Shortness of breath

Is it chronic obstructive pulmonary disease?

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BACKGROUND Of all the major diseases, chronic obstructive pulmonary disease (COPD) is the one for which the burden is increasing the fastest.

OBJECTIVE This article discusses the diagnoses and assessment of COPD, and provides management guidelines including smoking cessation, bronchodilator therapy, the use of inhaled corticosteroids, combination therapies, oxygen therapy, and rehabilitation.

DISCUSSION Diagnosis is by clinical suspicion in patients with an appropriate clinical history and airflow obstruction is confirmed using spirometry. Although smoking cessation and oxygen in selected individuals are the only interventions known to alter the natural history of COPD, many other treatments can significantly lessen breathlessness, reduce exacerbations, and improve exercise and quality of life.

A diagnosis of chronic obstructive pulmonary disease (COPD) should be considered in both men and women who have a risk factor (generally smoking) and who present with chronic respiratory symptoms of exertional breathlessness, chronic cough, regular sputum production, frequent winter 'bronchitis' or wheeze. The breathlessness in this situation is often mistakenly attributed to lack of fitness or the aging process. It is important to diagnose COPD as treatments can significantly improve symptoms and quality of life as well as potentially lengthening life years.

Definitions

The *Global initiative for chronic obstructive lung disease guidelines* (GOLD) define COPD as 'a disease state characterised by airflow limitation that is not fully reversible'.[1] The airflow obstruction is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases. Components of COPD that may co-exist include chronic bronchitis, emphysema, small airways disease (obstructive bronchiolitis), and chronic asthma with only partial reversibility.

Smoking is the major risk factor for developing COPD, contributing about 85% of the risk. Other exogenous irritants implicated causally in the development of chronic bronchitis include exposures to a range of respirable particulates and gases.

Diagnosing and assessing COPD

The presence of airflow obstruction is central to the diagnosis of COPD.

Spirometry

Spirometry is the only accurate method of measuring airflow obstruction in patients with COPD, and peak expiratory flow measurements are less useful than in asthma. The *Australian and New Zealand guidelines for management of COPD* (the COPD-X plan) emphasise the importance of obtaining spirometric measurements in all patients where COPD is suspected in order to determine both the presence and severity of COPD.[2] Although the place of spirometry as a screening test in all individuals who smoke is controversial and not of proven benefit, targeted spirometry in a symptomatic individual is fundamental to making a diagnosis of COPD. Besides COPD, the differential diagnoses of cough, sputum and shortness of breath include asthma, nonobstructive pulmonary diseases, and cardiac disease.

Although COPD is defined by the absence of significant reversibility, currently available drugs may induce significant improvements in FEV1 over time. Therefore, bronchodilator reversibility cannot serve as an absolute diagnostic criterion for separating COPD from asthma. On the other

hand, documentation of complete reversibility is useful in excluding COPD, and documentation of significant bronchodilator reversibility (a rise in FEV1 >400 mL) may identify those who are more likely to respond to therapy.

Assessing stages

Stages of COPD include:

- mild (postbronchodilator FEV1 <80%)
- moderate (FEV1 60–80% predicted), and
- severe (FEV1 <50% of predicted).

Interestingly, although FEV1 measures the severity of airflow obstruction and is the test most closely associated with mortality in COPD, it correlates poorly with symptoms (degree of shortness of breath and disability). Other features that may contribute to both the level of breathlessness and patient wellbeing include comorbidities such as cardiac disease, anxiety or depression, and lowered activity levels associated with deconditioning and therefore more noticeable exertional shortness of breath. Tests that may correlate better with symptoms include inspiratory capacity and other measures of lung hyperinflation. However, these tests are not widely used in practice. Investigators are developing scoring systems based upon multiple measures rather than simply the FEV1 as a more practical approach to classifying COPD and its effect on the individual. Recommendations for inclusion criteria include dyspnoea score, body mass index, arterial oxygen tension and assessment of exercise capacity.[3]

For those in whom airflow obstruction is already present, documentation of the severity of the impairment is important:

- to maximise the likelihood of smoking cessation if moderate or severe airflow obstruction is identified
- to document the presence of reversibility (defining an asthma component which may warrant more aggressive treatment)
- in order to monitor progress, and
- for prognostic reasons.

