Guidelines in the Management of Chronic Obstructive Pulmonary Disease

A Consensus Statement of the Ministry of Health of Malaysia, Academy of Medicine of Malaysia and Malaysian Thoracic Society

Introduction

Chronic obstructive pulmonary disease (COPD) is a common cause of illness in the community associated mainly with cigarette smoking. It is a progressive disease with considerable morbidity and mortality. Management of many patients remains suboptimal because of underdiagnosis and inappropriate treatment. Early detection and appropriate intervention can minimise the progression of COPD and a comprehensive management plan benefits all patients, including those with severe disease.

Several COPD management guidelines already exist, for example those by the American Thoracic Society[1], European Thoracic Society[2] and British Thoracic Society[3], but they do not take into account local conditions such as our health care system and sociocultural factors. The Malaysian Thoracic Society initiated efforts to produce COPD management guidelines in 1997 and the following document is aimed at improving overall management of COPD in Malaysia.

This report is not intended to be construed or to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as knowledge and technology advance and patterns evolve. The ultimate judgement regarding a particular clinical procedure and treatment must be made by the doctor in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

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Definitions

Chronic obstructive pulmonary disease is a condition characterised by persistent airflow obstruction, which is slowly progressive. It may be partially reversible and there may be features of airway hyperreactivity. Traditionally, it comprises chronic bronchitis and emphysema.

Chronic bronchitis is defined by the presence of increased bronchial secretions with chronic cough and expectoration on most days for at least 3 months a year in two consecutive years[1].

Emphysema is defined anatomically by permanent destructive enlargement of airspaces distal to the terminal bronchioles without obvious fibrosis[2].

Majority of patients show features of both conditions.

Epidemiology

According to the Ministry of Health annual reports from 1990 - 1995, respiratory diseases rank as the most common cause of medical consultations and the fourth leading cause of hospital admission[4]. There is

insufficient morbidity and mortality statistics for Malaysia but the incidence is probably rising. Data from the United States shows an increased prevalence of 41.5% since 1982[1]. Mortality rate has risen by nearly 32.9% between 1979 and 1991[1]. COPD is more common in men than in women, and it increases steeply with age. Exacerbations and respiratory failure in COPD may result in prolonged hospital stay and costly treatment. Undeniably, it leads to severe disability and reduced quality of life resulting in loss of productivity with substantial economic impact.

Risk Factors

Recognised risk factors are:

a) Cigarette smoking. It is the single most important cause of COPD. The greater the consumption the higher is the risk. Fig. 1 illustrates the decrease in the FEV_1 in a susceptible smoker compared to a lifelong non-smoker or a non-susceptible smoker. Smoking cessation at any age can reduce the rate of decline of lung function.

b) Passive smoking
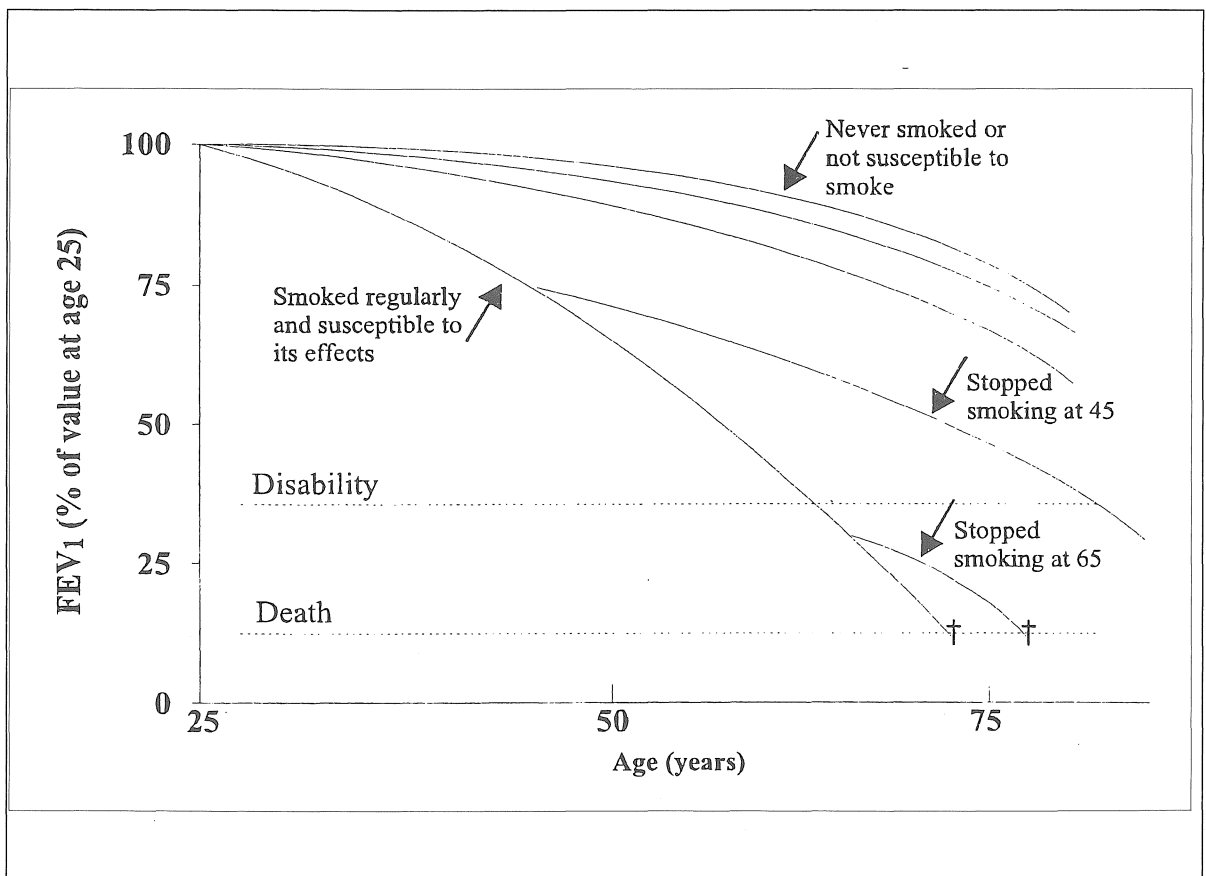
Fig. 1: The risks of developing COPD for smokers: the differences between the lines illustrate the effects that smoking, and stopping smoking, can have on the FEV_1. † = death, the underlying cause of which is irreversible chronic lung disease, whether the immediate cause of death is respiratory failure, pneumonia, cor pulmonale or aggravation of other heart disease by respiratory insufficiency. (Adopted from Fletcher and Peto)[5]

