Review Article

Oxygen Therapy: Important Considerations

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INTRODUCTION

Oxygen therapy is one of the most critical consideration in the management of diseases crossing different medical and surgical specialities. But this is one subject which remains poorly understood and inadequately practiced. Invariably, enormous errors are committed in the use of oxygen.[1-3] Oxygen prescription often comprises of a single written word — oxygen. Frequently, it is administered merely on verbal orders. Reports on assessment of uses and misuses of oxygen are almost universal including those from the developed countries of the West.[4-6] We have ourselves found gross inadequacies in oxygen-prescription on analysis of over a hundred indoor files and treatment charts.[7] A comprehensive overview of the subject is, therefore, important to rationalise treatment and achieve the maximum benefits.[7]

Oxygen is an atmospheric gas essential for survival of all living things. The presence of an "air" vital for survival of humans was recognised in the ancient Greek as well as in Vedic Hindu literature more than 2000 years ago.[8,9] But it was only in the eighteenth century that the gas was isolated by Joseph Priestley and its importance in respiratory physiology was described by Antoine Lavoisier.[10] Rapid developments took place in the subsequent years. The problems of oxygen deficiency as well as the need and indications for oxygen therapy were subsequently recognised. Soon, oxygen came to be known as a 'cure all' medicine used for conditions varying from cholera, arthritis, anaemia and syphilis to glaucoma, epilepsy, diabetes and cancers. It was around second decade of the twentieth century and later that the oxygen therapy was adopted for indications based on firm scientific foundations.[11]

INDICATIONS

Oxygen is now considered as an important drug required for the management of hypoxaemia and several other diseases characterised by hypoxic conditions. It is, therefore, used for a large number of pulmonary and non-pulmonary diseases for its definitive, supplementary or palliative role. The list of conditions keeps on expanding, especially with reference to the use of hyperbaric oxygen in acute conditions and domiciliary oxygen on long term basis for chronic respiratory diseases. The evidence in favour of several such 'new' indications is scanty and remains debatable.

HYPOXIA

Hypoxia which constitutes the most important indication for oxygen therapy, is defined as lack of oxygen at the tissue level. Hypoxaemia on the other hand, is low arterial oxygen tension (PaO_2) below the normal levels. There are numerous clinical conditions which could cause hypoxia. In clinical terms it is more useful to classify hypoxia with "hypoxaemic" and 'normoxaemic" categories based on PaO_2 levels.

Hypoxaemic Hypoxia

Oxygen deficiency results whenver the arterial blood oxygen tension is low.[12,13] The common causes of hypoxaemia include a decreased oxygen intake (such as at high altitude), hypoventilation, ventilation – perfusion (V/Q) abnormalities, right to left (R to L) shunt and diffusion defects at alveolo-capillary gas exchange levels. Most lung diseases responsible for hypoxia operate through one or more of these mechanisms. Ventilation-perfusion abnormalities, for example, are present in both obstructive and restrictive types of lung diseases which include chronic obstructive pulmonary disease (COPD), asthma and interstitial lung disease (ILD). Ventilation-perfusion mismatch and R to L shunt are also responsible for hypoxia in acute conditions such as pneumonias, pulmonary oedema and acute respiratory distress syndrome (ARDS).

Normoxaemic Hypoxia

Tissue hypoxia in the absence of low PaO_2 levels is difficult to measure quantitatively but is diagnosed from the presence of clinical features and indirect laboratory parameters. It develops when the tissue demands for oxygen are not supplied by the available oxygen stores. This could result from an inadequate supply of oxygenated blood to the tissues (circulatory

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hypoxia) when the blood flow is either decreased (*e.g.*, cardiac failure, shock, intravascular volume depletion) or it is altered in the presence of an excess of positive and expiratory pressure during mechanical ventilation, sepsis, abnormal body temperature or thyroid dysfunction.

Hypoxia will also result from failure of cellular matabolism (histotoxic hypoxia) in cases of tissue poisoning by toxic agents, endotoxaemia and septic shock, thiamine deficiency and some other systemic diseases. Anaemic hypoxia occurs due to deficiency of haemoglobin or an altered affinity of haemoglobin (Hb) to oxyen. This is seen in the presence of anaemia, haemorrhage, carbon monoxide poisoning, methaemoglobinaemia and haemoglobinopathies. Finally, hypoxia can also result when the demand for or utilisation of oxygen by the tissues is increased even though the oxygen delivery is normal or increased. This may occur during conditions of excessive stress, such as hyperpyrexia, thyrotoxicosis or other hypermetabolic situations.

Oxygen therapy is indicated during hypoxia characterised by hypoxaemia, which most often results from both acute and chronic diffuse pulmonary diseases.[14,15] On the other hand, the need of oxygen during normoxaemic hypoxia is somewhat difficult to determine and requires a careful assessment.

