Acute Exacerbations of Chronic Obstructive Pulmonary Disease

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. Spirometry is required to make the diagnosis; the presence of a post-bronchodilator FEV1/FVC < 0.70 confirms the presence of persistent airflow limitation. The most common respiratory symptoms include dyspnoea, cough and/or sputum production. In most outpatients, COPD is associated with significant concomitant chronic diseases (e.g. ischaemic heart disease and peripheral vascular disease), which increase its morbidity and mortality.

COPD may be punctuated by periods of acute worsening of respiratory symptoms beyond normal day-to-day variation, termed acute exacerbations. Acute exacerbations of COPD can be precipitated by several factors. The most common causes are respiratory tract infections.

When to prescribe antibiotics

Antibiotics, when indicated, can shorten recovery time, reduce the risk of early relapse, treatment failure, and duration of hospitalisation. Antibiotics should be given to patients (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 (invasive or non-invasive). (1)

Choice of antibiotics

The empirical antibiotic therapy in **Table 1** targets on the likely bacterial pathogens (e.g. *Haemophilus influenzae*, *Moraxella catarrhalis* and *Streptococcus pneumoniae*) and takes into account local patterns of antibiotic resistance (refer to Antibiogram for Common Bacterial Isolates under the Antibiotic Stewardship Programme in Primary Care in the Centre for Health Protection website at https://www.chp.gov.hk/en/features/49811.html). *Pseudomonas aeruginosa* and Enterobacteriaceae can occur in outpatients with advanced COPD. Additional risk factors for *Pseudomonas aeruginosa* infection include previous isolation of *Pseudomonas aeruginosa* from sputum, concomitant bronchiectasis on computed tomography, frequent administration of antibiotics, frequent hospital admissions and systemic glucocorticoid use. Amoxicillin, which was favored in the past, is no longer a recommended agent because it is inactivated by many strains of *H. influenzae* and *M. catarrhalis*, which are beta-lactamase producing. Amoxicillin-clavulanate or respiratory fluoroquinolone (e.g. levofloxacin) are recommended agents. U.S. Food and Drug Administration has recently warned against the use of fluoroquinolones in acute bacterial exacerbation of chronic bronchitis due to concern for serious side effects, unless there are no alternative options. (2) 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 serious side effects (e.g. joint or tendon pain, muscle weakness, tingling or pricking sensation, numbness in the arms or legs, confusion, and hallucinations) generally outweigh the benefits. The duration of antibiotic therapy for outpatients with a COPD exacerbation is usually 5 to 7 days, depending on the causative agent and response to therapy.

Prevention

Outpatients with COPD are recommended to receive seasonal influenza and pneumococcal vaccinations. (3,4)

Table 1: Antibiotics recommendation for treatment of Acute Exacerbations of Chronic Obstructive Pulmonary Disease

Drug (Route)	Dosage and Frequency, Adults (Usual)	Duration (Usual)	Remarks
First line			
Amoxicillin-clavulanate or other BLBLIs# (oral)	1g (875 mg /125 mg) twice daily; or 625mg (500 mg/125mg) three times daily	5 – 7 days	Amoxicillin-clavulanate is active against beta-lactamase-producing organisms (e.g. *H. influenzae, M. catarrhalis* and methicillin-sensitive *Staphylococcus aureus*).
Second line			
Ceftriaxone (IV or IM)	50 to 100 mg/kg/ day IV or IM in 1 to 2 divided doses (maximum: 4000mg per day)	5 – 7 days	For non-type 1 penicillin allergy. Daily doses greater than 2g are divided into 2 doses.
Cefpodoxime (oral)	200 mg twice daily	7 – 10 days	For non-type 1 penicillin allergy. Certain *S. pneumoniae* isolates may not be reliably covered by oral cephalosporins in the local setting.
Levofloxacin† **(oral)**	500 mg once daily	7 – 10 days	For outpatients who have either: - Failed the first line agent, or - Allergy (including type-1) to the first line agent, or - Documented infection by *S. pneumoniae* resistant to penicillin, or - Suspected *P. aeruginosa* infection.
Moxifloxacin † **(oral)**	400 mg once daily	5 – 10 days	

Beta-lactam-beta-lactamase inhibitor combinations e.g. ampicillin-sulbactam.
† Fluoroquinolones should be reserved for use in outpatients who have no other treatment options

Clinicians should tailor-make drug treatment based on clinical judgment. Definitive therapy should be based on microbiological and antibiotic sensitivity results if available. Management of outpatients with infections should be individualised. Doctors should check, document and get outpatients well informed about antibiotic treatment (e.g. indication, side effect, allergy, contraindication, potential drug-drug interaction, etc.). Outpatients should be reminded to take antibiotics exactly as prescribed by their family doctors.

References

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management and prevention of Chronic Obstructive Pulmonary Disease. 2017.
2. FDA updates warnings for fluoroquinolone antibiotics. U.S. Food & Drug Administration. https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm513183.htm (July 26, 2016)
3. Scientific Committee on Vaccine Preventable Diseases. Updated Recommendations on the Use of Pneumococcal Vaccines for High-risk Individuals. 2016.

4. Scientific Committee on Vaccine Preventable Diseases. Recommendations on Seasonal Influenza Vaccination for the 2017/18 Season. 2017.

Disclaimer:

This guidance notes is intended for medical professionals for reference only and is not intended to be prescriptive or a substitute for clinical judgment on management of individual patient. It is not a complete authoritative diagnostic or treatment guide. Medical professionals are recommended to obtain relevant information from other sources, and provide patient management based on clinical judgment.

This guidance notes will be kept updating thereafter. Please visit the website of Centre for Health Protection, Department of Health for the latest update and other information.

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