c) Air pollution especially SO_2 and particulates

d) Poverty and low socioeconomic status

e) Viral infection leading to airway hyperresponsiveness

f) Occupational exposure e.g. cadmium and silica

g) Genetic factor e.g. Alpha1 - antitrypsin deficiency

Prognosis

Factors associated with reduced survival are:

a) FEV_1 less than 1L

b) PO_2 less than 60mmHg (8kPa)

c) PCO_2 greater than 46mmHg (6.1kPa)

d) ECG or clinical evidence of cor pulmonale

e) FVC less than 2.5L

f) Continued smoking

Pathology

a) Chronic Bronchitis

Hyperplasia of the secretory cells and mucous gland enlargement are the histological hallmarks of chronic bronchitis, and these are the tissue correlates of increased sputum production[6]. These changes are due to repeated irritation by pollutants and infections. Airway wall inflammation, stenosis and distortion due to fibrosis may also be present[1,7]. The small bronchi and bronchioles are the main sites of the increased resistance to airflow.

b) Emphysema

Two main forms of emphysema are described. Centriacinar emphysema is characterised by focal destruction restricted to respiratory bronchioles and the central portion of an acinus, surrounded by relatively normal lung. Panacinar emphysema involves destruction of all the air spaces supplied by the terminal bronchiole. The current view is that emphysema occurs as a result of an imbalance between proteases and anti-proteases resulting in a relative increase in proteases and resultant destruction of lung tissue.

Clinical Consequences

COPD is often diagnosed late due to the paucity of symptoms in the early stages of the disease. At presentation patients are usually more than 40 years old and have functional evidence of moderate or severe airflow limitation. Chronic productive cough is often present. Dyspnea develops gradually as the years go by resulting in decreased effort tolerance. In moderate disease, patients may have prolonged expiration or wheezing. Later hyperinflation occurs with the characteristic increase in the anteroposterior diameter of the chest. In advanced disease features of respiratory failure and cor pulmonale appear.

Assessment

Spirometry is essential to diagnose and assess the severity of COPD. Airflow limitation can be demonstrated by a ratio of FEV_1 to FVC of less than 70%. The FEV_1 as a percentage of predicted values is more useful in the later stages of the disease. Mild COPD is characterised by a FEV_1 of more than 70% of the predicted value and severe COPD a FEV_1 of less than 50%.

Reversibility of airflow obstruction can be demonstrated either by a bronchodilator challenge or a trial of corticosteroids for two weeks with spirometry before and after. A positive spirometric response to bronchodilators or corticosteroids is considered to be present when the FEV_1 increases by 200ml and 15% of the baseline value.

Chest radiography may show features of hyperinflation, bullae, vascular attenuation, large pulmonary arteries and cardiomegaly. It also helps to exclude other causes of the symptoms.

More complex investigations are not normally indicated except in difficult cases.

Arterial blood gases is recommended for those patients with severe COPD and those in acute exacerbations.

Aims of COPD Management

The aims of management of COPD are to:

a) improve symptoms and quality of life

b) reduce the progressive decline in lung function

c) prevent and treat complications

d) prolong survival

e) reduce the number of exacerbations and need for hospital admissions

Management strategies include:
a) patient education
b) drug therapy
c) non-pharmacological treatment.