SHORT TERM OXYGEN THERAPY IN HOSPITALISED PATIENTS

Acute Respiratory Failure and Other Pulmonary Diseases

Presentation of acute respiratory failure is sudden in a previously healthy person while it is gradual in a patient with pre-existing chronic respiratory disease. There are signs and symptoms of hypoxaemia along with those of the underlying and / or complicating disease. The general features attributed to hypoxaemia are restlessness, palpitation, sweating, altered consciousness, headache, confusion and cyanosis. Blood pressure may initially rise, but it falls as the severity of hypoxaemia worsens. Hypercapnia accompanies hypoxaemia whenever there is hypoventilation. Diagnosis is made from the total clinical presentation of the disease and the relevant investigations. Acute respiratory failure is established by blood gas and pH determinations.

Higher concentrations of oxygen are required initially during acute respiratory failure.[16] This is achieved by higher flow rates via a face mask or a cannula. It is important to reduce the severity of hypoxaemia to prevent organ damage.Therapy is continuously monitored with gas-exchange parameters. In case hypoxaemia is not correctable, assisted ventilation may be required. It may also be stressed that correction of blood PaO_2 is not the only objective of therapy. Oxygen delivery to and its utilisation by the tissues are the major considrations.[17] Therefore, all the factors responsible for tissue delivery should be taken care of.

Acute Respiratory Distress Syndrome (ARDS)

Hypoxaemia of ARDS is not responsive to oxygen administered with cannulae or masks. It requires ventilator-controlled administration often with the use of positive end expiratory pressure (PEEP). The basic objective is to achieve a desirable PaO_2 of about 60 mmHg with the lowest possible inspired O_2 concentration (FiO_2).[16,18] In view of the high FiO_2 which is required, there is a serious risk of oxygen toxicity in these patients.[19] It is, therefore, desirable not to exceed an FiO_2 of more than 60% after the initial 24 hours. Some of the patients may need 100% FiO_2 initially. Continuation of those levels of FiO_2 beyond a few hours promotes oxygen toxicity almost invariably and proves counter productive.

Administration of PEEP of about 10 to 15 cm H_2O helps to reduce FiO_2. A higher PEEP may only increase the risk of barotrauma. Moreover, there is little evidence to suggest that a higher degree of PEEP shall help to reduce FiO_2. Therefore, a careful balance is required between FiO_2, PEEP and PaO_2.

Acute Severe Bronchial Asthma

Patients with acute severe asthma or status asthamticus have severe airway obstruction and inflammation. They are generally hypoxaemic. Arterial blood sample is immediately obtained and oxygen is started via nasal cannula or preferably via a face mask at flow rate of 4-6 L / min to achieve FiO_2 of 35 to 40 percent. Higher flow is unlikely to improve oxygenation. Flow rate is adjusted to maintain a PaO_2 of about 80 mmHg or near normal value.[20,21] Concurrent bronchial hygiene and administration of intravenous fluids, bronchodilators and corticosteroids should alleviate the problems in most of the situations. In view of the critical nature of the illness, it is advisable to start oxygen at home wherever possible. One important danger of oxygen therapy in severe airway obstruction is the precipitation of hypercapnia and narcosis resulting from CO_2 retention. This is more often seen in the presence of chronic airway obstruction due to chronic bronchitis and emphysema. It occurs rarely in severe asthma.

Administration of sedatives and tranquilisers must be avoided.[20] Sedatives may precipitate CO_2 retention not only in patients with chronic obstructive pulmonary disease (COPD), but also asthma. Assisted ventilation is required in case there is persistence of hypoxaemia and / or precipitation of hypercapnia.

Severe Pneumonias

Pneumonias can cause hypoxaemia and acute

respiratory failure, when severe and overwhelming. This is especially so in the presence of acute viral or bacterial bronchopneumonia.[22] Hyper-sensitivity and immunological insults or other organisms can also cause diffuse pulmonary involvement and acute respiratory failure. Oxygen is administered at a flow rate of 4-6 L / min with the help of nasal cannulae or face masks. It is desirable to achieve a PaO_2 of above 60 mmHg. Bronchial hygiene and treatment with antibiotics and other appropriate drugs should meanwhile continue.

Acute Exacerbations of COPD

Patients of COPD often have chronic hypoxaemia with or without CO_2 retention. An acute exacerbation of airway obstruction, mostly occurring after a respiratory tract infection causes worsening of hypoxia.[23,24] Oxygen in this situation is required until the exacerbation is settled. While a high FiO_2 of up to 100% can be initially administered in case hypoxaemia is severe, it is soon tapered to around 50-60% FiO_2. The goal of supplemental ogygen is to maintain a PaO_2 of 55-60 mmHg which corresponds to SpO_2 of about 90 percent.[25-27]

Higher concentrations of oxygen blunt the hypoxic ventilatory drive which may precipitate hypoventilation and CO_2 retention. It is not uncommon for CO_2 narcosis to occur following excessive concentrations of FiO_2. A recent study on 65 patients admitted with acute COPD exacerbations showed that a majority of patients who achieved a PaO_2 greater than and equal to 74.5 mmHg compared with those with a PaO_2 less than 74.5 mmHg had a longer hospital stay, more frequent admissions and greater use of non-invasive ventilation.[28] It is better to use a regulated flow device such as a venti mask which gurantees oxygen delivery to a reasonable extent. Once the patient is stabilised, one can shift to nasal prongs — a device which is more comfortable and acceptable to the patient.