Management of stable COPD

The goals of COPD treatment are to control symptoms, prevent exacerbations, and to improve lung function and health status. The only treatments for COPD which have been shown to alter mortality are:

- smoking cessation
- oxygen therapy in patients with significant resting daytime hypoxaemia, and
- noninvasive ventilation for management of acute exacerbations with accompanying ventilatory failure.

Other treatment modalities are primarily used with the aim of improving quality of life.

The COPD-X evidence based guidelines are adapted from the recently published GOLD guidelines for COPD management:[1]

- **C** – confirm diagnosis (through clinical assessment and spirometry)
- **O** – optimise function, through optimal drug therapy, smoking cessation and pulmonary rehabilitation
- **P** – prevent deterioration, through maintenance of smoking cessation, regular review and vaccinations
- **D** – develop a self management plan for use in stable COPD, and
- **X** – manage exacerbations.

Smoking cessation

Smoking is the most important risk factor for developing COPD and smoking cessation is the only effective means of slowing the accelerated decline in FEV1. The COPD-X guidelines emphasise the importance of smoking cessation using supportive therapy as well as pharmacological aids such as nicotine replacement therapy and bupropion, which have both been shown to improve quitting success rates. In a Polish study of patients offered smoking cessation therapy after spirometric testing, patients identified as having moderate to severe COPD were more likely to have successfully quit at 12 months after the intervention than those with normal lung function or only mild airflow obstruction.[4] Unless contraindicated, bupropion or nicotine replacement therapy combined with an appropriate support program should be used to optimise quit rates.

Bronchodilator therapy

In symptomatic patients with moderate and severe COPD, useful improvements in dyspnoea, quality of life, and functional exercise capacity can be achieved with bronchodilators. For patients who continue to experience symptoms despite the use of short acting drugs, long acting inhaled bronchodilators (anticholinergics such as tiotropium and/or long acting beta agonists [LABA] such as salmeterol or formoterol) may be used to control symptoms, improve exercise capacity and quality of life, and may also reduce exacerbations.[5] There are conflicting data as to whether combination long acting bronchodilator therapy (anticholinergic plus LABA) has significant benefits over either component alone, although the addition of formoterol to tiotropium produced substantially greater improvements in lung function than tiotropium alone.

Inhaled corticosteroids

The role of inhaled corticosteroids in the management

of COPD is contentious. Despite their anti-inflammatory effects in asthma they have not been found to be disease modifying in COPD. Nonetheless, for patients with moderate or severe COPD who suffer more than two exacerbations per year, inhaled corticosteroids may reduce the frequency of exacerbations and improve health status (through mechanisms not yet completely understood). In the absence of a test to predict potential corticosteroid responders from nonresponders, it has been recommended that all patients with COPD of moderate severity receive a trial of inhaled corticosteroids for 3–6 months, with continuation if there is objective benefit. The response may be assessed using spirometry, levels of dyspnoea, measures of exercise capacity and quality of life, frequency of exacerbations, or a combination of these. Some systemic absorption may occur, so the modest benefits of inhaled glucocorticoids must always be weighed against the potential risks of oropharyngeal and oesophageal candidiasis, easy bruising, cataract formation and possible contribution to osteoporosis.

Combination therapy

There are some data to suggest that combination therapy with long acting beta agonists plus inhaled corticosteroids provides greater symptomatic benefits than either component alone, but a recent Cochrane review suggests more data are needed.[6] Current studies are underway assessing the long term effects of various combination therapies. There are not as yet any published studies comparing the combination of a long acting anticholinergic agent with a combination inhaler of LABA plus inhaled corticosteroid. If patients have benefited clinically from a LABA in combination with tiotropium and are subject to frequent exacerbations, it would seem appropriate to use combination therapy to simplify the regimen and because of the known effect of moderately high dose inhaled corticosteroids in reducing exacerbation frequency. Potential benefits must, once again, be weighed against the known side effects.

Other drugs

Older drugs such as the oral bronchodilator theophylline and mucolytic agents may have a role in selected patients. A Cochrane review of mucolytic therapy showed improvements in symptoms and some reduction in exacerbation rates compared with placebo,[7] but criteria for predicting a response have not been established. Theophyllines are rarely used because of their narrow therapeutic index and potential for significant side effects, although some patients with disabling breathlessness may derive benefit from their use. Newer agents such as selective phosphodiesterase-4 inhibitors show promise of modest benefit in reducing exacerbations and improving health related quality of life.

