlet at the top to release the accumulating CO_2 that, being lighter than O_2, rises to the top. Although these devices theoretically deliver FiO_2 >0.5, they are best suited for patients who require <0.5 FiO_2.[23] There is no need for humidification; further, gastric distension and risk of airway obstruction by mucus are negligible.[24] The oxyhood is generally well tolerated. The disadvantages are the limitation on mobility (undesirable for prolonged oxygen therapy) and discontinuation of the enriched oxygen environment during feeding or suctioning.[25]

Non re-breather mask

Even though it is a low flow system it can work as a high flow system as it provides high FiO2. These are like masks but have a valve at the entry port that allows only oxygen from the source to enter the reservoir thus preventing re-breathing. It prevents room air from being entrained by an additional one way valve at the exhalation port. A well-fitting mask can provide up to 100% oxygen (Table I). When in doubt of the patient's requirements or if the patient is sick, as in the case of shock states, respiratory distress, cardiac failure, this is the mask to be chosen to

Table I. Oxygen percentages with different systems

Litres/min	Simple mask	Non re-breathing mask
5	40%	
6	45-50%	55-60%
8		60-80%
10		80-90%
12		90%
15		90-100%

institute oxygen therapy as it will provide maximum oxygen and build reserves, even prior to intubation. The oxygen flow should be set at a minimum of 10-15L/min (80-95% FiO_2).[26]

Venturi masks

These are high flow devices which allows precise measurement of oxygen delivered. Oxygen is delivered through a narrow orifice at a high flow based on Bernoulli principle. There are openings near the nozzle that allow room air to be sucked in, diluting the oxygen. Changing the size of the nozzle, the flow rates, as well as the ports, allows control of the amount of oxygen (Table II). This device guarantees fixed FiO_2 delivery and can save the oxygen costs as the high flow comes from the air at low oxygen concentrations. Increased rate of breathing does not affect the concentration of oxygen delivered. Each device will have a table on the package insert as a guide to flow rates required by that particular device.[27]

Continuous positive airway pressure (CPAP)

Continuous positive airway pressure (CPAP) is a type of positive airway pressure, where the airflow is introduced into the airways to maintain a continuous pressure to constantly stent the airways open, in people who are breathing spontaneously. It is indicated when the oxygen requirement is >60% with a PaO_2 of <60mm Hg. The background PEEP reduces the work of breathing, increases the FRC, recruits alveoli, increases static compliance and improves ventilation perfusion ratios. It maintains the set pressure throughout the respiratory cycle, during both inspiration and expiration and differs from bilevel positive airway pressure (BiPAP) where the pressure delivered differs based on whether the patient is inhaling or exhaling. These pressures are known as inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP).[28]

Table II. Venturi devices and delivery of oxygen

Litres/min (Oxygen / Total)	Oxygen concentration (percent)	Air: Oxygen ratio
2/53	24	25:1
4/45	28	10:1
6/47	31	7:1
8/45	35	5:1
10/33	40	3:1
12/32	50	5:3

In small neonates weighing <1400g, CPAP is best delivered using snug fitting nasal prongs. A pacifier may help in keeping the mouth snuggly closed. Various CPAP systems are available - the unit-made underwater seals and the more expensive bubble CPAP systems and ventilator systems. It could be tried prior to conventional ventilation in any spontaneously breathing patient who does not require emergency ventilation. Apart from nasal CPAP, other ways to provide CPAP are via nasopharyngeal tube or via face mask.[29]

High-flow nasal cannula

High flow nasal cannula (HFNC) oxygen delivery, also sometimes called heated humidified high flow nasal cannula (HHHFNC), is a relatively new non-invasive ventilation therapy that seems to be well tolerated in neonates and children with hypoxemic respiratory failure.[30] Before the advent of HFNC, clinicians were not comfortable administering a flow of >1 L/min via nasal cannula for newborns and >2 L/min in older children, due to the lack of adequate humidification.[31] The equipment includes traditional nasal cannula style prongs to deliver heated, humidified oxygen at flow rate starting at 1 L/kg/min that may be escalated to 2 L/kg/min based on work of breathing. An air-oxygen blender allows FIO_2 to be directly manipulated.[32]

Table III. Sample oxygen prescription

Name and hospital ID	Date and time
Current respiratory status	Respiratory rate Work of breathing Oxygen saturation
Target saturation range	
Reason to initiate oxygen support	
Mode of delivery	Nasal prongs Oxyhood Face mask Non re breather mask HFNC CPAP Mechanical ventilation
Flow rate and FiO_2	
Countersigning doctor and ID	

How to write an oxygen prescription

Since medical grade oxygen is classified as a drug, one needs to ensure that the prescription should detail: Patient information, drug (O_2), route (device), dose (flow/ FiO_2), target saturation, documentation and reason to start (Table III).

Contraindications to oxygen therapy

There are no absolute contraindications to oxygen therapy if indications are judged to be present. The goal of oxygen therapy is to achieve adequate tissue oxygenation using the lowest possible FiO_2. Some congenital heart defects can lead to an unbalanced circulation which may be made worse by administration of oxygen due to pulmonary vasodilation and subsequent systemic ischemia. This should be considered in a baby who presents unwell in the first two weeks of life with absent or weak femoral pulses and a heart murmur and is not improving with oxygen.[33] Supplemental O_2 should be administered with caution in patients suffering from paraquat poisoning and with acid inhalation or previous bleomycin lung injury.[34,35]

Cautions

In patients with chronic carbon dioxide retention, oxygen administration may cause further increases in carbon dioxide and respiratory acidosis.[36] Children with chronic neuromuscular disorders, chest wall deformities, cystic fibrosis, morbid obesity and chronic lung disease of prematurity are at risk. Evidence has also shown high concentration oxygen can cause a clinically significant increase in CO_2 in patients with severe exacerbations of asthma.[37] Other precautions/ hazards/ complications of oxygen therapy include drying of nasal and pharyngeal mucosa, oxygen toxicity, absorption atelectasis, skin irritation and fire hazard.[8]

Adverse effects

Dry or bloody nose, skin irritation around the nasal cannula or face mask, drowsiness, morning headaches and retinopathy of prematurity in newborn infants are common adverse effects due to injudicious administration of oxygen. Oxygen toxicity, caused by excessive or inappropriate supplemental oxygen, can cause severe damage to the lungs and other organ systems. High concentrations of oxygen, over a long period of time, can increase free radical formation, leading to damaged membranes, proteins and cell structures in the lungs. Prolonged high concentrations can be toxic to the pulmonary epithelium and hyperbaric oxygen can cause convulsions.[38]

Points to Remember

- ***Oxygen must be considered a medication that warrants a documented prescription before administration, except in emergency situations where written prescription is not mandatory to initiate the therapy***
- ***The prescription should include indication, target saturation range, mode of delivery and flow rate.***
- ***Choice of oxygen delivery device is based on clinical decision.***

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CLIPPINGS

Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults.

The clinical, laboratory, and chest CT features of 20 pediatric inpatients with confirmed COVID-19 infection were retrospectively analyzed during 23 January and 8 February 2020.

Procalcitonin elevation and consolidation with surrounding halo signs were common in pediatric patients which were different from adults. It is suggested that underlying coinfection may be more common in pediatrics, and the consolidation with surrounding halo sign which is considered as a typical sign in pediatric patients.

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