Interstitial Lung Disease (ILD)

Patients with ILD may either present with acute respiratory failure at the time of initial presentation in case of a fulminant onset, or during the course of an established disease whenever there is an intercurrent insult such as an infection.[29] Oxygen for acute respiratory failure is administered as per guidelines laid earlier.[14] Patients with ILD may require oxygen for prolonged periods.[30] Moreover, their lungs are already stiff and compliance is low. There is an increased risk of oxygen toxicity. It is, therefore, advisable to wean oxygen to an FiO_2 of about 40% as early as possible. Hypoxaemia in chronic ILD may not be seen during resting conditions but appears even after mild exertion. Such patients are often benefited with oxygen administered before and after physical activity.

Pulmonary Thromboembolism

Hypoxaemia in the presence of pulmonary thromboembolism is common but not essential. It depends upon the amount of occluded pulmonary circulation. A major pulmonary arterial embolism may induce hypoxaemia due to associated V / Q abnormality or pulmonary oedema. Hypocapnia is common due to the presence of hyperventilation. A fall in cardiac output and pulmonary artery wedge pressure also occurs.

Oxygen is definitely required whenever there is hypoxaemia and / or breathlessness. The area of lung devoid of arterial blood due to pulmonary thrombo-embolism continues to be supplied by the alveolar oxygen. Moreover, the systemic bronchial vascular anastomoses which are present in abundance expand immediately after pulmonary arterial occlusion and help prevent infarction.[31] Oxygen administration may help by enriching both the alveolar and the anastomotic blood supply. Oxygen (100%) has a therapeutic role in the treatment of air embolism.[32] It not only improves oxygenation but also helps in absorption of air bubbles by denitrogenating blood.

Spontaneous Pneumothorax and Pneumo-mediastinum

It is rare for hypoxaemia to occur following the occurrence of spontaneous pneumothorax or pneumomediastinum in a healthy person. On the other hand, such an event shall precipitate hypoxaemia in a patient with pre-existing lung disease. Oxygen in the presence of hypoxaemia is required to improve oxygenation. It is also used to absorb air from the pleural or the mediastinal cavity on similar principles as for the treatment of air embolism.[33] Administration of 100% oxygen causes denitrofication of the pleural / mediastinal air, which is then absorbed in the circulation. Such a modality should not be tried beyond 12-16 hours to avoid oxygen toxicity.

WHEN TO STOP OXYGEN

There is no purpose of continuing oxygen after its requirement has ceased. The thought of weaning should start the moment the patient is comfortable. There are several clinical and laboratory parameters which need to be continuously assessed. Symptoms and signs of hypoxaemia and tissue hypoxia should be carefully monitored. Weaning should be initiated once the patient's underlying disease process is stabilised and bedside evaluation of respiratory rate, heart rate, blood pressure, skin colour and pulse oximetry are normal.

Weaning can be gradually attempted by either discontinuing oxygen altogether or lowering its concentration for a fixed period and re-evaluating the clinical parameters and SpO_2. An initial attempt of

withdrawal for about 30 minutes is followed by longer periods. If there is no deterioration, oxygen may be completely withdrawn. In patients with underlying chronic respiratory diseases, oxygen may be required at lower concentrations for longer periods. Prospects of long term domicilary oxygen need to be discussed with the patient after the acute need is over.

MEDICAL DISORDERS

Oxygen has been used for a variety of medical and surgical disorders for its presumptive beneficial role. Many of the non-pulmonary disorders in this category have doubtful indications for oxygen therapy. But there are several other diseases for which oxygen has a genuine role to play.

Ischaemic Heart Disease

Oxygen is administrered to patients with coronary ischaemia on the premise that there is arterial and/or tissue hypoxia which can be reverted with oxygen administration. This is a routine practice for all patients with acture myocardial infarction.[34,35] Some degree of cardiac dysfunction and pulmonary congestion is present in most patients with acute myocardial infarction, even though there is no arterial hypoxaemia. But it is better to avoid arterial puncture for obtaining blood gas sample. Injury to skeletal muscles during the puncture may cause release of enzymes which are measured to assess myocardial infarction. Oxygen administration is useful to improve cardiac muscle and tissue oxygenation and relive breathlessness.