Patient education

The patient should be educated about:
a) the nature of the disease and its cause(s). Smoking cessation should be emphasised as an essential first step in preventing further damage to the lung. Even patients with advanced airflow obstruction show improved survival rates following smoking cessation[8]. Strategies to help patients quit their smoking habit include positive reinforcement, group support and nicotine replacement therapy.
b) its prognosis. The patient should be informed that although the disease is usually progressive and largely irreversible, symptoms can be improved and further deterioration may be preventable.
c) proper use of medications with emphasis on the use of inhaled medications.
d) non-pharmacological treatment: its modalities, indications and complications.
e) when to seek medical advice

Drug therapy

A major component of the management of COPD is pharmacological therapy. The inhaled route where applicable, is strongly recommended for delivery of drugs to the lungs. The recognised advantages of inhaled therapy include direct delivery to the site of action, rapid onset of action, small doses needed to achieve a therapeutic response, and fewer systemic side effects. A spacer device should be used for patients who are unable to coordinate inhalation with the activation of a metered-dose aerosol. Alternatively, dry powder inhalers or breath-actuated inhalers should be used.

Bronchodilators

Bronchodilator drugs are the mainstay of pharmacological therapy. These drugs relax bronchial smooth muscles and relieve bronchospasm and improve symptoms.

The three main groups of bronchodilators for use in COPD are:

i. anticholinergics
ii. beta$_2$ agonists
iii. methylxanthines

Anticholinergics

Onset of bronchodilation is relatively slower compared to beta$_2$ agonist. Significant bronchodilatation occurs within 30 minutes of inhalation and the maximum effect occurs 1.5 to 2 hours after inhalation. The duration of clinically significant bronchodilation is as long as 4 to 6 hours. Because quaternary anticholinergic agents are poorly absorbed into the circulation, they are virtually free of systemic side effects. Ipratropium bromide has been shown to be either equivalent to or more potent than beta$_2$ agonist as a bronchodilator in COPD[9,10]. Unlike beta$_2$ agonists, the efficacy of anticholinergics is maintained despite years of regular, continuous therapy because tachyphylaxis does not develop despite its prolonged usage. The recommended dose of 2 puffs (or 40mcg) of ipratropium bromide three to four times a day may be increased for patients with severe airflow limitation. Ipratropium bromide should be taken regularly rather than on a when-needed basis because of its relatively slow onset of action[11].

Example: ipratropium bromide (Atrovent)

Beta$_2$ agonists

Beta$_2$ agonists produce bronchodilation more rapidly than anticholinergic agents, acting within 15 minutes of administration with effects lasting 4 to 5 hours. They are useful as on-demand medications at times of acute dyspnoea. The main side-effects are tremor and palpitation. Since the number of beta$_2$ receptors decreases with age, the dose of a beta$_2$ agonist may have to be increased in older patients in order to achieve maximal bronchodilatation at the cost of increased side effects[12,13].

Examples:
inhaled beta$_2$ agonists : salbutamol (Ventolin, Respolin, Salamol, Buventol)
terbutaline (Bricanyl)
fenoterol (Berotec)
salmeterol (Serevent)
-long acting
formoterol (Foradil)
-long acting

oral long acting beta₂
agonists   : salbutamol (Volmax)
                       terbutaline (Bricanyl durules)
                       bambuterol (Bambec)
oral short acting beta₂
agonists   : salbutamol
                       terbutaline

At times of acute exacerbation and for patients with chronic severe airflow obstruction, these drugs should be administered using nebulisers. Alternatively, large volume spacers can be used to deliver larger doses of the drugs from metered dose inhalers. A combination of ipratropium bromide and a beta₂ agonist provides the combined rapid onset of action of the beta₂ agonist and the prolonged duration of action of ipratropium.

Examples: fenoterol combined with ipratropium bromide (Berodual MDI, Duovent nebuliser solution)
salbutamol combined with ipratropium bromide (Combivent MDI)

Methylxanthines

These drugs have comparable or less bronchodilator effect than anticholinergic agents or beta₂ agonists[14,15]. They are available in oral and parenteral preparations. They have a narrow therapeutic window and interactions with other drugs are common. Cimetidine, mexiletine, quinolones, allopurinol, macrolides, nifedipine, tetracycline, aluminium hydroxide, magnesium hydroxide and thiobendazole are known to increase the level of theophylline whereas phenytoin, rifampicin, phenobarbitone, carbamazepine, aminoglutethimide and isoproterenol may reduce it. Hepatic insufficiency, heart failure, cor pulmonale and viral pneumonia may also increase the blood theophylline level whilst cigarette smoking causes the opposite. Sustained release preparations taken at bedtime are useful for relieving nocturnal symptoms[11]. Some patients derive subjective benefit from theophylline which cannot be achieved with other bronchodilators. Theophylline has been shown to prevent respiratory muscle fatigue and to increase contractility of the fatigued diaphragm in the laboratory, but the clinical importance of these observations is not clear[16,17]. Other non-bronchodilatory

effects of theophylline include improved mucociliary transport and increased hypoxic respiratory drive. Blood levels of theophylline should be monitored when indicated such as when toxicity is suspected or when there is lack of response. Long acting preparations are preferred. Side effects of methylxanthines include gastric irritation, nausea, diarrhea, headache, tremor, irritability, sleep disturbance, convulsion and cardiac arrhythmia.

