Oxygen Therapy for Pulmonary Disease

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ABSTRACT

A reduction in lung capacity to oxygenize blood as well as in cardiovascular capacity to distribute blood may cause hypoxemia, which could then lead to tissue hypoxia and cellular death. The aim of oxygen treatment is to supply the minimum oxygen concentration needed to achieve adequate tissue oxygenation. There are various methods that can be used to supply oxygen, and the amount of oxygen requirement could also be calculated. Treatment methods are classified into STOT and LTOT. The benefit of oxygen treatment is increased survival, influence on the blood vessels, improved exercise capacity, and positive influence on the respiratory and neuropsychological systems. As with the case with pharmacological treatment, oxygen should be administered at certain doses to achieve greatest efficacy with the least toxicity.

Keywords: *hypoxemia, oxygen*

INTRODUCTION

History

Oxygen was discovered in 1775 in England by Joseph Priestley as a colorless gas. The gas was then named "oxygen" by Antoine Lavoisier. Its use was first reported in 1868 for dental anesthesia. In 1920, Alvan Barach reported the use of oxygen for treatment of bacterial pneumonia. During that era, oxygen was administered through a nasal cannula. Other administration methods developed afterwards. Fluid oxygen was first available in 1965. In 1967, Cherniack reported the administration of oxygenthrough a nasal cannula with a good flow without CO_2 retention.[1,2,3]

Background

A reduction in lung capacity to oxygenize blood as well as in cardiovascular capacity to distribute blood may cause hypoxemia, which could then lead to tissue hypoxia and cellular death. Such condition could be prevented by administering oxygen, aimed to improve and prevent hypoxemia, so that tissue hypoxia can be prevented and avoided.[2,4,5] At this moment, the indications for the use of oxygen treatment have increased in number. Several conditions that require oxygen treatment include acute cardiac infarction, anemia, carbon monoxide poisoning, and deficiency in oxygen transport. Long term oxygen treatment is recommended for chronic obstructive pulmonary disease (COPD) since it is also able to improve the patient's survival, even though the exact mechanism is still unclear. Patients with other chronic lung disease, such as interstitial fibrosis, SOPT, neuromuscular disease, kyphoscoliosis, and other chronic lung diseases may also receive oxygen treatment, even though the results are still unclear.[4,5,6]

HYPOXEMIA

Definition[7,8,9]

Hypoxemia is a condition where there is a reduction in arterial oxygen concentration (PaO_2) or arterial oxygen saturation (SaO_2) below the normal values of 85-100 mmHg for PaO_2 and 95% for SaO_2. Hypoxia is the term used to illustrate the condition of insufficiency in tissue oxygenation, or reduced tissue oxygen content with no regards to the cause or location.

Pathophysiology[7,8,9]

The four main causes of hypoxemia are as follows: 1) reduced amount of inhaled oxygen, 2) reduced alveolar ventilation, 3) poor connection between alveolar ventilation and capillary perfusion, and 4) intrapulmonary shunting. While the main cause of tissue hypoxia are arterial hypoxemia, reduced oxygen supply, and excessive oxygen use by the tissue.