Some people advocate the use of 100% oxygen for patients with complicated infarction, such as those with congestive heart failure or cardiogenic shock. Oxygen is administered to increase the oxygen content and delivery to the tissue.[36,37] It might also improve myocardial oxygenation and contractility. There is more definite and urgent indication in the presence of left ventricular failure with pulmonary congestion and/or oedema. Although inhalation of pure oxygen may not cause pulmonary toxicity for a few hours, it is not without complications when prolonged. Therefore, FiO_2 should always be guided by PaO_2 measurements and administration of 100% oxygen need not be prolonged.

The role of oxygen during uncomplicated episodes of angina or myocardial infarction is largely supplemental. Usually there is no demonstrable fall in arterial PaO_2. In such a situation, oxygen therapy can be useful only if the FiO_2 is high enough to cause a significant increase in the amount of oxygen dissolved in plasma. Such an FiO_2 is difficult to achieve in the ambulatory settings. Oxygen is administered to prevent or treat mild hypoxaemia. It is also debatable whether oxygen administration, when given in higher concentrations of 40% or more, reduces the extent of myocardial infarction.[38] There is some evidence to suggest that the short term use of oxygen transiently reduces the magnitude and the extent of electro-cardiogram (ECG) abnormalities. This is supported by the obsevations of experimental studies that an FiO_2 of 0.40 reduces the myocardial creatinine phosphokinase activity, amount of myocardial necrosis and infarct extension in dogs with ligated coronary arteries. The FiO_2 of 1.0 had no advantage over FiO_2 of 0.4. Even in documented myocardial infarction, the electro-physiological evidence of myocardial ischaemia could be diminished.

On the other hand, results of a double-blind clinical trial showed no clinically significant advantages in mortality or in the indices of morbidity, such as the use of analgesics, incidence of arrhythmias and systolic time intervals in the oxygen treated group. In fact, the incidence of sinus tachycardia and the levels of serum asparate amino-transferase levels in this group were higher. It is implied, therefore, that oxygen therapy in these patients should be given with caution. Although supplemental oxygen can be considered as rational and useful, the higher concentrations may be avoided.

Other Medical Disorders Characterised by Normoxaemic Hypoxia

There is a long list of disease-states where tissue hypoxia is either documented or clinically suspected, but arterial PO_2 is normal. The problem lies with either the oxygen transport or utilisation. Cerebrovascular disorders constitute another important indication for oxygen therapy. Hyperbaric oxygen (HBO) is shown to reduce cerebral oedema and intracranial tension following cerebral stroke.[39,40] Oxygen therapy started within first few hours after stroke could be used to "buy time" for the administration of thrombolytic or neuro-protective drugs.[41] Hyperbaric oxygen is the first line of treatment for gas embolism in the arterial circulation.[42]

Problems of Oxygen Transport

Oxygen is carried in haemoglobin and plasma when an adequate blood flow is maintained. Abnormalities of haemoglobin, low intravascular volume and/or inadequate blood flow can result in poor oxygen transport and tissue hypoxia. All those states are, therefore, potential indications for oxygen administration.[43, 44]

Chronic anaemias are well tolerated by most patients who do not need oxygen. Perhaps the tissues get acclimatised to the low oxygen supply. Most physicians in this country would recall patients with haemoglobins of around 5 gm% carrying on with routine activities. On the other hand, acute anaemia resulting from a massive bleeding or intravascular haemolysis is tolerated poorly. Administration of high concentration of oxygen is used as a short term measure. Adequate blood replacement is

required for a more definitive treatment. Role of oxygen for conditions associated with haemoglobin abnormalities, such as met-haemoglobinaemia or sickle cell disease, is not fully established. Oxygen is temporarily useful in acquired met-haemoglobinaemia, especially when severe. This is generally seen following toxic exposure to drugs or chemicals, such as nitrates, nitrites, sulfonamides and chlorates.

Oxygen is reported to diminish the number of sickle cells in the presence of sickle cell disease. In fact, it has been observed that the number of sickle cells in arterial blood is lower than in the venous blood and that administration of 100% oxygen reduces sickling. Therefore, oxygen has been used to treat acute sickle cell crises but the results are discouraging. In presence of pneumonias which are common in sickle cell anaemia, oxygen is administered to treat hypoxia. Hyperbaric oxygen has been tried with some success.

One important form of acquired haemoglobin abnormality, where oxygen is of definite help is carboxy haemoglobinaemia (COHb) resulting from acute carbon monoxide poisoning. Carbon monoxide poisoning is one of the absolute indications for hyperbaric oxygen therapy.[45] Affinity of carbon monoxide to haemoglobin is several times more than that of oxygen. To displace carbon monoxide, one needs to administer 100% oxygen which reduces the half-life of COHb from about 320 minutes to 60 to 80 minutes. Oxygen under hyperbaric conditions is much better as it reduces the half-life of COHb to 20 to 25 minutes.