Examples: oral sustained release preparations: Neulin SR, Theodur, Euphylline, Theo-24 intravenous preparation: aminophylline

Corticosteroids

These are anti-inflammatory drugs. Although corticosteroids are of undoubted benefit in asthma, their role in COPD has yet to be established[18]. Corticosteroids can be administered orally, by inhalation or intravenously. Corticosteroids may be beneficial during acute exacerbations[19].

During an exacerbation-free period, a trial of prednisolone, 30 - 40mg/day for 2 weeks, may be used to test reversibility of the airflow obstruction. About 10% of patients with stable COPD will show an improvement in FEV_1[20]. Once maximum improvement with oral prednisolone has been attained, high dose inhaled steroid therapy (e.g. at least 800mcg/day of beclomethasone dipropionate or budesonide) is commenced and prednisolone is tapered off. However, not all responders to prednisolone show a similar response to inhaled corticosteroids[21]. If high dose inhaled steroids for example, 2000mcg a day of beclomethasone or budesonide are not effective, prednisolone may be continued at the lowest effective dose.

Two local side-effects of inhaled corticosteroids, oral candidiasis and hoarseness, can be minimised by using large-volume spacers and by rinsing the mouth.

Examples of inhaled corticosteroids:
beclomethasone dipropionate (Becotide, Becloforte, Beclomet, Respocort, Aldecin)
budesonide (Pulmicort, Inflammide)
fluticasone (Flixotide)

Antibiotics

The airways of patients with COPD are colonised with *Streptococcus pneumoniae, Haemophilus influenzae* and *Moraxella catarrhalis* which are also frequently isolated from sputum during exacerbations[22,23]. Infections, frequently viral in etiology, are one of the most common precipitating factors of acute exacerbations of COPD. The sputum is usually purulent during an acute exacerbation but the chest radiograph seldom shows an infiltrate. Evidence of infection includes fever, leucocytosis, increased sputum volume and new lung infiltrates on chest radiograph. Sputum culture helps to determine appropriate antibiotic therapy but pathogens are difficult to identify during acute exacerbations. Therefore, treatment is often empirical with broad spectrum antibiotics such as tetracycline/doxycycline, ampicillin/amoxycillin, erythromycin, co-trimoxazole and cefaclor[24,25]. Second line antibiotics including second generation cephalosporins, ampicillin/sulbactam, amoxycillin/clavulanic acid, newer macrolides, and quinolones should be used if there is concern about beta-lactamase producing organisms or when there is failure to respond to first line antibiotics.

Others

The usefulness of mucolytic agents is unproven. Objective evidence of benefit is lacking[26] and widespread use of these agents cannot be recommended routinely based on the present evidence. Excessive mucus secretion is probably best controlled by avoiding inhaled irritants from cigarette smoke and exposure to environmental pollutants. Cough suppressants are undesirable for long-term therapy.

Stepwise Approach to Pharmacological Therapy for Stable COPD

The treatment strategies have to be tailored according to the patient's needs.

Step 1
Patients with mild to moderate continuing symptoms:

Ipratropium bromide MDI aerosol, 2 - 6 puffs (i.e. 40 -120mcg) every 6 - 8h
with or without
beta$_2$ agonist MDI aerosol 2 - 4 puffs (i.e. 200 - 400mcg) up to four times daily.

The use of a combination of ipratropium bromide and a beta$_2$ agonist in the same metered dose inhaler may help simplify therapy and improve compliance.

Step 2
If response to step 1 is unsatisfactory,

Add sustained release theophylline 400 - 600mg daily

N.B. While conclusive evidence for the use of sustained release beta$_2$ agonists or long acting inhaled beta$_2$ agonists is lacking, they may be tried in individual patients.

Step 3
If control of symptoms at Step 2 is suboptimal

Consider a trial of a course of prednisolone 30 - 40mg/day for 2 weeks
If improvement occurs:
taper prednisolone off
use high dose inhaled corticosteroids (≥800mcg/day)
if not effective, continue prednisolone at low daily or alternate day dose (e.g. 7.5mg)

If no improvement:
stop oral steroid
consider regular nebulised bronchodilators, combining anticholinergic and beta$_2$ agonist

