وزارة الصحة
Ministry of Health
الإدارة العامة للرعاية الصيدلية

Lower Respiratory Tract Infections Management Protocol

Abbreviation

IV: intravenous
IM: intramuscular
SC, SQ: subcutaneous
PO: oral
Min: minute
hr: hour
d: day
mo: month
q24hr: every 24 hours
q12hr: every 12 hours
q8hr: every 8 hours
q6hr: every 6 hours
q4hr: every 4 hours
mcg: microgram
mg: milligram
kg: kilogram
MDR: multi-drug resistance
MRSA: methicillin resistance staph. aureus
HAP/ VAP: Hospital acquired pneumonia/ Ventilator acquired pneumonia

Introduction

More than half of all antibiotics given to treat active infections in hospitals are prescribed for three infections where there are important opportunities to improve use: lower respiratory tract infection (pneumonia), urinary tract infection and skin and soft tissue infection (according to MOH hospitals reports). Availability of protocol and system to monitor the adherence is most important strategies to ensure that the use of antimicrobial in hospital setting is appropriately

Purpose: To help the MOH hospitals during establishment of Antimicrobials Stewardship Program at hospital settings

Aim and scope: The protocol is intended to provide guidance on the safe and cost-effectiveness treatment of most common community and hospital acquired infections and to decrease the antimicrobial resistance. For hospital acquired infection the choice between the recommended agents should be based on local resistance data (antibiogram)

Targeted population: Hospitalized immunocompetent patients who are diagnosed with Lower respiratory infection (Community acquired pneumonia, hospital acquired pneumonia and ventilator acquired pneumonia)

Targeted end users: Physicians**,** Pharmacists/clinical pharmacists and Nurses

Setup: Inpatient setting

Methodology:

Phase I: In 2014 the Antibiotic committee under the General Administration of Pharmaceutical Care developed the antimicrobial guideline by reviewing and adopting international guideline (Infectious Disease Society of America, American Thoracic Society, American Society of Health-System Pharmacists and European Society of Clinical Microbiology and Infectious Diseases) to cover 20 infectious diseases.

Phase II: In 2016, collaboration with General Administration of infection control a group of infectious disease consultants reviewed this guideline

Phase III: In 2020-2012 The specific indications were agreed by Antimicrobial Stewardship Program central team to be implemented and monitored in MOH hospitals as a strategy. For this reason, the lower respiratory infections sections updated by specialized clinical pharmacists according to recent international guideline, literature and MOH formulary and then reviewed by infectious disease consultants.

Conflict of interest:

This protocol developed based on valid scientific evidence, critical assessment of that evidence, and objective clinical judgment that relates the evidence to the needs of practitioners and patients. No financial relationships with pharmaceutical, medical device, and biotechnology companies.

Funding:

No fund was provided

Updating:

First version of this protocol created in 2020-2021. The protocol will be updated every 3 years or if any changes or updates released by international/national guidelines, pharmacotherapy references or MOH formulary

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Community Acquired Pneumonia [1]

Pneumonia Severity index (PSI) Prediction Tool for Patients with Community-Acquired Pneumonia

Definition of PSI: The pneumonia severity index is a rigorously studied prediction rule for prognosis that objectively stratifies patients into quintiles of risk for short-term mortality on the basis of 20 demographic and clinical variables routinely available at presentation. It is available on MOF formulary under the medical calculator section

Point Value	Risk	Risk Class	Disposition
≤70 points	Low	II	Outpatient care
71-90	Low	III	Outpatient vs. Observation admission
91-130	Moderate	IV	Inpatient admission
>130 total points	High	V	Inpatient admission (ICU)

* The American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) guidelines recommended that the patients with CAP should be treated for a minimum of five days. Before stopping therapy, the patient should be afebrile for 48 to 72 hours, breathing without supplemental oxygen (unless required for pre-existing disease), and have no more than one clinical instability factor (defined as heart rate >100 beats/minute, respiratory rate >24 breaths/minute, and SBP ≤90 mmHg).