Problems of Blood Volume and Cardiac Output

Oxygen transport and delivery to the tissues will also be inadequate whenever there are problems with either the total blood volume or the cardiovascular system. While acute blood loss may occur following an accident or a massive bleeding, plasma is lost in conditions associated with dehydration or burns. In view of a relatively small amount of oxygen carried in the dissolved form, loss of plasma shall not cause any significant change in the oxygen content of the blood. But in view of the diminished volume and hypotension, oxygen delivery is greatly impaired. Administration of oxygen is of limited value in such conditions.

Similarly, cardiovascular diseases responsible for the alteration in the heart rate, preload, after load and myocardial contractility adversely affect the oxygen supply. Such problems may arise in conditions associated with hypovolaemia, sepsis, myocardial dysfunction due to ischaemia or myocarditis and pulmonary thromboembolism. Oxygen therapy is useful as a supplement to the primary treatment of the disease. It should be administered in a higher concentration of 60 to 1000 percent for a short period of a few hours. Prolongation of such treatment is likely to cause problems of oxygen toxicity without accruing any significant benefits.

MISCELLANEOUS DISORDERS

Oxygen has been found useful is the treatment of cluster headaches.[46] It is administered at 7 to 8 L/min for about 10-15 minutes via a facemask. Significant relief is demonstrable in about 75% of patients. The effect is attributed to cerebral vasoconstriction due to oxygen administration.

Patients with terminal illnesses and advanced cancers have dyspnoea as a common problem. This could be attributed to pulmonary pathophysiological changes due to cancer, concurrent cardiopulmonary disease and general systemic manifestations. Oxygen therapy may improve breathlessness and other discomforts of cancer.[47, 78] In a recent study on 38 patients of primary or secondary lung cancer, oxygen and air were shown to ease the symptom of dyspnoea regardless of the patient's arterial oxygen saturation. It was suggested that a trial of 15-minute therapy at 4 L/min should be given to identify patients who are likely to benefit from the treatment. It was also suggested that benzodiazepines might potentiate the effect of oxygen.

SURGICAL INDICATIONS FOR OXYGEN THERAPY

Abnormalities of gas exchange in surgical patients are present in not only those with lung disease but also others, both during the surgical procedure and in the post-operative period.[49] Pulmonary complications especially infection, atelecatsis and thromboembolism are frequent in post-operative patients. This is especially so in patients who are smokers, obese, aged (over 60 years) and/or with a pre-existing lung disease. Hypoxaemia with or without CO_2 retention may occur because of the problems of ventilation-perfusion relationship and/or hypoventilation. Oxygen, along with other forms of treatment is required in all such patients with complications.

Postoperative State. Mild to moderate hypoxaemia is common in the first few hours after general anaesthesia especially when abdominal or thoracic surgery has been done. This is attributed to maldistribution of ventilation and increased physiological shunting. Central and peripheral ventilatory depression due to residual effects of anaesthetic and pain relieving drugs, shivering after anaesthesia and some degree of diffusion defect may also contribute to hypoxaemia. The effects of this hypoxaemia are likely to be serious in the presence of pre-existing risk factors or pre-operative low arterial oxygen tension. Such patients would require oxygen therapy for several hours depending upon the levels of PaO_2 and other clinical parameters. If PaO_2 measurements are not available, all such patients are given oxygen until fully awake and vital signs are normal and stable.[50,51] Most patients require only small

increases in FiO_2 administered with nasal cannulae at a flow rate of 5 to 6 L / min.

Oxygen for patients with significant cardio-pulmonary disease and after pulmonary or cardio-thoracic surgery is continued until blood gas estimations indicate that this is not required. In patients undergoing peripheral surgery, oxygen is generally not required unless complications occur.

LONG TERM DOMICILIARY OXYGEN THERPAY

Domiciliary oxygen therapy in use for over 100 years has been popularly employed in several chronic diseases.[52] There is substantial evidence in literature now to support the usefulness of long term oxygen in the overall maintenance therapy in patients having COPD. This was amply demonstrated with the help of two large and well controlled studies in these patients—the Nocturnal Oxygen Therapy Trial (NOTT) and the Medical Research Council (MRC) Working Party trial.[53,54] Results of both the trials are summarised below:

MRC Workig Party Trial[53]

A controlled trial of long term domiciliary oxygen therapy was conducted in U.K. on 87 patients who had COPD with severe arterial hypoxaemia and CO_2 retention. Patients were randomly distributed in two well-matched groups: the treatment group [oxygen (by nasal prongs) for at least 15 hours daily (flow rate of 2 L / min) was administered], and the control group [given no oxygen]. In the five-year follow-up period, mortality was less in the oxygen-treated group, although the survival-advantage became apparent only after a year and 135 days of treatment. Further, the oxygen therapy slowed down / stopped deterioration in those who survived longer. There was no evidence of any oxygen toxicity.