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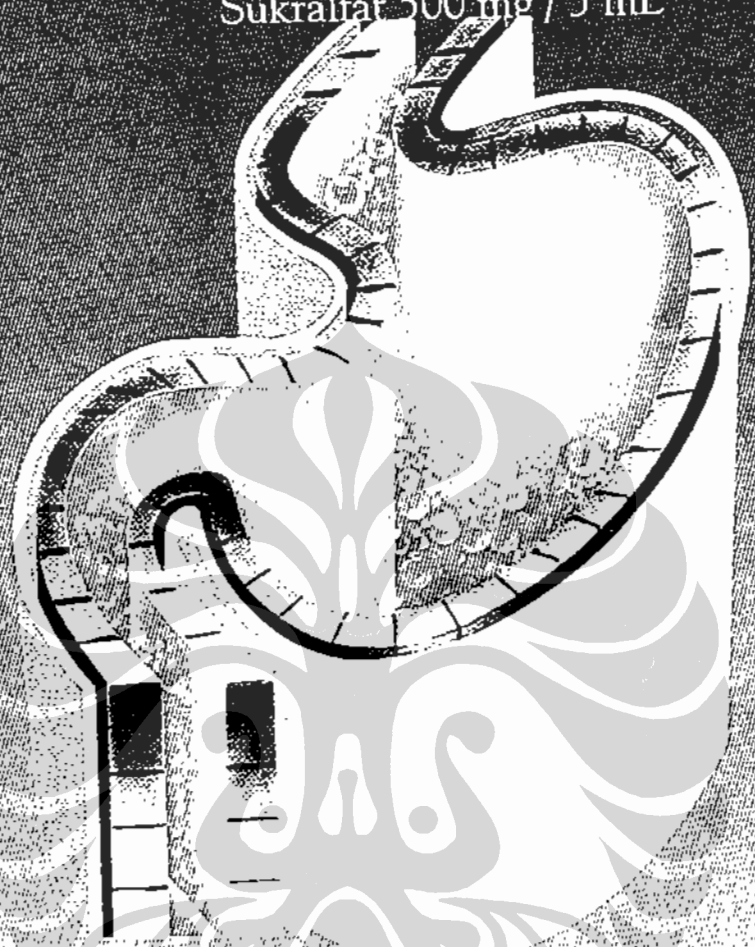

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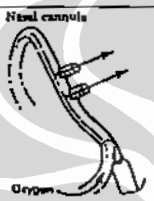
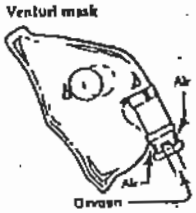
The mechanism of hypoxia is as follows: [7,8,9]

1. Aerobic metabolism requiring a balance of oxygen distribution (DO_2) and oxygen use (VO_2).
2. If the distribution of oxygen is reduced below the threshold (critical DO_2), or if oxygen use exceeds oxygen supply (heavy exercise), the tissue will switch from aerobic to anaerobic metabolism.
3. If there is excessive lactic acid production causing acidosis, cell metabolism is disturbed, resulting in cellular death.

OXYGEN TREATMENT IN PULMONARY DISEASE

Aim[1-6,8,10]

The principle of oxygen therapy is to improve tissue conditions and prevent hypoxemia by increasing the O_2 inspiration fraction (FiO_2). Oxygen is normally administered at the lowest dose, which could increase PaO_2 to over 60 mmHg, or O_2 saturation to over 90%.

	Type of equipment	Flow rate (L/minute)	FIO2 Threshold value (%)
1	Nasal cannula 	1-2	23-28
		3-4	28-38
		5-6	32-45
2	Simple mask 	3-4	25-30
		5-6	30-45
		7-8	40-60
3	Nonrebreathing mask 	8	70-100
4		> 8	50-60
5	Face tent or aerosol mask 	> 8	35-100
6	Venturi mask 	4	24
		4	26
		6	31
		8	35
		8	40

Method of Administration [1-4,11]

The oxygen used usually comes from an oxygen tube filled of compressed or fluid oxygen, with a capacity of 1340 and 3400 liters. The oxygen flows to the patient with a rate of ½ to 10 liters/minute. The choice of oxygen source largely depends on the duration of oxygen administration/day, the patient's age and activity. Several equipments to supply oxygen for therapy are as follows:[9]

How to Calculate Oxygen Requirement:

Case example:
a patient comes to the Emergency Room with the following blood gas analysis: $PaO_2 = 65$, $PaCO_2 = 50$
In this case, we use the formula:

$$PAO_2 = (P\ Bar - P\ H_2O)FiO_2 - \frac{PaCO_2}{0,8}$$

PAO_2 = alveolar O_2 pressure
P Bar = barometer pressure = 760 mmHg
PH O = surface steam pressure = 47 mmHg
FiO_2 = oxygen inspiration fraction (%)
R = respiratory quotient = 0.8

$$\rightarrow PAO_2 = (P\ Bar - P\ H_2O)\ FiO_2 - \frac{PaCO_2}{0.8}$$

$$= (760-47)\ 0.21 - \frac{50}{0.8}$$

$$= 713 \times 0.21 - 62.50$$

$$= 149.73 - 62.50 = 87.23$$

We would thus correct the hypoxia up to $PaO_2 = 80$
And then use the following ratio:

$$\frac{PaO_2}{\text{Previous } PAO_2} = \frac{PaO_2}{\text{Expected } PAO_2}$$

$$\frac{65}{87.23} = \frac{80}{PaO2}$$

$$PaO_2 = \frac{87.23 \times 80}{65} = 107.36$$

And then we return to the previous formula, assuming that there has not been a change in PaCo2.

$$\rightarrow PaO_2 = (P\ Bar - P\ H_2O)\ FiO_2 - \frac{PaCO_2}{0.8}$$

$$107.36 = 713 \times FiO_2 - \frac{50}{0.8}$$

$$FiO_2 = \frac{107.36 + 62.50}{713} = \frac{169.86}{713}$$

$$= 0.23$$ (and then refer to the concentration table)

Table 1. Oxygen Concentration According to the Equipment Used

Equipment	O_2 (l/minute)	FIO_2
Nasal cannula	1	0.21- 0.24
	2	0.23-0.28
	3	0.27-0.34
	4	0.31-0.38
	5-6	0.32-0.44
Venturi	4-6	0.24-0.28
	8-10	0.35-0.40
	8-11	0.50
Simple mask	5-6	0.30-0.50
	7-8	0.40-0.60
Rebreathing	7	0.35-0.75
	10	0.65-1.00
Non-rebreathing mask	4-10	0.40-1.00

Based on the table above, we can see that $FiO_2 = 0.23$ is achieved by using a nasal cannula with an O_2 flow rate of 1-2 liters/minute.

Indication [5,7,8,10]

Specific indications for oxygen therapy for lung disease are as follows:

1. Acute and chronic respiratory failure due to chronic obstructive pulmonary disease
2. Hypoxia due to pulmonary infiltrates
3. Cardiopulmonary edema
4. Primary pulmonary hypertension
5. Interstitial pneumonitis

More controversial indications are cystic fibrosis, restrictive lung disease, kyphoscoliosis, and tuberculosis-associated neuromuscular/skeletal disease.

Oxygen Treatment Methods

Oxygen treatment can be classified into short-term and long-term treatment.

a. Short-term Oxygen Therapy/STOT
Short term oxygen therapy is usually indicated for acute hypoxemia, cardiac and respiratory failure, hypotension, reduced cardiac flow, and metabolic acidosis, as well as respiratory distress.

b. Long-term Oxygen Therapy/LTOT[1-7,10]
Long-term oxygen therapy is usually indicated for chronic obstructive pulmonary disease. The aim of LTOT is to correct chronic hypoxemia without causing hypercapnia, reduce polycitemia, reduce the cost of care, and improve survival. LTOT may be administered continuously or intermittently.

Continuous LTOT is administered if the patient's resting blood gas analysis results are as follows:

- $PaO_2 < 65$ mmHg or oxygen saturation < 80%
- PaO_2 between 56 – 59 mmHg or an oxygen satura-

tion of 89% accompanied by cor-pulmonale
- Polycitemia (Ht > 56%)
- PaO_2 > 59 mmHg or oxygen saturation > 89%

Oxygen is administered for 15-18 hours/day for 4-8 weeks.

Intermittent/nocturnal LTOT is administered if the patient's blood gas analysis results are as follows:
- During exercise: PaO_2 55mmHg or oxygen saturation 88%
- During sleep: PaO_2 55mmHg or oxygen saturation 88% accompanied with complications such as pulmonary hypertension, somnolence, and arrhythmia

The patient's clinical condition, such as reduced breathing difficulty, headache, sleep disturbance, frequency, and the duration of exacerbation must be evaluated at least 1 (once) a month, as well as the arterial oxygen pressure and saturation, to determine oxygen volume during rest, activity, and sleep. The efficacy and saturation of the equipments to administer the oxygen should also be monitored continuously.