Patient group	Therapy (Dosing Regimen)	
Previously healthy outpatients; no antibiotic use in past 3months	1❒ 2❒ 3❒ 4❒	Amoxicillin 1 g PO q 8hr (5-7 days) Azithromycin 500 mg PO on day 1 followed by 250 mg q24hr on days 2-5 Clarithromycin 500 mg PO q12hr (5-7 days) Doxycycline 100 mg PO q12hr (7-10 days)
Outpatients with comorbidities or antibiotic use in past three months	1❒ 2❒ 3❒ 4❒ 5❒ 6❒	Cefuroxime 500 mg PO q12 hr + Clarithromycin 500 mg PO q12hr (5-7 days) Cefuroxime 500 mg PO q12 hr (7 days) + Azithromycin 500 mg PO on day 1 followed by 250 mg q24hr on days 2-5 Amoxicillin 1 g PO q8hr + Clarithromycin 500 mg PO q12hr (5-7 days) Amoxicillin 1 g PO q8hr (5-7 days) + Azithromycin 500 mg PO on day 1 followed by 250 mg q24hr on days 2-5 Amoxicillin-clavulanate 1 g PO q12hr + Clarithromycin 500 mg PO q12hr (5-7 days) Amoxicillin-clavulanate 1 g PO q12h (5-7 days) + Azithromycin 500 mg PO on day 1 followed by 250 mg q24hr on days 2-5 <u>In case of allergy:</u> Levofloxacin 750 mg q24hr (5 days) Moxifloxacin 400 mg q24hr (5-7 days) Note: don't use it due TB >>>> confirmed with ID administration
Inpatients, non-severe	1❒ 2❒ 3❒ 4❒	Ceftriaxone 1- 2 gm IV q24hr + Clarithromycin 500 mg PO q12hr (7 days) Ceftriaxone 1- 2 gm IV q24hr (7 days) + Azithromycin 500 mg PO on day 1 followed by 250 mg q24hr on days 2-5 Amoxicillin-clavulanate 1 g IV q8hr + Clarithromycin 500 mg PO q12h (7 days) Amoxicillin-clavulanate 1 g IV q8hr (7 days) + Azithromycin 500 mg PO on day 1 followed by 250 mg q24hr on days 2-5

	5❒ 6❒ 7❒ 8❒ 9❒ 10❒ 1❒ 2❒	Cefotaxime 1–2 g q8hr + Clarithromycin 500 mg PO q12hr Cefotaxime 1–2 g q8hr (7 days) + Azithromycin 500 mg PO on day 1 followed by 250 mg q24hr on days 2-5 Amoxicillin-clavulanate 1 g IV q12hr + Doxycycline 100 mg PO q12hr (7-10 days) Ceftriaxone 2 gm IV q24h (7 days) + Doxycycline 100 mg PO q12hr (7-10 days) <u>In case of allergy:</u> Levofloxacin 750 mg q24hr (5 days) Moxifloxacin 400 mg q24hr (5-7 days) **Add:** - If prior Respiratory Isolation of MRSA **Or** - If Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for MRSA **and the MRSA screening is positive** Vancomycin IV loading dose (in case of acute- sever illness) of 25-30 mg/kg then 1g q8hr (7 days) Linezolid IV 600 mg q12hr (7 days)
Inpatients, severe	1❒ 2❒ 3❒ 4❒ 5❒ 6❒	Ceftriaxone 1-2g IV q24hr+ Clarithromycin 500 mg PO q12hr (7 days) Ceftriaxone 1-2g IV q24hr (7 days) + Azithromycin 500 mg PO on day 1 followed by 250 mg q24hr on days 2-5 Ceftriaxone 1-2g IV q24hr + Levofloxacin 750 mg IV q24hr (5-7 days) Ceftriaxone 1-2g IV q24hr +Moxifloxacin 400 mg IV q24hr (7 days) Cefotaxime 1–2 g q8hr + Levofloxacin 750 mg IV q24hr (5-7 days) Cefotaxime 1–2 g q8hr + Moxifloxacin 400 mg IV q24hr (7 days)
		Add if: / **Replace B-lactam with** antipseudomonal antibiotics **if:**
	1❒ 2❒	Prior Respiratory Isolation of MRSA or Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for MRSA Vancomycin IV loading dose (in case of acute- sever illness) of 25-30 mg/kg then 1g q8hr (7 days) Linezolid IV 600 mg q12hr (7 days)
		Prior Respiratory Isolation of Pseudomonas aeruginosa or Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for P. aeruginosa 1 ❒ Piperacillin-tazobactam 4.5 g q6hr (7 days) 2 ❒ Cefepime 2 g q8hr (7 days) 3 ❒ Ceftazidime 2 g q8hr (7 days) 4 ❒ Aztreonam 2 g q8hr (7 days) 5 ❒ Meropenem 1 g q8hr (7 days) 6 ❒ Imipenem 500 mg q6hr (7 days)
Influenza virus	1❒	Oseltamivir (Tamiflu) 75mg q12hr for 5 days

