Acute exacerbations of chronic obstructive pulmonary disease: treatment and prevention

Terence Seemungal
Jadwiga A Wedzicha

Abstract
An acute exacerbation of chronic obstructive pulmonary disease (COPD) is sustained worsening of dyspnoea and sputum production in patients with COPD. They may be managed in the community with oral steroids and antibiotics but hospital referral is required where there is doubt about the diagnosis or if there are features of severity such as confusion, respiratory distress or haemodynamic instability. Regular review is required as failure to improve should prompt consideration of another diagnosis. In the emergency department, nebulized β₂-agonists and anticholinergic bronchodilators should be given and arterial blood gases assessed. Patients with an arterial pH of 7.35 or less should be assessed for non-invasive ventilation. Patients who are stable and are not in type 2 respiratory failure should be considered for discharge if there is adequate home support. Warded patients should be discharged if they are stable for 24 hours and if both patient and doctor are confident that they can manage at home with outpatient follow-up at 4 to 6 weeks. About 25% of COPD patients may not have recovered to baseline lung function at this time.

Keywords acute exacerbations; antibiotics; chronic obstructive pulmonary disease; nebulizer; oral steroids; respiratory distress

Exacerbations of chronic obstructive pulmonary disease (COPD) are an important cause of morbidity and mortality in the condition, and their incidence increases with its severity. Some patients suffer frequent exacerbations leading to hospital admission, with considerable impact on their quality of life and activities of daily living. COPD exacerbations are associated with physiological deterioration and increased airway inflammatory changes caused by factors such as viruses, bacteria and, possibly, common pollutants. Current evidence suggests that appropriate management and prevention of exacerbations may modify the long-term course of COPD.

Aetiology
Table 1 lists the common microbial agents associated with exacerbations of COPD. Respiratory viruses have been shown to cause prolonged exacerbations and are associated with increased lower airway inflammation. There is evidence that chronic infection or prolonged carriage after acute infection may occur with adenovirus and respiratory syncytial virus.

The role of bacteria is complex. The common bacteria identified in COPD are:
- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Moraxella catarrhalis*

In severe COPD, gram-negative organisms are also of importance, especially *Pseudomonas aeruginosa*. Patients with bacteria in their sputum are more likely to suffer exacerbations and experience prolonged recovery and greater severity. Many studies have shown no change in bacterial species during exacerbations, though changes may be seen in the bacterial strains obtained from patients.

Diagnosis and differential diagnosis
COPD has four principal symptoms:
- dyspnoea
- cough
- sputum volume
- sputum purulence.

The diagnosis of an acute exacerbation is based on an acute sustained deterioration in sputum purulence and increased volume, and dyspnoea.¹² These may be associated with symptoms of an upper respiratory tract infection (cold or sore throat).

The differential diagnosis includes:
- pneumonia
- pulmonary embolism
- pneumothorax
- pleural effusion
- cardiac disease (congestive cardiac failure, arrhythmias)

### Micro-organisms associated with COPD exacerbations

<table>
<thead>
<tr>
<th>Viruses</th>
<th>Bacteria</th>
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<tbody>
<tr>
<td>Rhinovirus</td>
<td>Non-typable <em>Haemophilus influenzae</em></td>
</tr>
<tr>
<td>Coronavirus</td>
<td><em>Streptococcus pneumoniae</em></td>
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<tr>
<td>Respiratory syncytial virus</td>
<td><em>Moraxella catarrhalis</em></td>
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<tr>
<td>Influenza virus</td>
<td><em>Pseudomonas</em></td>
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<tr>
<td>Parainfluenza virus</td>
<td><em>Staphylococcus aureus</em></td>
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Table 1
• rib fracture
• inappropriate use of sedatives.