NOT Trial Group[54]

Six treatment centres in the USA recruited 203 patients of hypoxaemic COPD over 27 months and randomly allocated to either continuous oxygen therapy or 12-hour nocturnal oxygen therapy (NOT). Each surviving patient was followed for at least one year. Overall mortality in the nocturnal oxygen therapy group was 1.94 times than in the continuous oxygen therapy group. Continuous oxygen therapy not only benefited patients with CO_2 retention and poor lung function, but also those with low mean pulmonary artery pressure and pulmonary vascular resistance. Although continuous oxygen had shown better results, this did not mean that nocturnal oxygen alone was not useful. In fact, "some oxygen was better than none and continuous oxygen was better than nocturnal".

Benefits of Long Term Oxygen Therapy

Singificant improvements are shown in several parameters of chronic respiratory insufficiency of COPD.[55-58]

1. Duration of survival. An increase in the duration of survival was the most significant benefit seen in both the studies mentioned earlier. The same observations have been made in most of the subsequent studies and clinical experience.

2. Intellectual functions. There is significant improvement in memory, motor coordination, mood and other hypochondrial symptoms on long term oxygen therapy.

3. Pulmonary hypertension. There is a decrease in pulmonary vasoconstriction and vascular resistance. This improves the severity of right heart failure.

4. Red cell mass. Long term oxygen decreases red cell mass and haematocrit levels. Therefore, complications of polycythaemia are diminished.

Potential Benefits. There are reports on improvement of several other parameters.[55,57] Although some of these benefits are not necessarily proved with placebo-controlled studies. These include the following: *(i)* increased exercise ability; *(ii)* improved quality of life, patients resuming gainful employment and participating in their own care, more actively; *(iii)* decrease in dyspnoea; *(iv)* decrease in hospitalisation and exacerbations of respiratory failure, and *(v)* delayed development of cor-pulmonale.

There is little evidence to support oxygen supplementation during exercise training in COPD patients during pulmonary rehabilitation.[59] But evidence does support the use of oxygen supplementation for patients with severe hypoxaemia at rest or with exercise.[60]

SELECTION OF PATIENTS

All patients with chronic hypoxaemic lung disease are potential candidates for long term oxygen therapy.[57,61,62] Following guidelines are used to select patients for instituting the treatment:

1. A definitive documented diagnosis responsible for chronic hypoxaemia;
2. An optimal medical treatment should be in effect;
3. Patient in a stable condition; and
4. Oxygen administration should have been shown to improve hypoxaemia and provide clinical benefits.

It is important to ensure that the patient is compliant with the general medical regimen and follows instructions, such as to quit smoking. Continued smoking not only aggravates the disease process but also reduces the full physiological benefits of oxygen and poses inherent safety risk of accidental fires.

Following specific indices are used while prescribing long term oxygen:

1. At rest in non-recumbent position, the PaO_2 of 55

mmHg or less.

2. Patients with PaO_2 of more than 55 mmHg are considered in the following conditions:
   (a) patient on optimal medical treatment with demonstrable hypoxic organ dysfunction, such as secondary pulmonary hypertension, cor-pulmonale, polycythaemia or CNS dysfunction;
   (b) when there is a demonstrable fall in PaO_2 below 55 mmHg during sleep, associated with disturbed sleep pattern, cardiac arrhythmias or pulmonary hypertension. These patients may be benefited by nocturnal oxygen therapy; and
   (c) when there is a demonstrable fall in PaO_2 during exercise and oxygen administration is shown to improve exercise performance, duration or capacity. These patients may benefit by oxygen during exercise. They may also be administered supplemental oxygen before and after the exercise.

It is important to mention that PaO_2 (55 mmHg or less) is not the only guide to prescribe oxygen, but it is the presence of a chronic hypoxaemic pulmonary disease. Healthy people living at an altitude of 10,000 feet or more do not require oxygen. They are able to acclimatise to even severe degrees of hypoxaemia. In fact, man has survived without oxygen even at the top of Mt. Everest (altitude 29028 ft). It is a patient with a chronic pulmonary disease who loses the ability to adapt and needs long term oxygen.

OXYGEN DOSAGE

Most of the COPD patients are prescribed low flow concentrations at 1-2 L per minute. Higher flow rates are required for some of the patients, especially those with other chronic respiratory diseases. The treatment is guided by PaO_2 which should be maintained at 60 mmHg or so (SaO_2 of 85-90%). During the period of exercise, sleep or other activities, the flow rate may be increased by another 1-2 L / min. While continuous therapy is required for patients who show hypoxaemia at rest, intermittent treatment during specific periods may be used for patients who demonstrate intermittent hypoxaemia.

EQUIPMENT FOR OXYGEN THERAPY

A variety of equipment are required for oxygen administration which include the supply sources, regulatory and delivery devices, conservation and humidification system.[63-66]

Supply Sources

There are three main types of systems commercially available for supply of oxygen at home: compressed gas cylinders, liquid oxygen and oxygen concentrators.