Benefits of Oxygen Therapy [5,7-10,13]

Improved Survival

Long term oxygen therapy can improve the survival of patients with chronic obstructive pulmonary disease. This is in accordance with a study by the British Medical Research Council in hypoxemia patients who randomly received continuous oxygen for 15 hours per day, while the rest did not receive oxygen therapy. A 5-year evaluation demonstrated that 19 out of 42 patients that received oxygen had died, while 30 out of 45 patients that did not receive oxygen therapy had died. The Nocturnal Oxygen Therapy Trial (NOTT) on 203 patients with chronic obstructive pulmonary disease with hypoxemia who randomly received oxygen therapy for 24 hours even though they actually received an average of 19 hours of oxygen therapy daily, while the reminder of the group received 12 hours of oxygen therapy. Evaluation at 26 months demonstrated that a lower mortality rate in the group receiving 24 hours of oxygen therapy daily. According to the two studies above, we can see that there is an increase in the survival rate of patients receiving long term oxygen therapy, which need to be evaluated in 2 months to determine whether the patient continues to suffer from hypoxemia. Studies demonstrate that over 40% of patients receiving long-term oxygen therapy undergo improvements within a month.

Influence on Pulmonary Vessels

Administration of oxygen can improve the pulmonary blood circulation and reduce cardiac workload. In 16 patients with chronic obstructive pulmonary disease that underwent right heart catheterization and suffered from hypoxemia for the previous 41 months, not long after and 31 months after receiving oxygen therapy, patients that did not receive oxygen therapy demonstrated an average increase in pulmonary arterial pressure of 1.47 ± 2.3 mmHg, while patients that received oxygen therapy went through an average reduction in pulmonary arterial pressure of 2.15 ± 4.4 mmHg. The study by NOTT concluded that oxygen administration for 6 months produces a significant improvement on pulmonary arterial pressure, peripheral blood vessel pressure and cardiac volume during resting as well as during activity, as well as prevent alveolar hypoxia.

Improved Rresting Capacity

Reduced ventilation is a factor that reduces the circulation of patients with obstructive respiratory disease during activity. Administration of oxygen can improve the patient's ability to walk, and increase the patient's strength in the treadmill test as well as cycle ergometer test in patients with hypoxemia who suffer from oxygen de-saturation during activity. Oxygen administration increases oxygen supply and utilization by muscles during activity. Oxygen administration also reduces ventilation/minute, respiratory frequency, and improves the function of respiratory muscles during activity by stimulating respiratory muscles and increasing diaphragmatic capacity to support the effort of the respiratory muscles. Oxygen administration also reduces the feeling of breathlessness and increases strength, which directly reduces the activity of respiratory chemoreceptors.

Influence on Respiratory System Activity

As mentioned above, oxygen administration could reduce ventilation/minute, even though the mechanism is still unclear. A beneficial effect of oxygen treatment towards ventilation and respiratory system activity is to reduce the feeling of breathlessness in patients with mild hypoxemia.

Influence on The Neuropsychological System

Hypoxemia (PaO_2 45-60 mmHg) could cause reduced consciousness, a disturbance in brain function and memory in young adults. Such hypoxemia may reduce the neuropsychological manifestations in patients with chronic obstructive pulmonary disease. The study by NOTT on the neuropsychological findings in 203 patients with an average PaO_2 of 51 mmHg, and the Canadian

Intermittent Positive Pressure Breathing Trial on 100 patients with an average PaO_2 of 66 mmHg both demonstrated increased neuropsychological disturbance with reduced PaO_2.