Hospital Acquired Pneumonia/Ventilator acquired pneumonia [2]

-**For hospital-acquired infection the choice between these agents should be selected based on local resistance data (antibiogram)**
-Patient should be shifted to specific antibiotic depend on the culture result within **3-5 days**
-Daptomycin (inactivate by surfactant), tigecycline (lower clinical cure rate in RCT) are not recommended in management of HAP/VAP
-In patients with suspected VAP/HAP, avoiding aminoglycosides (poor clinical response, poor lung penetration, and risk of toxicity) and colistin (increase resistance, nephrotoxicity and increase mortality over long term) if alternative agents with adequate gram-negative activity are available
-The guideline recommends against using of an aminoglycoside as the sole antipseudomonal agent

<table>
<tr><td colspan="3">• Empiric regimens for suspected S. aureus (MSSA), P. aeruginosa, and other gram-negative bacilli</td></tr>
<tr><td>• In patients without risk factors for antimicrobial resistance
• If the patient treated in ICUs where <10%–20% of S. aureus isolates are methicillin resistant and <10% of gram-negative isolates are resistant to the agent being considered for monotherapy</td><td colspan="2"><u>Seven days' regimen</u>
❒ Piperacillin-tazobactam 4.5 g IV q6hr
❒ Cefepime 2 g IV q8hr
❒ Levofloxacin 750mg IV q24hr
❒ Imipenem 500mg IV q6hr (lower dose if pt wt < 70 kg to prevent the seizure)
❒ Meropenem 1g IV q8hr</td></tr>
<tr><td colspan="3">• Empiric regimens for suspected S. aureus (MRSA) , MDR P. aeruginosa, and other gram negative bacilli</td></tr>
<tr><td rowspan="7">For patients with HAP/VAP who have:
• a risk factor for MRSA and MDR infection (i.e, prior intravenous antibiotic use within 90 days)
• hospitalization in a unit where >20% of S. aureus isolates are methicillin resistant and >10% of gram-negative isolate are resistance or the prevalence of MRSA& MDR is not known</td><td>2 antipseudomonal antibiotics from different classes</td><td>Plus</td></tr>
<tr><td>❒ Piperacillin-tazobactam 4.5 g IV q6hr</td><td rowspan="6">❒ Vancomycin IV loading dose (in case of acute- sever illness) of 25-30 mg/kg then 1g q8hr

Or
❒ Linezolid IV 600 mg q12hr</td></tr>
<tr><td>❒ Cefepime 2 g IV q8hr
❒ Ceftazidime 2 g IV q8h</td></tr>
<tr><td>❒ Imipenem 500mg IV q6h
❒ Meropenem 1g IV q8hr</td></tr>
<tr><td>❒ Azetreonam 2 g IV q8hr</td></tr>
<tr><td>❒ Levofloxacin 750mg IV q24hr
❒ Ciprofloxacin 400 IV q8hr</td></tr>
<tr><td>❒ Gentamicin 5–7 mg/kg IV q24hr
❒ Amikacin 15–20 mg/kg IV q24hr</td></tr>
</table>

• who are at high risk for mortality (On or need ventilator support due to HAP OR septic shock)	avoiding aminoglycosides if alternative agents with adequate gram-negative activity are available	
Proven MSSA	❒ Cloxacillin 2g IV q4hr ❒ Flucloxacillin 2g IV/IM q4hr ❒ Cefazolin 1-1.5 g IV/IM q8hr	
Proven a carbapenem-resistant	❒Colistin 5 mg/kg IV × 1 (loading dose) followed by 2.5 mg × (1.5 × CrCl + 30) IV q12hr (maintenance dose) ❒Polymyxin B Loading dose, 2 to 2.5 mg/kg (20,000 to 25,000 international units/kg) IV over 1 hr, followed by maintenance dose of 1.25 to 1.5 mg/kg (12,500 to 15,000 international units/kg) IV every 12 hr -The guideline recommends against using of colistin as the sole agent ❒Ceftazidime/Avibactam 2.5g IV q8hr ***Please follow MOH formulary restriction regulation during prescribing or dispensing of these antibiotics**	

References:

1. Joshua P. Metlay, Grant W. Waterer. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. American Journal of Respiratory and Critical Care Medicine, Volume 200, Issue 7, 1 October 2019, Pages e45-e67
2. Andre C. Kalil, Mark L.Infectious. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clinical Infectious Diseases, 2016, (63):5: e61–e111