Compressed gas cylinder. The commonly used gaseous system in the home consists of H or K cylinders containing compressed oxygen. A pressure regulator and a flow meter are required to adjust the amount delivered to the patient. When continuously used at 2 L / min, each cylinder will last about two-and-a-half days and thus, necessitating frequent fillings. They are also heavy giving an unsightly look to the bedroom. Moreover, regulation of pressure and flow require some effort and additional help. For the present, compressed gas cylinders are most commonly used for domiciliary use in India. It is because of its lower costs and relatively easy availability in even small towns compared to the other systems. Gas cylinders also form a good back-up facility in case of a failure of other systems. Portable D and E cylinders are available for ambulatory use. Aluminium cylinders are also available. These are lighter in weight than the cast iron cylinders. They are better suited for portability, but are costlier.

Liquid oxygen system (LOX). The LOX system for use at home is a smaller version of the bulk liquid system used in the hospitals. The reservoir (stationary) unit contains about 70 to 90 pounds of oxygen in the liquid state at -273 ^oF. It lasts for 4-½ to 10 days at a continuous flow rate of 2 L / min. The vessel is about 3 to 4 feet tall and about 18 inches in diameter. The internal pressure is about 22 to 50 psi which can generate flow rates of 0.25 to 15 L / min. In addition to the stationary unit, there is a light weight portable unit which can be carried by the patient on the shoulder for ambulatory and outdoor activities. The portable units are designed to be filled from the stationary reservoir unit with safety.

There is a minor loss of gaseous oxygen from the liquid gas units at a rate of about one lb per day. Therefore, the units should not be stored in small and closed space to aovid gaseous accumulation posing a fire hazard. Liquid gas system is more practical but expensive. It is not easily available in this country as yet.

Oxygen concentrator. It is an electrical device that provides oxygen from the atmospheric air. It employs a molecular "sieve" that filters out the nitrogen molecules, water vapour and other trace gases.[67] It can deliver 85% to 90% oxygen at a flow rate of upto 4 L / min. The polymeric membrane concentrators can deliver 30% to 40% oxygen at flow rates of up to 10 L / min.

A concentrator is ideal for use at home. It obviates the need of regular filling of the tank. Its initial cost is high but the running cost is negligible. Proper maintenance of the equipment and replacement of filters is required. A back-up source of oxygen supply (*e.g.*, compressed oxygen cylinder) is necessary in case of a power failure. There is generation of some noise and heat that some patients may find bothersome. This can be avoided by placing the concentrator in an

adjacent room and using a longer oxygen tube. This may increase the back pressure necessitating the use of a pressure compensated flow meter to assure accurate oxygen flow.

Delivery Devices

Devices used to deliver oxygen include canulae, prongs and masks.[68] Those are essentially the same as used in the hospitals. Nasal cannulae and prongs are preferred because of the cosmetic reasons. It is easy to conceal oxygen tubing by applying it to ordinary thick rimmed frames of eye-glasses ("Oxyspecs"). Different kinds of "oxyspecs" and other devices are now commercially available for this purpose.

There is no difference in the type of delivery devices used with different types of oxygen sources. Humidification is not essential at flow rates of less than 4 L / min unless the patient complains of dryness of the nose or mouth, nasal irritation or crusting. Humidifier is a potential source of infection and needs regular cleaning and disinfection. Disposable humidifiers significantly increase the costs. Oxygen canisters are carried by patients on their shoulders while ambulating. This is quite troublesome in those with lower residual exercise capacity. A simple walking aid consisting of a full weight canister transported using a small wheeled cost pulled by the patient is shown to be helpful.[69]

Oxygen-conserving Devices

Oxygen therapy on long term basis is a costly proposition. Many patients tend to conserve oxygen by reducing the flow as well as the duration of administration. Moreover, the standard oxygen supply devices allow the flow of oxygen, both during inspiration and expiration. In fact, it is only 15% to 20% part of respiratory cycle during inspiration which delivers the oxygen to the alveoli effectively. Therefore, a lot of oxygen delivered to the patient is wasted in the surroundings.

In recent years, several methods have been devised to conserve oxygen.[70,71] It is possible to save up to 50% oxygen with some of these methods. The three types of devices commercially available for this purpose are as follows:

1. Reservoir oxygen delivery. With this method, oxygen which is stored during exhalation in a reservoir (approx. 20 mL) becomes available at the beginning of inhalation. There are two types of reservoir cannulae in use:

(a) Pendant reservoir (Oxymizer pendant). The reservoir coupled to the nasal prongs consists of a collapsing chamber that hangs at the chest. It saves oxygen between 2:1 to 4:1 over continuous flow oxygen therapy.

(b) "Moustache configured" Oxymizer. The reservoir sits right on the face thus being noticeable and cosmetically unsightly. Its efficiency is similar to that of pendant reservoir.