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Acute Exacerbations

Assessment of acute exacerbation

History :	Previous performance status when stable
	Duration and progression of current symptoms
	Decrease in effort tolerance
	Sputum characteristics and volume
	Previous and concomitant medications
Examination :	Temperature
	Respiratory rate
	Pulse rate and blood pressure
	Wheezing
	Cyanosis
	Use of accessory muscles
	Evidence of cor pulmonale
	Evidence of pneumonia
	Conscious level
	Evidence of co-morbid conditions, e.g. myocardial infarction, uncontrolled diabetes, carcinoma of the lung, pneumothorax, cardiac failure and tuberculosis
Laboratory measurements :	PEFR (<100L/min)
	FEV1 (<1L)
	Pulse oximetry SO_2 (<90%)
	PaO_2 (<8kPa, 60mmHg)
	$PaCO_2$ (>6kPa, 45mmHg)
	ECG
	Chest radiograph
	White cell count
	Sputum culture and sensitivity
	Blood glucose and electrolytes
	Theophylline levels when indicated
	(Values in brackets indicative of a severe attack)

Management of acute exacerbation

a) Oxygen therapy

Oxygen should be given to increase the arterial oxygen saturation (SO_2) to more than 90% and arterial oxygen tension (PO_2) to more than 8.0 kPa (60mmHg) with care not to depress pH to less than 7.25 and / or elevate PCO_2 to more than 8.0 kPa (60mmHg). Oxygen may be administered via masks beginning at 24% (or nasal prongs at 2 litres a minute) and the concentration may be increased to achieve desired levels with regular monitoring of blood gases. For further information, refer to page 402.

b) Bronchodilators

Inhaled beta$_2$ agonists and anti cholinergics given by nebuliser or metered dose inhalers with spacers should be administered. Beta$_2$ agonists may be repeated every 30 minutes if necessary. If there is poor response, beta$_2$ agonists may be administered parenterally eg. salbutamol or terbutaline 3 - 20mcg per minute.

Ipratropium is given by either nebuliser (0.5mg every 4 - 8 hours) or metered dose inhaler (6 - 8 puffs every 3 - 4 hours).

Combination therapy with both beta$_2$ agonists and anticholinergics may have additional synergistic effects and there is no evidence of increased side effects with the combination.

c) Methylxanthines

Methylxanthines are continued or added if the bronchodilators above are ineffective. For initiation of intravenous therapy in patients not previously receiving methylxanthines, the recommended loading dose of aminophylline is 6mg per kg. The maintenance dose of intravenous therapy is 0.5mg/kg per hour and the levels should be maintained at 8 to 12mcg/ml.

d) Corticosteroids

Corticosteroids may be useful but they should be tailed down as soon as possible. Evidence supporting the use of oral or intravenous steroids in acute COPD exacerbations is however limited. Initial dosages are 30 - 40mg per day of prednisolone or 100 - 200mg of intravenous hydrocortisone 6 - 8 hourly.

e) Antibiotics

Purulent sputum is usually an indication for empirical antibiotics as previously described.

Indications for the use of antibiotics include increased sputum volume, purulent sputum and worsening dyspnoea.

Oxygen Therapy

In COPD, the prevention and correction of hypoxaemia is of utmost priority. Long term oxygen therapy improves organ function, reverses secondary polycythemia, alleviates right heart failure, improves quality of life and prolongs survival. Two large studies have shown survival advantage of oxygen therapy in stable, hypoxic COPD patients[27,28]. In the British Medical Research Council (MRC) study patients who received 15 hours of oxygen per day had better survival than those who did not receive oxygen. In the National Heart, Lung and Blood Institute's Nocturnal Oxygen Therapy Trial (NOTT), patients receiving continuous oxygen therapy (average 19 hours/day) had less mortality than those on 12 hours/day. The mechanism for improved survival is not fully understood; however, lowering pulmonary artery pressure with oxygen may reduce cardiac work and relate to improved tissue oxygenation.

Indications:
There are three settings where oxygen therapy is indicated:
a) long term oxygen therapy
b) exercise
c) acute exacerbation.

Long term oxygen therapy (LTOT)

LTOT is indicated when either of the following is present under stable condition:

a) PO_2 is less than 55mmHg or SO_2 is less than 88%. or
b) When PO_2 is between 55 - 59mmHg or SO_2 is more than 89% with the presence of cor pulmonale. Cor pulmonale is defined as ECG changes of p pulmonale, haematocrit of more than 55% and signs of right heart failure.

Systems:
Oxygen may be supplied from a cylinder in the form of compressed gas or liquid or from oxygen concentrator. Compressed oxygen gas from cylinder and concentrator are more commonly used. While the initial cost for cylinder is low (about RM900), the long term cost is

Table I
Comparison of Oxygen Systems

Type	Gas	Liquid	Concentrator
Availability	Common	Limited	Common
Reliability	Good	Possible inaccurate setting, freezing of connector	Good, needs regular service
Cost	Moderate	High	Low
Refill	Needed	Needed	Not needed
Power	None	None	Needed
Ambulatory use	Yes	Yes	No

high (about RM3,000 per year) and requires frequent refilling of the cylinder (twice per week). Oxygen concentrator on the other hand costs around RM7,000 and the only other cost is electrical charges of about RM2 a day and a periodic change of filter and servicing.

