Oxygen: Friend or Foe?

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Objectives

- Brief history of oxygen as a therapeutic agent
- Quick review of the indications of oxygen therapy
- A breakdown of the potential detrimental affects of oxygen therapy with a focus on oxygen toxicity and absorption atelectasis.
- How can we minimize the negative affects of oxygen therapy while maximizing the physiologic needs and benefits of oxygen therapy.
The History of Oxygen as a therapeutic agent

Oxygen was discovered as a separate gas in the late 18th century. Although its life supporting role was well understood early in this period, it took about 150 years for it to be used properly for patients. It was around the end of World War I that the use of inhaled oxygen became more scientifically established as a therapeutic agent.
Oxygen gas, when respired in the human lungs, generally produces a sensation of agreeable warmth about the region of the chest, and some say that they experience a comfortable sensation through the whole body.
Derose recommends the use of oxygen by the subcutaneous method in cases of tuberculosis with dyspnoea, and remarks that "the temperature falls and a feeling of well-being immediately prevails, for which the patient is very grateful, and sleep, previously impossible, becomes soothing and refreshing." He suggests its employment for 1) the toxic dyspnoea of uraemia, 2) eclampsia, 3) carbon di-oxide poisoning, 4) in certain cases of diabetes, 5) emphysema, 6) pertussis, 7) asystole, and 8) in those cases where mechanical obstruction is precisely located in the air passages.
THE THERAPEUTIC ADMINISTRATION OF OXYGEN,

- Where, in lung affections, an addition of oxygen to the inspired air is needed in order to combat want of oxygen, it is evidently desirable to continue the administration over long periods.
- In cases where the source of danger is failure of the circulation, the inhalation of oxygen may also be of use, and I have seen the cyanosis in a case of valvular disease clear up at once on the administration of oxygen.
- The probable risks of prolonged administration of pure oxygen must be borne in mind, and if necessary balanced against the risks of allowing the oxygen want to continue. No fixed rule can be given.
OXYDOG: THE DISCREET MOBILE OXYGEN CONCENTRATOR

*OXYCAT ALSO AVAILABLE

NEW PRODUCT SPOTLIGHT
Indications of Oxygen Therapy

Tissue hypoxia with arterial hypoxemia
Ventilation-perfusion (V/Q) mismatch
(pneumonic and atelectatic lung zones)
Alveolar hypoventilation
(drug overdose, neuromuscular disorders)
Right to left shunting
(pneumonia, pulmonary embolism, arteriovenous channels)

Tissue hypoxia without arterial hypoxemia
Myocardial infarction
Low cardiac output states
Carbon monoxide poisoning
Chronic lung disease
Detrimental Affects of Oxygen Therapy

Hyperoxia is not well defined, but likely occurs whenever oxygen tension is over 21% of atmospheric pressure.

Hyperoxia can then result in any of the following:

- Depression of Ventilation
- Retinopathy of prematurity
- Bacterial infection associated with humidifiers.
- Absorption atelectasis
- Oxygen toxicity
Depression of ventilation can occur as a result of hyperoxic hypercarbia. This is the phenomenon of increased PaCO2 associated with increases in FiO2 in individuals with chronic compensated respiratory acidosis.

There are several mechanisms that act together to cause this phenomenon.
Depression of Ventilation

The Haldane effect: An increased amount of CO2 is dissolved in blood due to the fact that oxyhemoglobin binds CO2 less avidly than deoxyhemoglobin.

Increase in Dead Space Ventilation: With supplemental oxygen, there is a drop in hypoxic pulmonary vasoconstriction which then leads to redistribution of blood flow from well ventilated to poorly ventilated aveoli.

A small decrease in minute ventilation can occur due to decreased stimuli from the peripheral chemoreceptors to the central respiratory center.
Depression of Ventilation

Anxiolytic and antidyspneic affects of oxygen therapy can promote sleep which then results in loss of voluntary drive to breathe. Respiration is then sustained only by metabolic control mechanisms which then can contribute to increasing hypercarbia.

Hypoventilation resulting from the above mechanisms then decreases inspiratory flow demand reducing the amount of entrained air, especially with low flow oxygen systems, which then may increase the FiO2 delivered to the patient when then can exacerbate the above mechanisms further.
Retinopathy of Prematurity

- Premature birth
  - Decreased: Maternally derived factors (ω-3 PUFA, IGF-1)
  - Supplemenal oxygen
  - Vasoobliteration

- Increased
  - ROS: Free radicals, Lipid peroxidation, Prostanoids and isoprostanes, trans-AAs, Nitration

- Decreased
  - HIF-1 stabilization
  - Growth factors (VEGF, Epo, IGF-1)
  - ω-3 PUFA

- Hypoxia: Increasing metabolism
- Neovascularization

- Current prevention
  - Vitamin E?
  - Limiting O₂ supply

- Improved rate and outcome of ROP

- Future strategies
  - Antioxidants
  - Antinflammatorys
  - Modulators of metabolite signaling
  - Growth factors
  - ω-3 PUFA
  - Stem cell therapy

- Current therapy
  - Cryotherapy
  - Laser photocoagulation
  - Anti-VEGF therapy (under evaluation)
Bacterial Infections Associated with Humidifiers

Contamination of oxygen humidifiers occurs more commonly on long term oxygen devices such as home concentrators.