The chest radiograph is not required for the diagnosis of a COPD exacerbation but it is useful in the establishment of many of the above. Briefly, patchy mainly air space shadowing chiefly in a lobar distribution is indicative of a community-acquired pneumonia, unilateral absence of lung markings at the periphery of the lung field together with a visible lung border in the apex indicates a pneumothorax, bat’s wing shadowing with cardiomegaly indicates congestive cardiac failure. Where the chest radiograph is equivocal, brain-type natriuretic peptide, a useful marker of cardiac failure, is indicated. A rib fracture may be seen on a radiograph to be coincident with an area of localized chest wall tenderness.

The differentiation between a pulmonary embolism and a COPD exacerbation may always be difficult but is more so in severe COPD. In severe COPD, the chest radiograph may show little more than hyperexpansion with large pulmonary arteries. The ECG shows a right ventricular strain pattern in both conditions. However, a low systolic blood pressure and an inability to elevate the arterial oxygen tension above 8 kPa (60 mmHg) in spite of use of high flow oxygen favours an embolic phenomenon.

Severity

A staging system for COPD exacerbations has not yet been agreed. However, it is generally accepted that the following features in the history are suggestive of a worse prognosis:
• severity of underlying COPD
• history of more than 3 exacerbations per year or 1 or more previous hospitalizations for COPD-related illness in the previous year
• presence of comorbidities.¹

Signs of severity are use of accessory muscles, haemodynamic instability, worsening or new-onset central cyanosis, peripheral oedema, signs of cor pulmonale and, importantly, acute confusion.

Community management

Initial treatment of an exacerbation of COPD comprises more frequent use of bronchodilators (e.g. salbutamol, ipratropium bromide) with an inhaler or in nebulized form temporarily. Antibiotics are indicated in patients with any two of increased dyspnoea, increased sputum volume and increased sputum purulence. There are insufficient comparative studies to guide us on the choice of antibiotic; hence clinical judgement according to local sensitivities is suggested.

Community-based care is suggested where there is no evidence of decompensated type 2 respiratory failure and where there is supportive, usually nurse-led, care.

Use of oral corticosteroids has been related to more rapid physiological recovery from exacerbations in the community and improved lung function, and may decrease the risk of relapse.²,³ The mechanism of these effects in COPD is largely unknown, and relatively short courses (about 2 weeks) are effective. However, the beneficial effects must be balanced against the side effects. Current guidelines suggest that oral corticosteroids (prednisolone, 30–40 mg once daily) should be used, but in patients already taking oral corticosteroids, the dose is reduced over a longer period.

Failure to improve should prompt consideration of an alternative diagnosis but it is also to be noted that a significant proportion of patients may not recover completely even after 1 month of treatment, and the authors suggest a review of all patients treated in the community regularly and at 2 weeks after diagnosis.

Referral to tertiary centre

Regular assessment is required after initiation of therapy in the community. Referral to hospital should be considered when there is no improvement or the patient deteriorates. Referral should also be considered for those with a severe exacerbation (see above) and when any of the following criteria apply:
• presence of a new cardiac arrhythmia
• insufficient home support
• elderly patient
• uncertain diagnosis.

Hospital management

Accident and emergency department

Initial management – rapid management of these patients may prevent complications requiring intensive care. Airway, breathing and circulation should be assessed immediately on arrival. Controlled oxygen should be given via a Venturi mask to patients with an arterial oxygen saturation (SaO₂) of less than 90% or an arterial partial pressure of oxygen (PaO₂) of less than 8 kPa. Because carbon dioxide retention occurs insidiously with rising PaO₂ in these patients, the aim is to maintain SaO₂ at 92–94%. Arterial blood gases should be rechecked at 30 minutes to assess the pH. While this is performed, a postero-anterior chest radiograph and ECG are requested. Spirometry may be helpful; a forced expiratory volume in 1 second (FEV₁) of less than 1.0 litre is considered an index of a severe exacerbation. Haemoglobin concentration and blood potassium levels should be measured.

While the patient is in the A&E department, nebulized bronchodilator therapy with both β₂-agonists and anticholinergic agents should be started, oral corticosteroids administered and aminophylline considered. Most studies of intravenous aminophylline have demonstrated only minor benefits in COPD exacerbations, though the sample size in these studies has been relatively small. Antibiotics may be prescribed as above.