Small cylinders for ambulatory use and as emergency back-up are recommended for all patients to be used in addition to large cylinders or concentrators. Table I summarises the advantages and disadvantages of various oxygen systems.

Delivery Methods:
a) Continuous flow dual-prong nasal cannula. This is the most commonly used delivery method. It is cheap, simple and comfortable to wear.
b) Oxygen conserving devices. This conserves up to 7 times of oxygen and are particularly useful when used with oxygen cylinder. Oxygen delivery is regulated by a sensor which delivers oxygen during early inspiration.
c) Transtracheal oxygen. Although cosmetically attractive, this method is more invasive and not generally popular among patients.

A tube of up to 50 metres may be used for oxygen delivery from its source which allows mobility within house and sometimes around the house.

Each litre per minute of oxygen flow delivers 3 - 4% of oxygen above atmospheric air (21% oxygen) - Table II.

Humidification:
Humidification is not necessary when oxygen is delivered via nasal cannula but necessary when delivered via transtracheal route.

Assessment:
Prior to initiating LTOT, at least 2 arterial blood gases (ABG) must be studied at 3 weeks apart when patients are in stable condition. If changes fulfil the criteria for LTOT on both occasions as stated earlier, patients may be treated with LTOT.

Settings:
The concentration of oxygen to be given to a patient should be assessed with pulse oximeter or ABG. The aim is to achieve a PO_2 of $\geq$60mmHg (8kPa) or SO_2 >90%. Because of the shape of oxyhaemoglobin dissociation curve, further increases of oxygen above 60mmHg add little benefit but may increase the risk of carbon dioxide retention. An increase of 1L/min is often required during sleep and exercise.

Reassessment:
The adequacy of treatment must be assessed from time to time, preferably every 1 to 3 months. This should be done

Table II
Relationship Between Nasal Cannula Flow Setting and FiO₂

Nasal Cannula Flow L/min	FiO₂ (%)
1	24
2	28
3	32
4	35

when the patient is clinically stable and receiving adequate medical treatment. If the patient is clinically well and does not fulfil the criteria for LTOT, oxygen therapy may be discontinued. If the concentration of oxygen prescribed does not correct the oxygenation to a satisfactory level, an increase in oxygen concentration may be necessary. With the exception of a few, most patients would need to continue LTOT for the rest of their lives[29,30].

Oxygen therapy during exercise

Patients with COPD are encouraged to remain active. Many patients who are hypoxaemic at rest deteriorates during exercise whilst others may only be hypoxaemic during exercise. The aim of oxygen therapy during exercise is to relieve dyspnoea and improve exercise tolerance.

Baseline ABG and/or SO_2 should be taken before and repeated during exercise while adjusting the oxygen level to maintain SO_2 above 90%. Pulse oximetry is more advantageous for this purpose as it allows continuous monitoring and is noninvasive. Patients should be evaluated using the same oxygen system that they are expected to use at home. As a rough estimate, patients require 1L/min more oxygen during exercise than at rest.

Oxygen therapy during acute exacerbation

Aim:
The aim of oxygen therapy during acute exacerbation is to correct or prevent life-threatening hypoxaemia (maintain PO_2 >60mmHg/8kPa or SO_2 >90%).

Delivery Methods:
a) Dual-prong nasal cannula
   This is inexpensive and generally well accepted by patients. The FiO_2 is affected by the geometry of the nose, mouth breathing, ventilating rate, tidal volume and oxygen flow rate. This is a delivery method of choice for low FiO_2 (<35%) as high FiO_2 will require higher flow setting which causes discomfort to the nasal mucosa. Refer to Table II for flow setting.

b) Venturi mask (Ventimask)
   Venturi mask maintains a fixed ratio of oxygen to room air, thus maintaining a constant FiO_2. It reduces the risk of CO_2 retention. FiO_2 of 24 - 50% can be achieved. This is preferred to a simple face mask.

c) Simple face mask
   FiO_2 of 35 - 55% can be achieved with a flow of 6 - 10L/min when used with simple face mask. Oxygen flow of higher than 5L/min is recommended to wash out CO_2 and prevent CO_2 retention. The face mask is less comfortable and affects communication and feeding.

d) Non-rebreathing mask with reservoir and one way valve (High Flow Mask)
   FiO_2 of 90% can be delivered through non-rebreathing mask with reservoir provided the mask is tightly sealed on the face. The risk of CO_2 retention is greater since high FiO_2 is delivered.

