Chronic obstructive pulmonary disease (COPD) is a disease state characterised by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases.1 It is a common disease worldwide with a significant morbidity and incurs heavy utilisation of health care resources. In Hong Kong, COPD was the 5th leading cause of death, and accounted for at least 4% of all public hospital acute admissions in 2003. The prevalence of COPD among elderly Chinese (age ≥70 years) living in Hong Kong is estimated to be 9%.2

Acute exacerbation of COPD (AECOPD) is characterised by a sustained worsening of symptoms from stable condition that is acute in onset and this worsening of symptoms is beyond the day to day variation of symptoms as experienced by the patients. The symptoms usually include increased breathlessness, sputum purulence or increased sputum volume and in some patients, these are accompanied by other problems such as increasing cough, wheeze, chest tightness or fatigue.3 AECOPD is defined by some authorities using strict criteria with at least two of the following major symptoms (including increased dyspnoea, increased sputum purulence, increased sputum volume), or one major and one minor symptom (nasal discharge/congestion, wheeze, sore throat, cough) for at least two consecutive days.4,5 However, the severity of exacerbations can be extremely heterogeneous, ranging from mild increase in symptoms to serious and severe respiratory failure.

Infectious agents are recognised as a major pathogenic factor in AECOPD. Other contributing factors for exacerbations include air pollution6, low temperature, and interruption of regular treatment. A 1-year prospective study from 2004 to 2005 in Hong Kong has shown a positive sputum culture rate of 32.3% in patients admitted to hospital with AECOPD.7 Haemophilus influenzae was the commonest organism identified in sputum culture (13.0%), followed by Pseudomonas aeruginosa (6.0 %) and Streptococcus pneumoniae (5.5%). A positive viral culture from nasopharyngeal aspirate specimen was noted in 9.7% of our patients, with influenza A, respiratory syncytial virus and influenza B being the commonest viral pathogens.7 In contrast, previous studies using polymerase chain reaction technique in examining respiratory specimens have found rhinovirus as the commonest viral pathogen.8 The role of bacteria in causing AECOPD has been controversial as the same organisms may be isolated in some patients at clinical stability.3 Evidence to support the causative role of bacteria in AECOPD includes the identification of a new strain of bacteria using the technique of cell lysate polyacrylamide-gel electrophoresis.9 The benefits to patients seen in trials of antibiotics for AECOPD also support bacteria as an important trigger for the exacerbations.10

Patients with mild acute exacerbations can be managed as out-patients, but more severe cases require hospitalisation. The major components in managing AECOPD include the use of short acting inhaled beta-2 adrenergic agonist, anti-cholinergic bronchodilator, systemic corticosteroid and antibiotic.1 In some patients, controlled oxygen therapy and/or non-invasive positive pressure ventilation (NPPV) may be beneficial. More severe exacerbations may require invasive mechanical ventilation.

Bronchodilators provide relief of lung hyperinflation, with improvement of shortness of breath, chest tightness and wheeze. The advantage of using inhaled short acting beta-2 adrenergic agonists for AECOPD is its fast onset of bronchodilatation. Anticholinergic bronchodilator is often used in combination with beta adrenergic agonists to produce bronchodilatation in excess of that achieved by either agent alone. Meta-analyses have shown no difference in the efficacy of delivering the bronchodilator therapy via a nebuliser over inhalation via a spacer device for patients with AECOPD.11 There is currently no strong evidence to support the use of long acting bronchodilators in the treatment of exacerbations. The role of aminophylline in the treatment of AECOPD remains controversial. Recent studies have suggested that low dose theophylline (at plasma concentrations below 10 mg/l) has some anti-inflammatory effect on the COPD airway.12,13 The proposed mechanism of its inflammatory effect includes reversal of steroid resistance of the airway by restoring the activity of histone deacetylase to normal levels. However, meta-analysis has failed to confirm the benefits in terms of improvement of lung function and symptoms of patients with AECOPD treated with aminophylline.14 In addition, there was a significant increase in adverse events such as nausea and vomiting in the aminophylline-treated patients.14

Systemic (oral or intravenous) glucocorticosteroid therapy is recommended for treating AECOPD as it significantly reduces treatment failure and need for additional medical treatment.15,16 Use of systemic corticosteroid for patients hospitalised for AECOPD...
accelerates the rate of lung function improvement and improves the sensation of dyspnoea over the first 72 hours of treatment although its use is associated with an increased rate of drug related adverse reactions.16 The Global Initiative for Chronic Obstructive Lung disease (GOLD) guideline recommends a 10–14 day course of 30–40 mg/day of oral prednisolone for treatment of AECOPD.1

