National Clinical Guideline Centre

Pneumonia

Diagnosis and management of community- and hospital-acquired pneumonia in adults

Clinical guideline <…>

Appendix N

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Disclaimer
Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

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1 Classifications for the purposes of data pooling

1.1 Rationale for using antibiotic classification

1.1.1 Community-acquired pneumonia

Streptococcus pneumoniae is the most frequently identified cause of community-acquired pneumonia (CAP). *Staphylococcus aureus*, *Mycoplasma pneumoniae, Legionella pneumophila* and *Haemophilus influenza* are also implicated as causes of CAP, depending on the population type and underlying risk factors. *Moraxella catarrhalis*, *Chlamydophyla* spp. and *Coxiella burnetti* are less common causes of CAP.

Our search protocols placed antibiotics into narrow and broad spectrum categories based on their predicted antibacterial activity. Narrow-spectrum agents were subdivided into class 1 agents (benzylpenicillin and oral penicillin V) covering penicillin-susceptible *S. pneumoniae* and class 2 agents (ampicillin and amoxicillin) providing additional cover against amoxicillin-susceptible *H. influenzae*. Broad-spectrum agents including beta-lactam antibiotics with additional activity against beta-lactamase-producing community pathogens (*H. influenzae*, *M. catarrhalis*) and methicillin-susceptible *S. aureus* were split into beta-lactamase stable penicillins (isoxazolyl penicillins such as flucloxacillin, beta-lactam–beta-lactamase combinations, such as co-amoxiclav) and cephalosporins. For CAP, cephalosporins were grouped together due to their similar broad-spectrum activity against susceptible community pathogens.

Tetracyclines are broad-spectrum agents with activity against *S. pneumoniae*, *S. aureus*, *H. influenzae* and atypical pathogens such as *M. pneumoniae* and *C. burnetti*.

Fluoroquinolones were subdivided into those with inadequate anti-pneumococcal activity (ciprofloxacin, ofloxacin) and the newer respiratory fluoroquinolones with broader anti-Gram-positive activity (levofloxacin, moxifloxacin).

1.1.2 Hospital-acquired pneumonia

In addition to community pathogens, aerobic Gram-negative rods such as *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* play a major role in hospital-acquired pneumonia (HAP). Beta-lactam agents with additional anti-pseudomonal activity (carbapenems, monobactams, certain third generation cephalosporins such as ceftazidime and beta lactam-beta–lactamase combinations such as piperacillin-tazobactam) were specifically considered under the HAP category. Other antibiotics with predominant activity against hospital-related pathogens (glycopeptides, aminoglycosides and the oxazolidinones such as linezolid) were also considered.

Table 1: Antibiotic classifications - separate columns denote drugs considered suitable for pooling in meta-analysis

BETA-LACTAMS					FLUOROQUINOLONES			
Narrow-spectrum beta-lactams		Broad-spectrum beta-lactams						
Class 1	Class 2	Beta-lactamase stable penicillins	All cephalosporins[1]	All carbapenems (HAP only)	Non-respiratory fluoroquinolones (1st and 2nd generation)	Respiratory fluoroquinolones (3rd and 4th generation)	MACROLIDES	TETRACYCLINES
Penicillin G (benzylpenicillin)	Ampicillin	Co-amoxiclav	1st GENERATION	Imipenem	Ciprofloxacin	Levofloxacin	Clarithromycin	Doxycycline
Phenoxymethyl-penicillin (penicillin V)	Amoxicillin	Piperacillin-tazobactam	Cefalexin	Meropenem	Ofloxacin	Moxifloxacin	Clindamycin	Tigecycline
		Timentin (ticarcillin-clavulanic acid)	Cefradine	Ertapenem			Erythromycin	Tetracycline
		Flucloxacillin	Cefadroxil				Azithromycin	Minocycline
		Co-fluampicil	2nd GENERATION					
			Cefaclor					
			Cefuroxime					
			3rd GENERATION					
			Cefotaxime					
			Ceftriaxone					
			Ceftazidime					
			Cefixime					
			Cefpodoxime proxetil					
			4th					

BETA-LACTAMS					FLUOROQUINOLONES			
Narrow-spectrum beta-lactams		Broad-spectrum beta-lactams						
Class 1	Class 2	Beta-lactamase stable penicillins	All cephalosporins[1]	All carbapenems (HAP only)	Non-respiratory fluoroquinolones (1st and 2nd generation)	Respiratory fluoroquinolones (3rd and 4th generation)	MACROLIDES	TETRACYCLINES
			GENERATION					
			Cefepime					
			5th GENERATION					
			Ceftaroline fosamil					

[1] *All cephalosporins except for first generation agents are considered beta lactamase stable*