Choice and Setting:
The choice of delivery method and the setting of flow of oxygen depend on the condition of the patient and patient's tolerance to the delivered FiO_2. ABG should be assessed before and while on oxygen therapy to determine the adequacy of treatment and preventing unacceptable CO_2 retention. Pulse oximetry may be used but when CO_2 retention is suspected, ABG must be performed. Oxygen setting is aimed at maintaining or achieving a PO_2 >60mmHg (8kPa) or SO_2 >90%. If CO_2 retention occurs, the decision to alter the setting will depend on the pH. If pH is normal and SO_2 is >90%, the high CO_2 may be acceptable indicating chronic CO_2 retention which is well compensated. If CO_2 retention is associated with acidaemia (pH <7.25), a change in flow setting or treating with venturi mask or mechanical ventilation may be needed. Table III summarises the recommended therapeutic decision to be taken based on the patient's ABG results. It must be remembered when titrating the supplemental oxygen, it can take up to 20 to 30min to achieve a steady state after a change in FiO_2. Therefore, ABG sampling at shorter interval can be misleading.

Non-pharmacological Treatment

Assisted ventilation

Some patients treated in the ICU may show deterioration despite aggressive pharmacological and controlled oxygen therapies. These patients will require some forms of ventilatory support during this phase of acute on chronic respiratory failure. They usually exhibit fatigue and deteriorating mental status as a result of worsening acidosis and hypoxaemia.

Table III
Adjustment of Oxygen Settings Based on Arterial Blood Gases (Adapted from Carter)[31]

PO$_2$ (mmHg)	PCO$_2$	pH	Therapeutic Decision
>60	Normal	Normal	No change in O$_2$ flow
>60	Mild rise	Normal	No change, monitor ABG
>60	High	Normal	No change, monitor ABG
>60	High	Low	Venturi Mask, if unsuccessful mechanical ventilation
<60	No rise	Normal	Raise O$_2$, monitor ABG
<60	Mild rise	Normal	Raise O$_2$, monitor ABG
<60	High	Low	Venturi Mask/Mechanical ventilation

The decision to institute or withhold ventilatory support will depend on several considerations outlined in the table below[3]:

Factors to encourage use of assisted ventilation

* A demonstrable remedial reason for current decline - e.g radiographic evidence of pneumonia or drug overdosage.
* The first episode of respiratory failure.
* An acceptable quality of life or habitual level of activity.

Factors likely to discourage use of assisted ventilation

* Previously documented severe COPD that has been fully assessed and found to be unresponsive to relevant therapy.
* A poor quality of life - e.g being housebound, in spite of maximal appropriate therapy.
* Severe co-morbidities - e.g pulmonary oedema or neoplasia.

N.B. Neither age alone nor the PCO$_2$ are a good guide to the outcome of assisted ventilation in hypercapnic respiratory failure due to COPD. A pH of >7.26 is a better predictor of survival during the acute episode[32].

Ventilatory support can be instituted invasively via an endotracheal tube or by non-invasive IPPV via facial masks (NIPPV).

IPPV via endotracheal intubation remains the preferred and most widely used method in most centres treating acute exacerbation of COPD. It also provides a route for bronchial suctioning in patients with copious secretion.

NIPPV is only available in some hospitals with specialist facilities and staff support. It is highly labour intensive and its success depends heavily on the patient's mental alertness, tolerance of the appliances, haemodynamic stability and capability to clear secretions. Comparative studies of NIPPV with intubation and mechanical ventilation have not demonstrated an improved clinical outcome in terms of patient survival.

The duration of ventilation and hence the timing of weaning remains a contentious issue. It is rarely justifiable to prolong ventilation beyond 14 days. Those who fail weaning should be considered for tracheostomy.

Pulmonary rehabilitation

Pulmonary rehabilitation is a multidimensional continuum of services directed to persons with pulmonary disease and their families, usually by an interdisciplinary team of specialists, with the goal of achieving and maintaining the individual's maximum level of independence and functioning in the community[33].

The programme should be developed with the primary aim of increasing exercise tolerance and improving the quality of life of COPD patients, who are often physically

deconditioned by disabling dyspnoea. However, there are no prospective randomised controlled studies that provide conclusive evidence of survival benefits.

Patients who should be referred to a pulmonary rehabilitation programme are those on optimal medical therapy and who continue to:
a) have severe respiratory symptoms
b) have several emergency room visits per year
c) exhibit limited functional status
d) have impaired quality of life

Such programmes are usually provided on an outpatient basis; the frequency and duration vary in different programmes. Team members would include physicians, dieticians, respiratory therapists and psychologists.

Patients must be highly motivated, non smokers and must undergo stress testing to exclude silent cardiac disease. Education of the patient and his family is an important component, in order to ensure compliance and behaviour change.

The components of a comprehensive rehabilitation programme are:
a) Exercise training
i) Lower extremity exercises. Example, walking and cycling, on average 3 - 5 times perweek.
   This can improve quality of life and reduce dyspnoea.
ii) Upper extremity training
   Can improve dyspnoea by decreasing the metabolic and ventilatory requirements for arm exercise. This can in turn improve dyspnoea following simple activities such as lifting objects or combing the hair.
iii) Inspiratory muscle training
   May improve ventilatory muscle function and/or alleviation of symptoms for some patients. However, it is not clear whether it can be recommended for routine use.

b) Psychosocial support
Many patients experience anxiety and depression; also, they may have problems in acquiring and retaining new information, forming new concepts and performing complex perceptual-motor manoeuvers.

