Hypoxia & Oxygen Use

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November 9, 2016
Objectives

 State cause of hypoxia and conditions for which $O_2$ is beneficial
 Identify physiologic signs of hypoxia and situations where oxygen may be useful
 Identify types of and appropriate use of oxygen delivery devices
 State benefits, limitations, and contraindications of oxygen use
 Discuss supportive research guiding oxygen use

*Personal Disclosures: None
What is oxygen?

- The term “Oxygen" comes from a Greek word that means “acid-former”.

- The air we breathe is composed of 21% percent oxygen (O$_2$).

- Oxygen is a colorless, odorless, tasteless gas that is essential for the body to function properly and survive.
The Great Exchange
The Great Exchange

Deoxygenated blood from pulmonary artery

Air

Alveolus

capillary
Hypoxemia/Hypoxia

- Hypoxemia is defined as an abnormally low level of oxygen in the blood.

- Hypoxia is defined as a condition where the oxygen supply is inadequate either to the body as a whole (general hypoxia) or to a specific region (tissue hypoxia).
Causes of Hypoxia

- Troubles can arise from any part of the respiratory system or can occur at level of blood vessels or any part of the cardiopulmonary system.

- Damage to lung tissue (COPD/Intestinal Lung Disease/Fibrosis)
- Lung infections (Bronchitis/Pneumonia/ARDS-air flow obstruction)
- Pulmonary edema (fluid fills the tissue of the lung)
- Pleural effusion/Empyema (fluid or pus fills pleural space)
- Pneumothorax (Air/blood/other fluid fills pleural space)
- Areas of lung collapse (atelectasis/collapsed lung/trapped lung)
- Pulmonary embolism (blood clot to artery in the lung)
- Other Pulmonary Vascular Problem (AVM, Pulmonary HTN)
- Heart troubles (heart failure, arrhythmias, MI)
- Trauma to the chest (pulmonary contusion/broken ribs/flail chest)
- Neuromuscular weakness (leading to decreased breathing efforts)
- Pain issues in chest or abdomen (shallow breathing leading to atelectasis)
- Encephalopathy (No signal sent from brain to take a breath)
- Airway Obstruction (Foreign body/tumor/sleep apnea/stridor/tracheal stenosis/mucous)
- Hematologic Problem (Acute Blood Loss, Anemia, Carbon Monoxide Poisoning)
Pathophysiology of Hypoxia

Difficulty can occur in the bronchioles (main wind pipes) or the alveoli (little air sacs) that make it more difficult for oxygen exchange to occur.
Pathophysiology of Hypoxia

- Often seen in many different lung diseases where there is damage to the lung tissue.

- Notice that in the case of emphysema, there is less surface area for oxygen exchange to take place.
Pathophysiology of Hypoxia

Inflammation or scarring diseases of the lung, such as interstitial lung disease or pulmonary fibrosis causes difficulty with the exchange of oxygen and carbon dioxide at the level of the alveoli.
Infections

- Occurs with infections.
- Puss will fill the spaces between the alveoli and blood vessel, making it hard for oxygen and carbon dioxide molecules to exchange between lung and blood vessel surfaces.
Pulmonary Edema

- Fluid overload and pulmonary edema interfere with oxygen exchange.
- Fluid fills the sacs, decreasing the surface area that oxygen can be exchanged.
Effusions/Lung Collapse/Atelectasis

Pleural effusion: The fluid accumulates outside of the lung, taking up the space the lung would normally fill, causing the lung to collapse.
Pneumothorax

Pneumothorax occurs either when air escapes from the lung itself (ruptured bleb), or trauma to outside of lung (like a punctured rib) causing pleural space to fill up with air/blood/fluid, causing the lung to collapse.
Pulmonary Embolism (PE)

Pulmonary embolism or a blood clot to the lung, obstruct blood flow to the lung and this inhibits the exchange of oxygen since blood will not circulate to the affected area of the lung.
Pulmonary Hypertension

Pulmonary Hypertension: The capillaries in the lungs become narrowed, blocked, or destroyed, causing the blood pressure within the lungs to become high, making it difficult for blood to flow through the lungs.
Decreased Cardiac Output

Reduced cardiac function (whether due to heart failure, arrhythmia, myocardial infarction or chronic illness) causes less blood flow to the lungs and this reduces the ease of oxygen exchange in the lungs at the pulmonary vascular level.
Neurogenic/Hypoventilation

Encephalopathy or other problem in the brain can cause cessation of respiratory efforts. This can be from stroke, brain trauma, or chemical imbalance like hypercapnia or drug overdose.
Upper Airway Obstruction

- Any obstruction of the airway (foreign body obstruction, tracheal stenosis, sleep apnea, stridor) will cause decreased air exchange and lead to hypoxia.
Hematological Problem

- Hematological Problems:
- Anemia/blood loss—there is not enough blood to carry oxygen to cells.
- Carbon monoxide poisoning—blood cells not able to pick up oxygen molecules.
Oxygen Consumption

- Definition: The rate at which oxygen is removed from the blood for use by the tissues.