Both the reservoirs provide equivalent oxygen saving at flow rates of 0.5 L / min. But the Pendant reservoir can be operated at 0.25 L / min to achieve the oxygen saturation similar to those of a flow of one litre per minute with a steady flow delivery system. The reservoirs maintain a saving of 3:1 to 4:1 over steady flow during exercise as well.

2. Electromechanical pulsing devices. The electromechanical demand devices deliver oxygen only during inhalation.[71] Delivery of oxygen during exhalation is saved. It consists of a box shaped unit attached to the outlet of the oxygen source and a solenoid valve, which opens on sensing the decrease in pressure as the patient inhales. A "pulsed" volume of 15 to 35 mL of oxygen is delivered each time. It reduces the amount of oxygen usage by 35% to 75%, producing a saving of about 7:1 compared with continuous flow system.

Electronic demand devices are also available for use with portable cylinders as well as with piped-in-oxygen system in the hospitals. Some of the demand devices available in the Western market include Pulsair, DO_2 S and Oxymatic, etc. They significantly add to the costs and produce a "clicking" sound at the bedside. Both these factors make it unacceptable to many of the patients.

3. Transtracheal catheters. It is a narrow lumen catheter which resembles an angiocatheter.[72] It is inserted directly into the trachea. Oxygen is delivered through a tubing attached to a small fitting at the neck. There are several reasons to believe that is more effective: *(i)* oxygen is delivered ahead of the nasopharynx bypassing some of the anatomical dead space, *(ii)* the upper airways serve as a reservoir towards the end of expiration, and *(iii)* the oxygen delivered is not diluted with atmospheric air prior to entering the respiratory tract.

Transtracheal catheters are useful for patients receiving very high litre flows. They save oxygen by an efficiency factor of 2:1 to 3:1. Its efficiency can be further enhanced by combining it with pulsed oxygen delivery. Intratracheal catheter is more acceptable to the patient since the look is not unsightly. There is nothing on the face and it can be easily hidden beneath the collars. Moreover, there is no nasal or auricular irritation, it does not get dislodged during sleep.

There is a small risk of infection and subcutaneous emphysema when the catheter is introduced. It can get plugged with mucus and thick secretions. Therefore, it should be cleaned on daily basis. Some of the transtracheal catheters available commercially are the Heimlich Microtrach, the SCOOP catheter and the intratracheal oxygen catheter (ITOC). The ITOC is implanted through a subcutaneous tunnel from the chest wall to the trachea. It is of more permanent nature. Patients with transtracheal catheters should have conventional cannuale at home for use in an emergency,

when the transtracheal catheter gets blocked due to kinking or plugging.

Risks of Long Term Oxygen Therapy

There are three types of risks associated with long term use of oxygen: physical, functional and cytotoxic.[73] The risks are higher particularly with high FiO_2 of over 50 percent.[74]

Physical risks. Since oxygen supports combustion, the oxygen tanks are potential risks of fire hazard and tank explosion. In fact, these risks are rather small. It is highly desirable that smoking is stopped with its use. The supply source (such as a cylinder) should not be kept in a small closed room to avoid accumulation of the vented gas. The other minor risks of oxygen therapy include the injury to the nose and face from catheters and masks. Dryness and crusting may occur from dry, non-humidified gas. In a recent case report, a patient who used a nasal cannula for oxygen supplementation suffered deep second-degree burns to his nose and left leg while his mobile phone served as the heat source to ignite fire.[75]

Functional risks. Oxygen therapy may accentuate hypoventilation in patients with COPD.[76] This may include hypercapnia an carbon dioxide narcosis. Pre-hospital hyperoxia from excessive oxygen administration in COPD patients is shown to be dangerous.[77] In practice, with low flow oxygen therapy, the risk is rather small. Therefore, chronic carbon dioxide retention is not considered a contraindication for long term oxygen therapy. It has been suggested that arterial pH is a better guide to monitor therapy than $PaCO_2$. Patients with carbon dioxide retention also tolerate and benefit from long term oxygen as long as the pH dose not show acidaemia.

Cytotoxic damage. Oxygen administration can cause structural damage to the lungs.[78,79] Both proliferative and fibrotic changes of oxygen toxicity have been shown at autopsy on COPD patients treated with long term oxygen. But there is no significant effect of these changes on clinical course or survival of these patients. Most of the structural damage attributable to hyperoxia results from high FiO_2 administration in acute conditions.[79] Oxygen administration in newborns is particularly fraught with grave risks.[80,81] It is responsible for complications such as retrolental fibrosis and bronchopulmonary dysplasia.

In India, some of the important problems stated by most of the patients relate to difficulties of procurement and costs. There are limited sources of supply. Moreover, the medical expertise and advice to supervise domiciliary treatment is lacking. Patients' resources to afford the treatment are also scanty. There are no clear guidelines available regarding reimbursement of costs on oxygen and the apparatus — a facility available to government and several other private / public sector employees for other treatments. One does expect that most of the difficulties shall resolve in due course of time.

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