Careful assessment of psychological status is required and pharmacological intervention may be needed in some patients.

c) Breathing retraining
The aim is to relieve and control breathlessness. Techniques include diaphragmatic and pursed lips breathing to improve ventilatory pattern and improve synchrony of abdominal and thoracic muscles.

Surgery

Patients with COPD may be considered for surgical management of extrapulmonary diseases or pulmonary diseases which may or may not be related to COPD.

Pre-operative evaluation

The principal consultant managing the patient with COPD must assess carefully the risk benefit ratio of surgical management. This depends on the indication for the surgery, the site of surgery (thoracic/abdominal/non thoracoabdominal), the experience of the surgical team, type of anaesthesia and the severity of COPD. Patients with mild COPD have similar operative risk as the general population.

Multidisciplinary consultations must be encouraged prior to surgery. Whenever possible, thorough assessment is performed well before surgery so that patient's condition can be optimised. These include cessation of smoking, bronchodilator therapy, steroid therapy (whenever appropriate), chest physiotherapy and if indicated, antibiotics.

Pre-operative assessment includes:
a) thorough history
b) physical examination
c) chest radiograph
d) spirometry
e) arterial blood gases
f) cardiovascular screening (at least ECG and if necessary echocardiography)

Patients who have a FEV_1 of more than 50% predicted, and normal arterial blood gases would normally have minimal risk for non-thoracic surgery.

Non-thoracic surgeries

The further the surgery from the chest or diaphragm the lesser the risk of complication related to COPD. Ophthalmic, orthopaedic and ENT surgeries are generally safe and have no COPD related complications.

Urological, gynaecological and colorectal procedures for patients with FEV_1 ≥50% predicted should be performed under local or epidural anaesthesia whenever possible. Patients should preferably be observed in ICU post-operatively.

Upper abdominal surgery is associated with an increased risk of post-operative pulmonary complications and mortality[34,35,36]. The risks are particularly high in patients who are obese, still smoking, elderly and those with concomitant heart disease. Whenever possible laparoscopic procedure should be considered. ICU care is advisable for all patients during the post operative period.

Thoracic surgeries

a) Thoracic surgery for diseases unrelated to COPD
Lung nodule/mass may need to be removed surgically in patients with COPD. The risk of post operative respiratory insufficiency or death is higher in patients undergoing a pneumonectomy with a pre-operative $FEV_1 < 2L$ or ≤50% predicted, or a carbon monoxide diffusion of <60% predicted. Pneumonectomy may reduce lung function by 50%, lobectomy by 20% and segmentectomy by 10%. Post-operative FEV_1 of less than 40% - 50% predicted normal is associated with higher morbidity and mortality. Pre-operative assessment should include spirometry and blood gases, and if possible quantitative lung scintigraphy, carbon monoxide diffusing capacity (DLCO) and exercise testing.

b) Thoracic surgery related to COPD
Resection of large bullae compressing normal lung tissue may improve lung function and symptoms. The difficulty is to distinguish compressive bullae from non compressive emphysema. CT thorax may help to differentiate between these two conditions. Resection of bullae occupying more than one-third of hemithorax produces the best results.

Lung volume reduction surgery, whereby part of the lung (the most emphysematous area) is removed has shown some promising results[37]. However, more data is needed especially regarding the selection of patients and the safety of such procedures.

Lung transplantation, single or double improves quality of life and survival for patients with advanced COPD. This is reserved for younger patients with no chronic broncho-pulmonary infection. However, lack of donor organs and cost factor limit this form of treatment to very few patients.

Lung transplantation for the management of COPD is currently not performed in Malaysia but it is hoped that this will be available in the future.

Conclusion

Since tobacco smoking is the main cause of COPD, all patients who smoke should be encouraged to stop in order to prevent progressive decline in lung function. The main goals of COPD management are to improve symptoms and quality of life, to reduce airflow limitation, to prevent and treat complications and to prevent death due to complications. Outpatient treatment should be administered using a stepwise approach depending on the severity of disease. Inhaled anticholinergic treatment offers the greatest bronchodilator benefit with fewest side effects. This therapy may be supplemented by an inhaled $beta_2$ agonist or sustained release theophylline preparation for added bronchodilator effect. About 10% of patients with stable COPD will show an objective response to a trial of oral steroid therapy, and for these patients inhaled corticosteroids or oral steroids at the lowest effective dose may be added. Antibiotics are only used during acute exacerbations. Patients with limitation of activity despite optimal medical therapy may benefit from a pulmonary rehabilitation programme. Correction of hypoxaemia is a priority and long-term oxygen therapy prolongs survival in chronically hypoxaemic COPD patients. In a few carefully selected patients, surgery in the form of lung volume reduction surgery or bullectomy may be of benefit.

Acknowledgement

CONSENSUS STATEMENT

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