Antibiotic Guidance Notes in Community Setting

Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous lung condition characterised by chronic respiratory symptoms as a result of airway and/or alveolar abnormalities. It is caused by combination of environmental factors (e.g. passive smoking, outdoor and indoor air pollution, occupational exposure to air-borne pollutants) and host factors (e.g. smoking, advancing age)[1,2]. In Hong Kong, the prevalence of COPD is 0.5% among individuals aged 15 or above. It is most common among the 75 - 84 age group (2.2%), with a male predominance[3].

Clinical features and Causes of Exacerbation

The most common respiratory symptoms include dyspnoea, cough and/or sputum production. COPD is diagnosed by forced spirometry that shows a post-bronchodilator FEV1/FVC <0.7. COPD is associated with co-morbidities such as cardiovascular diseases, hypertension and lung cancer[4–6].

COPD may be punctuated by acute exacerbations, defined as acute episodes of increased respiratory symptoms worsening over <14 days, which may be accompanied by tachypnoea and/or tachycardia, and is often associated with local and systemic inflammation[7]. Acute exacerbations of COPD are mainly triggered by respiratory viral infections (e.g. influenza A, rhinovirus), although bacterial infections and air pollution can also trigger these events[7–10]. Common bacterial isolates in patients hospitalised with COPD exacerbations are *Haemophilus influenzae (H. influenzae)*, *Streptococcus pneumoniae (S. pneumoniae), Pseudomonas aeruginosa* and *Moraxella catarrhalis (M. catarrhalis)*[9,11–13].

When to prescribe antibiotics

Appropriately prescribed antibiotics may shorten recovery time, reduce the risk of early relapse, treatment failure, and duration of hospitalisation. Antibiotics can be prescribed when there are clinical signs of a bacterial infection. Evidence suggests that sputum colour and purulence can predict the presence of a bacterial infection. In a pooled analysis, green or yellow sputum showed a sensitivity of 94.7% and a specificity of 15% for the presence of bacteria[14]. Studies also showed that a positive bacterial culture was obtained in 77-84% of patients with purulent sputum[15,16]. According to the 2024 Global Strategy for Prevention, Diagnosis and Management of COPD Report, antibiotics should be given to patients in the community (a) with three cardinal symptoms: increased dyspnoea, increased sputum volume and increased sputum purulence; or (b) with increased sputum purulence and one other cardinal symptom; or (c) requiring mechanical ventilation[7].

Choice of antibiotics

The empirical antibiotic therapy in **Table 1** targets likely bacterial pathogens responsible for COPD acute exacerbation and takes into account local patterns of antibiotic resistance[17]. *P. aeruginosa* and/or Enterobacterales infection may occur in outpatients with advanced COPD. Risk factors for *P. aeruginosa* infection include: chronic colonization or previous isolation of *P. aeruginosa* from sputum, very severe COPD (FEV1 <30% predicted), bronchiectasis on chest imaging, broad-spectrum antibiotic use within the past three months and chronic systemic glucocorticoid use[18–21]. Amoxicillin and macrolides are not recommended considering the high resistance rates in Hong Kong. Local data in the community shows reduced susceptibility of *S. pneumoniae* to penicillin (23-51% resistance to penicillin), and to macrolides (82% resistance to erythromycin)[17,22]. In addition, 50% of *H. influenzae* isolates were resistant against ampicillin, and nearly all (99%) *M. catarrhalis* isolates produced beta-lactamase[17]. Amoxicillin-clavulanate or respiratory fluoroquinolone (e.g. levofloxacin) are recommended agents. For patients who cannot take amoxicillin-clavulanate due to Non-type I penicillin allergy, cephalosporins, for example cefpodoxime and cefuroxime, may be considered as an alternative. Fluoroquinolones should be reserved for use in outpatients who have no other treatment options for acute bacterial exacerbation of chronic

bronchitis because the risk of severe adverse effects causing aortic dissections or ruptures of an aortic aneurysm, significant decreases in blood sugar, disabling side effects of the tendons, muscles, joints, nerves, central nervous system and mental health[23–25]. In relation to treatment duration, a systematic review indicated that short-course antibiotic treatments (≤5 day) were not significantly different from long-course treatments (≥6 days) regarding clinical cure and bacterial eradication in outpatients with exacerbations of COPD. Another systematic review and meta-analysis demonstrated that short-course antibiotics (<6 days) were not significantly different from long-course antibiotics (>7 days) in terms of clinical success or bacteriological eradication. In addition, there were significantly fewer adverse events with short-course antibiotics[26–28]. Based on the evidence, a 5-day course of antibiotics will generally be adequate to treat a mild to moderate acute exacerbation of COPD due to bacterial infection.

Table 1: Recommended antibiotic treatment for acute exacerbation of COPD

Drug (Route)	Dosage and Frequency (Usual)	Duration (Usual)	Remarks
First line			
Amoxicillin-clavulanate or other beta-lactam-beta-lactamase inhibitors combinations* (oral)	1 g (875 mg/125 mg) twice daily or 625 mg (500 mg/125 mg) three times daily	5 days	Amoxicillin-clavulanate is active against beta-lactamase-producing organisms (e.g. *Haemophilus influenzae, Moraxella catarrhalis* and methicillin-sensitive *Staphylococcus aureus*).
Second line			
Cefpodoxime (oral)	200 mg twice daily	5 days	For Non-type I hypersensitivity to penicillin†. Antacid may decrease the absorption of the drug. Dosage should be adjusted appropriately in patients with renal insufficiency.
Cefuroxime (oral)	500 mg twice daily	5 days	For Non-type I hypersensitivity to penicillin†.
Ceftriaxone (IM)	1 g once daily	5 days	For Non-type I hypersensitivity to penicillin†.
Levofloxacin (oral)	500 mg once daily	5 days	For outpatients who have: • Type I and Non-type I hypersensitivity to the first line agent†, or; • Documented infection by *S. pneumoniae* resistant to penicillin Consider levofloxacin if *P. aeruginosa* infection is suspected.
Moxifloxacin (oral)	400 mg once daily	5 days	

* Beta-lactam-beta-lactamase inhibitor combinations e.g. ampicillin-sulbactam.

†Type I hypersensitivity: Reaction typically occurs within 1 hour after drug exposure. Symptoms usually manifest as urticarial (hives and/or angioedema), bronchospasm, gastrointestinal symptoms (abdominal pain, diarrhoea), or anaphylactic shock. Non-type I hypersensitivity: Reaction usually occurs more than 1 hour after exposure, up to days or weeks. Lesions may last from days to weeks. Cutaneous manifestations are not urticarial in nature, and include maculopapular or morbilliform rashes, erythema multiforme, fixed drug eruptions, and/or contact dermatitis[22,29].

Prevention

Outpatients with COPD are recommended to receive seasonal influenza, pneumococcal and COVID-19 vaccinations[30,31].

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