Pulmonary rehabilitation

For patients with persisting shortness of breath and impaired exercise capacity despite pharmacological therapy, multidisciplinary pulmonary rehabilitation programs of 7–8 weeks duration improve both exercise capacity and quality of life (level A evidence).[8] Added benefits may include reduced hospital presentations and admissions, although the data are not as robust in this area. Ideally all symptomatic patients with COPD should be referred for pulmonary rehabilitation. Unfortunately, currently fewer than 2% of Australian COPD patients have access to such programs. If they are not available in the patient's area, a simple home based exercise program may be of benefit. A 'Pulmonary rehabilitation toolkit' is soon to be released by the Australian Lung Foundation and should provide a useful user friendly manual to assist interested health professionals in setting up and running a pulmonary rehabilitation program.

Oxygen therapy

Supplemental oxygen may be appropriate therapy for patients who are hypoxaemic at rest (PO2 <55 mmHg or 55–59 mmHg with evidence of end organ effects of the hypoxaemia). It is generally delivered via a concentrator and has been shown to prolong life in those with hypoxaemic COPD. If patients do not perceive a symptomatic improvement from oxygen in this situation, they may be reluctant to use it for the prescribed period (at least 16 hours per day) which is known to maximise mortality benefit. When prescribing oxygen in this circumstance, it is important for patients to understand the aim of treatment is improved longevity.

The role of oxygen for use during exertion or nocturnally for those who do not fulfil the abovementioned criteria is unclear. Although studies have demonstrated improvements in exercise capacity and oxygenation with oxygen therapy during acute exertion in the testing laboratory, there has only been one trial suggesting that modest benefits in quality of life can be observed in the longer term through the use of portable oxygen therapy in patients not fulfilling criteria for long term continuous oxygen therapy but who desaturated acutely with exertion.[9] The recently revised Thoracic Society of Australia and New Zealand position statement on 'Adult domiciliary oxygen therapy'[10] recommends that evidence of desaturation with exertion and of benefit with supplemental

oxygen should be documented before portable oxygen is provided for such patients.

There is a lack of uniformity of provision of portable oxygen across the states in Australia, no doubt because the evidence for benefit is unclear. Further research is required in this area. Nocturnal oxygen may be used to relieve demonstrated sleep desaturation to SpO2 ≤88% (PaO2 <55 mmHg) in the presence of hypoxia related sequelae such as pulmonary hypertension or cor pulmonale, or when such desaturations occur for more than one-third of the night. An absence of data supporting a mortality benefit and conflicting data as to any improvements in pulmonary haemodynamics with this treatment means this recommendation is consensus based (level D evidence).

Treatment of exacerbations

Many patients with COPD do not suffer frequent exacerbations while others are beset by frequent flare-ups. Recent studies confirm that increasing numbers of exacerbations impact adversely on lung function, and lung function decline is more rapid in those who have frequent exacerbations.[11] Anything that can be done to prevent exacerbations should be beneficial in the short and long term for these patients.

The frequency of exacerbations should be reduced by appropriate use of inhaled corticosteroids and bronchodilators, and vaccinations (influenza, pneumococcus). The impact of exacerbations may be minimised by giving self management advice on how to recognise and respond promptly to a change in symptoms; by starting appropriate treatment with oral corticosteroids and/or antibiotics; and by providing adequate support. If patients require hospitalisation and are hypercapnoeic, noninvasive ventilation is now the gold standard for management leading to reduced lengths of stay, less requirement for intensive care and invasive ventilation, and reduced mortality. Pulmonary outreach nursing for 'frequent flyers' has recently been shown in a New Zealand study[12] to impact favourably upon hospital admissions for COPD, although more randomised controlled studies are needed in this area.

Resource

Further information including a checklist for COPD is available through the Australian Lung Foundation website at: www.lungnet.com.au

Conflict of interest: the author has spoken at several drug company sponsored meetings in Australia (GlaxoSmithKline, Astra Zeneca, Boehringer Ingelheim/Pfizer).

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