Common Bacterial species found included *Klebsiella aerogenes*, *Pseudomonas species*, *Streptococcus viridans*, *Streptococcus epidermidis*

Pathologic infections are rare in spite of this finding.

Hospital based disposable humidifiers do not appear to pose a significant threat even up to 12 weeks as long as they are maintained properly with appropriate changes of tubing and use of reservoir bags in patient lines.
Absorption Atelectasis

High doses of supplemental oxygen can cause nitrogen washout of the aveoli there by leading to alveolar collapse.

Absorption atelectasis appears to be more likely under certain circumstances:
• A low ventilation-perfusion ratio
• Qualitative or Quantitative abnormalities in surfactant that promote alveolar collapse
• High rate of oxygen uptake due to increase in metabolic demand.
• An impaired pattern of respiration that fails to correct atelectasis
Loss of nitrogen in the blood causes less total venous pressure. This leads to the collapse of the alveolus.
Absorption Atelectasis

Shunting resulting from absorptive atelectasis can rise to as high as 11% in older otherwise healthy volunteers breathing 100% oxygen for 30 minutes.

Treatment:
- Rapid titration of FiO2 to the lowest fraction necessary to maintain SaO2 >90%.
- Initiate other strategies to correct atelectasis and improve alveolar ventilation.
In the event of a sudden loss of cabin pressure, an oxygen mask will drop from the compartment above your head. For $15.00 you can activate it....
Oxygen Toxicity

Oxygen toxicity can cause damage at multiple levels

1. System wide cellular injury
2. Airway injury
3. Lung parenchymal injury
Oxygen Toxicity

Cellular Injury

Cellular injury occurs through the production of Reactive oxygen species:
1. Superoxide Anion
2. Hydroxyl Radicals
3. Hydrogen Peroxide

There are antioxidant defenses within cells that reduce these species:
Manganese superoxide dismutase
Superoxide dismutase
Oxygen Toxicity

Cellular Injury

If there is an increase in oxygen reactive species and/or a decrease in superoxide dismutase activity, the increased oxygen radicals will impair the function of essential intracellular macromolecules resulting in cell death.
Oxygen Toxicity
Airway Injury

Airway Injury: Many healthy volunteers will experience substernal heaviness, pleuritic chest pain, cough and dyspnea within 24 hours of breathing pure oxygen.

This is a result of tracheobronchitis and absorptive atelectasis.

Erythema and edema can be observed on bronchoscopy in patients treated with 90%FiO2 for 6 hours.

Concentration of reactive oxygen species in exhaled gas increases after only 1 hour of breathing 28% oxygen, regardless of the presence of underlying lung disease.
Oxygen Toxicity
Airway Injury

Bronchopulmonary dysplasia or BPD

• A disease in neonates following recovery from neonatal from neonatal RDS.
• attributed to barotrauma and/or oxygen toxicity.
• Characterized by epithelial hyperplasia and squamous metaplasia in the large airways, thickened alveolar walls, and peribronchial and interstitial fibosis.
Oxygen Toxicity
Parenchymal Injury

Progressive worsening of airspace disease can be observed in patients with ARDS who are sustained on mechanical ventilation due to various factors:

1. Underlying process which produced the ARDS
2. Development of ventilator induced pneumonia
3. Barotrauma
4. Diffuse alveolar damage from oxygen toxicity
Summary

Potential adverse clinical consequences of supplemental oxygen are wide ranging and have both intrapulmonary and extrapulmonary consequences. There appear to be other factors which influence the amount of oxygen that each individual can tolerate before damage occurs.
The single most important recommendation is that FiO₂ should be titrated to the lowest concentration required to meet oxygenation goals. This goal should be in the range of 60-65mmHG PaO₂ or oxygen saturation of 90-92%.

However clinical judgement for each individual patient is vital as some patients may tolerate hypoxemia poorly.
Areas of Future Study

Augmentation of Antioxidants ie Superoxide dismutase

Immune modulators: Manipulation of specific groups of inflammatory factors in the body may permit modification of the deleterious inflammatory response provoked by hyperoxia.