Patients experiencing AECOPD with clinical signs of airway infection (e.g., increased sputum volume and change of colour of sputum, and/or fever) may benefit from antibiotic treatment.1 The choice of antibiotic should reflect the local patterns of antibiotic sensitivity to Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis. In Hong Kong, beta-lactamase activity was noted in 10.1% and 54.5% of the admissions with positive sputum culture for Haemophilus influenzae and Moraxalla catarrhalis respectively. At least intermediate resistance to penicillin was noted in 69.0% of hospital admissions with sputum that grew Streptococcus pneumoniae.7 The Hong Kong Interhospital Multi-disciplinary Programme on Antimicrobial Chemotherapy (IMPACT) guideline in 2003 has recommended oral/intravenous amoxicillin-clavulanate or ampicillin/sulbactam as the anti-microbial therapy for patients with AECOPD.17 Alternative antibiotics include cefotaxime or a new anti-Gram positive fluroquinolone. A recent Cochrane review has also supported the use of antibiotic therapy for patients who are moderately or severely ill with AECOPD with increased cough and sputum purulence, as antibiotic treatment is associated with reduction in mortality, treatment failure and sputum purulence.10

Controlled oxygen therapy is needed for hypoxic patients. In patients with decompensated hypercapnic respiratory failure, the use of NPPV can decrease mortality and need for intubation. In addition, NPPV use has led to a reduction in treatment failure, and a more rapid improvement within the first hour in both respiratory rate and pH in blood gas measurement. Furthermore, the hospital length of stay and complications associated with treatment for AECOPD are both reduced in the NPPV treatment group compared to medical treatment alone.18 The use of central respiratory stimulants such as doxapram for treatment of respiratory failure has gone out of favour since the introduction of NPPV. The use of doxapram is commonly associated with side effects, particularly agitation. NPPV is much more effective in correcting respiratory failure than doxapram.19 In addition, NPPV use is associated with much less side effects when compared with doxapram use.19

Recurrent AECOPD is associated with harmful health effects and poor outcome. Local data have shown that COPD patients have an average 2.2±1.8 episodes of re-admissions to hospital for AECOPD within one year.20 For those patients whose COPD exacerbations were severe enough to warrant application of NPPV respiratory support, the 1 year mortality rate was 49.1%.21 Previous studies have shown that pulmonary function and quality of life are adversely affected by frequent exacerbations, particularly in active smokers.1,2

As recurrent episodes of AECOPD have such harmful health effects, it is important to prevent exacerbations and the possible strategies include smoking cessation, pulmonary rehabilitation, use of long acting bronchodilators, use of inhaled corticosteroid and influenza vaccination. There is some evidence that the use of long acting bronchodilator such as tiotropium may lengthen the time of first COPD exacerbation and reduce health care utilisation for exacerbations.23 In the Inhaled Steroids in Obstructive Lung Disease in Europe (ISOLDE) trial, the use of the inhaled corticosteroid fluticasone propionate in patients with moderate to severe COPD was associated with fewer exacerbations and a slower decline in health status when compared to patients on placebo.24 Withdrawal of inhaled steroid from stable COPD patients was associated with increased rates of exacerbations and hospital admissions.25, 26 In a major randomized placebo-controlled study in 50 centers, N-acetylcysteine was shown to be ineffective in preventing deterioration in lung function during an acute exacerbation of exacerbations in patients with COPD.27 There is currently some evidence to support the role of pulmonary rehabilitation post acute exacerbations in reducing the risk of readmissions to hospital and mortality,28 but more data from randomized controlled trials are needed. In addition, there is suggestion that integrated care programme may help decreasing exacerbations of COPD in certain European countries.29 The integrated intervention consists of an individually tailored care plan upon discharge shared with the primary care team, and accessibility to a specialized nurse case manager through a web-based call centre. Whether a similar type of integrated care model is suitable for COPD patients in Hong Kong needs further investigation. Influenza vaccination has been shown to be effective in the prevention of influenza-related acute respiratory illness in COPD patients30 and the GOLD guideline recommends annual influenza vaccination for all COPD patients.1

In summary, AECOPD causes harmful health effects on the patients and imposes a considerable burden on the health care system. Prompt treatment of acute exacerbations and prevention strategies to avoid recurrent exacerbations among COPD patients are needed to improve their health status and reduce utilisation of health care resources.

References