The incidence of such disturbance is approximately 27% in patients with a PaO_2 of less than 50 mmHg. The NOTT study also demonstrated a difference in alertness, motor reflex, and grip strength, but does not have any influence on emotional status and quality of life.

Complications of Oxygen Therapy[4,5,14]

One of the risks of oxygen treatment is oxygen intoxication. Intoxication may occur if oxygen is administered at an FiO_2 of over 50% continuously for 1-2 day. Another risk is CO_2 gas retention and atelectasis. The exact level and duration of oxygen treatment that causes toxicity is often hard to determine. Toxicity is also determined by patient tolerance, effective dose, and duration of exposure. From the three factors above, patient tolerance is most difficult to determine.

Factors that Determine Oxygen Toxicity[14]

Factors that increase toxicity	Factors that decrease toxicity
Corticosteroid	Intermittent exposure
Hypercapnia	Hypothermia
Hyperthermia	Anti-oxydant
Epinephrine	Chlorpromazine
Thyroid hormone	Anesthesia
X-ray	Sodium bicarbonate
Insulin	Reserpine
Athropine	Immaturity

The free radical theory of oxygen toxicity is already widely accepted, and it is said that the partial generation rate increase in oxygen products is accountable for toxicity. An increase in certain oxygen products, including superoxyde anions(O_2^-), hydrogen peroxyde (H_2O_2), and radical hydroxide (HO) could disturb normal cell metabolism through the lipid peroxydase process. Cell damage and death are also suspectedly caused by a loss of membrane integrity.[15]

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SYMPTOMS OF OXYGEN TOXICITY [4,5,14]

Oxygen intoxication does not manifest clinically within the first 24 hours of 100% O2 exposure at a pressure of 1 atm, but this does not mean that there will not be toxicity at cellular levels.

There are three phases of oxygen intoxication:

Initial Phase

The first clinical symptom is cough due to tracheobronchitis, starting with mild tracheal irritation at the carina. Afterwards, the cough becomes uncontrollable and there is severe pain during inspiration. The patient then has short and heavy breaths. Migratory chest pain is a dominant symptom. Such condition is always accompanied with a reduction of vital capacity. It takes several days to return the vital capacity to its original level. The cause of such vital capacity is unknown, but it is not associated with pain or alveolar lung edema. The above symptoms occur in subjects exposed to 1 atm of O_2 for 30-74 hours. Difficulty breathing does not occur, even after over 60 hours of exposure.

Advanced Phase

The advanced phase of O_2 intoxication influences the alveolar-capillary gas exchange. In patients without a history of lung disease, toxic O_2 is reported to occur after 4 days of 91% O_2 exposure. During this advanced phase, chest x-rays would demonstrate diffuse, bilateral infiltrates without cardiomegaly, accompanied by the production of purulent, white, or reddish sputum. Chest pain is not a common complaint, perhaps because patients are generally intubated and have difficulty communicating. Alveolar atelectasis occurs with various frequencies and is associated with absolute FiO_2 levels. The higher the FiO_2, the higher the rate of atelectasis.

Terminal Phase

In the terminal phase, there is progressive consolidation of the lungs and lung fibrosis. Generalized radioopacity can be seen in the chest x-ray, and gas exchange can no longer take place, and the patient finally dies.

The best way to prevent oxygen toxicity is by administering oxygen at a minimum concentration.

CONCLUSION

1. The aim of oxygen therapy is to administer oxygen at the minimum concentration required to achieve adequate tissue oxygenation.
2. The indication of oxygen therapy in lung disease is acute and chronic respiratory failure due to chronic obstructive pulmonary disease, hypoxia due to lung

infiltrate, cardiopulmonary edema, primary pulmonary hypertension, and interstitial pneumonitis.

3. Studies demonstrate that long term oxygen therapy in chronic obstructive pulmonary disease can reduce mortality, increase activity and quality of life, reduce the frequency of hospitalization, and reduce pulmonary arterial pressure.
4. As with drugs, oxygen should be administered at certain doses to achieve efficacy and reduce toxicity.

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