- Increased oxygen needs occur when....
  - Exercising
  - Infection/Fever
  - Stress on the body
  - Burns or wounds
  - Increased work of breathing (seen in lung diseases)
  - Feeding
Signs & Symptoms of Hypoxia

- Diaphoresis
- Low oxygen sats
- Cardiac arrhythmia
- Juglar venous distension (if related to RV failure)
- Adventitious lung sounds or decreased/absent lung sounds
- Altered Mental Status

- Dyspnea
- Restlessness
- Anxiety
- Cyanosis
- Confusion
- Tachypnea
- Tachycardia
- Dizziness
Most Important Consideration

Identify and Correct the cause of the hypoxia; in the meantime, supportive cares, including supplemental oxygen and ventilator assistance is crucial.
Oxygen Delivery Devices

Conventional Nasal Cannula
Most commonly used oxygen delivery device
High Flow Devices

High Flow Nasal Cannula
High flow oxygen (HFO) therapy system can deliver a high flow air/oxygen blend through a nasal cannula or tracheal adapter, providing an alternative to other forms of ventilation. By providing flow rates of up to 60 LPM, high molecular humidity, and precise oxygen delivery.

Comfort Flow Oxygen
Type of High Flow Oxygen system, can deliver up to 40 liters flow and 100% FiO$_2$
High-Flow Oxygen Therapy

- Oxygen via nasal cannula whereby heated and humidified oxygen is delivered to the nose at high-flow rates. These flow rates generate low-level positive pressure in the upper airways, and the fraction of inspired oxygen ($\text{FiO}_2$) can be adjusted by changing the fraction of oxygen in the driving gas. These flow rates may also decrease physiological dead space by flushing expired carbon dioxide from the upper airway.

- Benefits include better comfort to the patient and improved oxygenation as compared to standard oxygen delivered via face mask as standard flow rate.
Oxymizer: Specialized nasal cannula with high luminal diameter and oxygen reservoir thought to deliver higher oxygen concentration breath by breath in order to increase oxygenation.
Oxygen Masks

Simple Face Mask

Non-Rebreather Mask
Venturi Mask

“Jets” for Venturi regulate FiO₂ delivered
Oxygen Delivery Devices

Oxygen Tent Mask

Oxygen Hood
Oxygen Delivery Devices

Trach Collar

T-Piece
Oxygen Delivery Devices

CPAP and BiPAP
Variety of Masks
Oxygen Delivery Devices

Bag Mask Valve
(Ambu Bag)

Mechanical Ventilator
Oxygen Delivery Devices

ECMO: ExtraCorporeal Membrane Oxygenation

Used as life sustaining measure for patient with acute heart and lung failure. Also used for coronary bypass surgery.
Use of Oxygen in COPD

Benefits of Oxygen in Stable COPD

- Reduces symptoms of dyspnea
- Improves exercise endurance/tolerance
- Increase cardiac output when used with activity
- Decreases hypoxic pulmonary vasoconstriction, thus improving pulmonary hemodynamics (increased systemic oxygen delivery and improved respiratory muscle function)
- Oxygen flow may stimulate upper airway and facial receptors, which appears to reduce the intensity of dyspnea
- Reduction in overall mortality for COPD
Use of Oxygen in COPD Exacerbation

Oxygen-induced hypercapnia proposed mechanisms

- Increased V/Q mismatching within the lungs, possibly due to reversal of hypoxic vasoconstriction, increasing perfusion of poorly ventilated lung units.

- Haldane Effect—oxygenated hemoglobin has lower carbon dioxide binding capacity than does deoxygenated hemoglobin, and as the proportion of oxygenated hemoglobin increases, there is a consequent rightward shift of the CO\textsubscript{2}-hemoglobin dissociation curve, resulting in increased PaCO\textsubscript{2}. This is usually overcome by increasing VE, however, patients with severe COPD are unable to do this and worsening hypercapnia results.
Use of Oxygen in COPD Exacerbation

- Rebound Hypoxia can occur upon the abrupt withdrawal of supplemental oxygen because the oxygen and carbon dioxide displace each other. If there is a sharp fall in the alveolar PaO$_2$, the remaining PaCO$_2$ displaces the oxygen. For this reason, oxygen therapy should always be stepped down gradually.