Further treatment – early discharge from the A&E department with out-patient follow-up may be considered in patients who suffer an uncomplicated exacerbation without severe symptoms, in those with no respiratory failure, and when adequate home and community nurse support is available. Otherwise, the patient should be admitted to the ward.

Non-invasive positive-pressure ventilation (NIV) should be considered in patients with an arterial pH of less than 7.35 on maximal medical therapy. NIV has been shown to improve mortality and reduce the need for intubation and duration of hospital stay in these patients. In the absence of NIV or delay in its application, doxapram (a respiratory stimulant that may be helpful in acute respiratory failure) may be considered, with cardiac monitoring. A Cochrane Review suggests that doxapram ‘may improve blood gas exchange in the short term’.⁴ Patient monitoring is crucial at this stage because mortality increases once the pH declines below 7.26; ideally, patients should be cared for in a high-dependency unit. Referral to an intensive care unit is required for those who deteriorate further with increasing hypoxia and worsening pH.
In-hospital management: continued monitoring of arterial blood gases is required while respiratory failure is still present, and attention to fluid status is vital. In-hospital treatment of acute COPD exacerbations with antibiotics is associated with reduced treatment failures and mortality. Fluid management and fluid balance are essential. Deep vein thrombosis prophylaxis is considered in the immobilized, polycythaemic or dehydrated patient. Physiotherapy to induce sputum clearance is recommended.

As the patient’s symptoms improve, medication should be tapered back to the levels used before admission. Spirometry is used to confirm the severity of disease before discharge. Serial peak flow measurements are not helpful during exacerbations; they may vary little, and the median decrease at exacerbation is small.

Discharge – the median duration of stay in hospital is about 1 week. Discharge is considered when:

• the patient has been clinically stable for 24 hours, and understands how to administer his or her treatment
• home and follow-up care arrangements are completed
• the patient, family and physician are confident that the patient can manage successfully at home.

Out-patient follow-up
Hospital assessment at 4–6 weeks is recommended for all patients, to consider their coping skills and measure FEV₁. About 75% of patients have fully recovered by this time. Inhaler technique and the long-term need for nebulizers are assessed, and the patient may be given advice on how to recognize symptoms of a COPD exacerbation.5

There is evidence that an appropriate home-care package with specialist nurse advice in the outpatient setting reduces readmission.1,2

Prevention of exacerbations
Frequent COPD exacerbations are associated with poor quality-of-life scores, greater levels of hospitalization, greater health burden, more rapid decline in lung function and greater airway inflammation. Figure 1 shows the significant proportion of the quality-of-life scores accounted for an exacerbation frequency of greater than 3 per year. Measures to reduce the risk of exacerbation are therefore important. Viral infections are important possible therapeutic targets, though there are currently few appropriate interventions. Influenza vaccine is strongly recommended for all COPD patients, and patients are advised to avoid upper respiratory tract infections. The pneumococcal vaccine, though recommended for patients with chronic lung disease, has been shown to be effective only in some subsets of COPD patients in randomized controlled studies. Systematic reviews have not supported the use of oral bacterial extracts as immunostimulants in COPD.

Both inhaled corticosteroids and long-acting anticholinergic agents have been shown to reduce the frequency of exacerbations. Mucolytic agents are used in several countries worldwide but the current weight of evidence does not support their use in exacerbation prevention. Several non-pharmacological therapies have been shown to be useful in exacerbation prevention and, of these, pulmonary rehabilitation has received much attention. Both long-term oxygen therapy and non-invasive ventilation reduce COPD-related hospitalization.

REFERENCES

Practice points

• Acute exacerbations of COPD are defined by symptoms
• Cardiac failure is an important differential diagnosis
• Antibiotics are indicated when there are sputum changes
• Oral steroids hasten recovery and decrease the risk of relapse
• Patients with acute exacerbations treated in the emergency department must be treated proactively to prevent rapid deterioration