- Evidence points to titrating oxygen therapy to correct hypoxia, while avoiding hyperoxia is the best approach to oxygen therapy in patient with COPD exacerbation. Target SaO$_2$ range of 88-92% (which should yield PaO$_2$>55) is generally the accepted goal for patients at risk of developing hypercapnia.

**Information found in review article, “Oxygen therapy in acute exacerbations of chronic obstructive pulmonary disease” International Journal of COPD 2014:9 1241-1252.**
Oxygen Therapy for Patients with COPD [Chest 2010; 138 (1):179-187]

Current Evidence and the Long-term Oxygen Treatment Trial
James K. Stoller, MD, MS, FCCP; Ralph J. Panos, MD, FCCP; Samuel Krachman, DO, FCCP; Dennis E. Doherty, MD, FCCP; Barry Make, MD, FCCP; and the Long-term Oxygen Treatment Trial Research Group

Long-term oxygen therapy recommendations [based on review of Nocturnal Oxygen Therapy Trail (NOTT) and the Medical Research Council (MRC) studies]

- Oxygen therapy should be used for a minimum of 15 hours per day to ensure maximal benefit in patients with moderate to severe chronic hypoxemic lung disease ($\text{PaO}_2 \leq 55$).
- There is significant benefit with relative risk of death of 1.94 (95% CI, 1.17-3.24) with use of nocturnal oxygen.
- Use of long term oxygen therapy in patient with mild to moderate hypoxemia ($\text{PaO}_2 \leq 59$) showed no mortality benefit.
- Use of oxygen in patient’s with mild hypoxia ($\text{PaO}_2 \leq 59$) should be restricted to patients having complications including pulmonary hypertension, polycythemia, or peripheral edema.

**Results of both studies showed that COPD patients with resting hypoxemia, some oxygen is better than no oxygen, and continuous oxygen is better than nocturnal oxygen alone.**

**Results of other short-term trials have suggested beneficial effects, other than survival in patients with COPD and moderate hypoxemia at rest, including improved exercise performance.**
Benefits of an Oxygen Reservoir Cannula versus a Conventional Nasal Cannula during Exercise in Hypoxemic COPD Patients: A Crossover Trial
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- Trail of 43 patient with COPD testing endurance; each patient used nasal cannula for 2 session and then the oxymizer for 2 exercise sessions in pulmonary rehabilitation program.

- Endurance time was significantly higher (+12%) when patient’s cycled while using oxymizer in comparison to nasal cannula (858 +/- 754 vs. 766 +/- 652) a difference of 92 seconds cycling duration.

- O₂ sats at “isotime” (total duration of exercise) was significantly higher with the oxymizer (93.5 +/- 5.4 vs 90.4 +/- 5.3%; p=0.027)

- Conclusion: O₂ delivery via the Oxymizer is superior to nasal cannula in regard to endurance capacity and oxygenation during exercise in patient’s with severe COPD; In particular, patient’s with a higher demand (≥4 lmp) may benefit more for oxymizer use.
High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

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Multicenter, open labeled trial from February 2011 through April 2013: Patient’s randomly assigned without hypercapnia, who had acute hypoxemic failure with ratio of PaO2:FiO2 of 300 or less to high-flow oxygen therapy, standard oxygen therapy delivered via face mask, or non-invasive positive-pressure ventilation. N=310 (94 to standard O2 group, 106 to high-flow O2 group, 110 to non-invasive ventilation group). The primary outcome was the proportion of patient intubated at day 28; secondary outcomes included all-cause mortality in the ICU and at 90 days and the number of ventilator free days at day 28.
Results

- The number of ventilator-free days at day 28 was significantly higher in the high-flow oxygen group (24+/-8 days, vs 22+/-10 in the standard oxygen group, and 19+/-12 in the non-invasive-ventilation group.

- Rate of intubation at day 28 was 38% in high-flow oxygen group, 47% in the standard oxygen group, and 50% in the non-invasive ventilation group.

- The hazard ratio for death at 90 days was 2.01 (95% confidence interval, 1.01 to 3.99) with standard oxygen vs high-flow oxygen (p=0.046) and 2.50 (95% CT, 1.31 to 4.78) with noninvasive ventilation vs. high-flow oxygen (p=0.006).

- At 1 hour after enrollment, patients reported reduced dyspnea scores, rating the intensity of respiratory discomfort lower with the use of high flow oxygen as compared to either the standard oxygen therapy group or the non-invasive ventilation group.
Conclusions of High-Flow O₂ Study

- In patients with acute hypoxemic respiratory failure (non-hypercapnic), treatment with high-flow oxygen, standard oxygen, or non-invasive ventilation did not result in significantly different intubation rates.
- Treatment with high-flow oxygen as compared to either standard oxygen therapy or non-invasive ventilation resulted in more ventilator-free days.
- There was a significant difference in the favor of high-flow oxygen in 90-day mortality (improved survival rate).
- There is improved patient comfort with less reported dyspnea in patient’s treated with high-flow oxygen as compared to standard oxygen or non-invasive ventilation.
Management of Spontaneous Pneumothorax: British Thoracic Society Pleural Disease Guideline 2010

Andrew MacDuff, 1 Anthony Arnold, 2 John Harvey, 3 on behalf of the BTS Pleural Disease Guideline Group

*Also linked as guideline for American Thoracic Society Guidelines*

- Primary or Secondary Spontaneous Pneumothorax and Tension Pneumothorax: should be admitted to hospital and receive supplemental oxygen. Most require decompression/drain placement.

- Use of oxygen in patient’s with Pneumothorax has been shown not only to correct arterial hypoxemia, but also results in four-fold increase in the rate of pneumothorax resolution.

- BTS guidelines recommend the use of high-flow oxygen (10L/min) in symptomatic patients; however, caution must be taken in patient with COPD/chronic hypercapnia.
Pneumothorax: Why oxygen helps

- Gas in the pleural cavity is absorbed by diffusion

- Oxygen is absorbed 62 times faster than nitrogen, carbon dioxide is absorbed 23 times faster than oxygen.

- When the patient inhales more oxygen, nitrogen will disappear from the pleural cavity, leaving oxygen in its place, which is absorbed faster from the pleural cavity into the veins.

- Even in the absence of hypoxia, oxygen is helpful in resolving pneumothorax.
Air Versus Oxygen in ST-Segment–Elevation Myocardial Infarction

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- 638 patients with STEMI, but without hypoxia given 8L flow oxygen vs no oxygen
- Mean troponin between groups, no difference
- Significant increase in mean peak CK in oxygen group compared to no oxygen group
- At 6 months, the oxygen group had significant increase in MI size on cardiac magnetic resonance imaging (20.3 gm vs 13.1 gm)
- Conclusion: Supplemental oxygen in patients with STEMI but without hypoxia may increase early myocardial injury and was associated with larger myocardial infarct size, assessed at 6 months.
N=318 patient with sleep apnea (AHI 15-50) randomly assigned to CPAP vs oxygen vs sleep hygiene/healthy lifestyle (control group)

On average patient wore oxygen 4.8±2.4 hours/night and CPAP use was 3.5±2.7 hours/night

The adjusted 24-hour mean arterial pressure at 12 weeks was significantly lower in the group receiving CPAP than either the control group or the group receiving supplemental oxygen (-2.4 to -2.8 mm Hg). No significant difference was detected between group receiving oxygen and the control group

Meta-analysis of 61 observational studies showed that a reduction in 2 mm Hg SBP would reduce mortality from stroke by 10% and from ischemic heart disease by 7%
Respiratory rate ≤12 in patient no in physiologic sleep strongly suggests acute opioid intoxication.

Persistent hypoxemia after the administration of naloxone may signify the presence of negative pressure pulmonary edema. Mild hypoxia may resolve, but if significant hypoxia persists intubation/positive pressure ventilator should be initiated.

Complication of pulmonary edema can arise; this is thought to be related to attempted inspiration against a closed glottis leading to decreased intrathoracic pressure, causing fluid extravasation; another theory suggests neurogenic pulmonary edema r/t similar mechanism. It is not shown to be related to Naloxone itself.

As alternative to Naloxone administration, patient may be intubated to ensure safe ventilation and oxygenation, providing protection against aspiration while the opioids are metabolized.
Future Studies

- Long-term Oxygen Treatment Trial, currently underway, randomization of >1000 patient; study details found at Clinicaltrials.gov

- Oxygen therapeutics (use of biotechnology to develop “artificial blood" or a "blood substitute“) research efforts have been directed toward developing products to perform the oxygen-carrying and gas transport function of red blood cells. Inability to obtain regulatory approval and sustain investor support resulted in the withdrawal of many products from clinical trials. In 2009, the remaining two companies ceased manufacture of their oxygen therapeutics and filed for bankruptcy. Currently, there are no clinical trials underway in the US for this.
Future Studies

Use of AccuO2 measures SpO₂ to adjust oxygen pulses to achieve a target SpO₂. Has been shown to be superior when compared with continuous flow and a standard oxygen conserving device, improving the overall efficiency of oxygen delivery. Studies underway for use in ambulatory setting.