Principles of Antibiotic Use - The 6 Step Plan

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Choosing an Antibiotic

Disease/Site

Non-infectious  Viral  Bacterial

No Antibiotic-Patient education

Choose Antibiotic Wisely
Clinical Response

- Improved
- Unchanged
- New Infection

Stop Antibiotic

Re-culture/Rethink

Step 1.
Is it an Infection?

- Tips for Diagnosing Allergy:
  - Recurrence
  - Blocked nose a dominant feature
  - Allergic facies
  - Family history
  - Allergy testing
Step 2.
Is it a Viral infection?

- Common Cold:
  - Winter predominance
  - Sniffles
  - Mucus (even green)
  - Not localised
  
  - 30% of individuals cough for more than 10 days

Step 2.
Is it a Viral infection?

- Bronchiolitis:
  - Hyperinflation
  - Noisy breathing

  - Aetiology: Rhinovirus/RSV/PIV/Influenza/HMP
Step 3.
Picking an Antibiotic for a Bacterial Illness?

- PK/PD
- Break points
- MIC
- Amoxil TDS/Augmentin BD (slow release formulation)
- Guidelines
Selecting Antibiotics

- Concentration
- AUC/MIC
- Mode of killing
- PK/PD
- Time
- Above MIC
- Adverse events

Dosage

- Consider antibiotic for relevant organisms
- Consider dosage interval and total dose depending on the antibiotic mode of killing (pk/pd principles)
- PK = Effect of body on drug (absorption, availability, metabolism, excretion)
- PD = Effect of drug on body (receptor binding, tissue penetration)
Present URTI Guidelines

- Diagnose URTI
- Decide if antibiotic necessary
- Oral amoxycillin 90mg/kg/day
- Alternative therapy = Augmentin/Cefpodoxime

Brink A, et al. SAFPJ 2009;51:105-113

Treatment CAP

- Antibiotics for all – Amoxicillin (90mg/kg/day tds 5 days) – (IV Ampicillin) or Cephalosporin that works
- < 2 months add aminoglycoside/cephalosporin
- > 5 years add macrolide
- HIV-infection add aminoglycoside
- HIV-exposed < 6 months add cotrimoxazole
- AIDS add cotrimoxazole
Treatment of Bronchiolitis

- Humidified oxygen: Beneficial
- ?? Antibiotics - associated infection
- ?? Efficacy of Bronchodilators
  - Inhaled & oral B2 agonists
  - Inhaled ipratropium bromide
  - theophyllines
- ?? Use of corticosteroids
- ? Use on leukotriene antagonists
- ? Efficacy of immunoglobulin

Selecting Antibiotics

- MIC
- Concentration
- Time
- Palatability
- Adverse events
Step 4.
What Dose of Antibiotic?

- High dose: 90 mg/kg/day – Pneumococcus
- Add clavulanate – H’flu

Dosage

- Correct antibiotic dosages and duration
- Correct antibiotic administration
  - Concentration dependent antibiotics (Aminoglycosides, quinolones) = single daily concentration
  - Time dependent antibiotics (B-lactams, vancomycin, pip-taz, carbapenems, linezolid) = continuous infusion over 24 hours (3-4 hours for carbapenems, TDS for linezolid)
Predictors of Bacterial Eradication: PK/PD Profiles

Time-Dependent Agents

Includes:
- Penicillins
- Cephalosporins
- Linezolid

Clinical and bacteriologic success correlates with length of time bacteria are exposed to agent at concentration that exceeds MIC

Concentration-Dependent Agents

Includes:
- Fluoroquinolones
- Aminoglycosides
- Tetracyclines

Successful therapy correlates with parameters that involve blood concentration of agent and MIC

Break point

- MIC that allows ideal PK/PD of antibiotic
- = 40-50% for time dependent killers
- = Peak concentration > 90% above MIC for concentration dependent killers
Persistence of organisms after Amoxil/clav use

Step 5.
What Duration of Antibiotics?

- Pakistan data pneumonia
- ?URTI
Pneumonia Study

- Seven sites in 5 Pakistan cities
- Children with severe pneumonia
- Randomised to ambulatory group (oral amoxicillin 80-90 mg/kg/day in 2 doses x 5 days or
- Hospitalised group (IV ampicillin 100mg/kg/day in 4 doses) x 48 hours then oral amoxicillin.

Results:
1. 2037 children aged 3-59 months
2. Treatment failures:
   - hospitalised group 8.6%
   - ambulatory group 7.5%
3. Deaths within 14 days:
   - hospitalised group 4
   - ambulatory group 1

Hazi T, Fox LM, Fox MP, et al for the New Outpatient Short-Course Home Oral Therapy for Severe Pneumonia Study Group
Lancet 2008;371: 49-56
Step 6.
What About a New Infection?

- HAP
- ESBL
- MRSA
- Pseudomonas

E coli
- < 1960 – Sensitive Ampicillin
- 1963 – B-lactamase production
- 3rd Generation Cephalosporin use
- CTX-M15 Production – Escape DNA into plasmids
- 3rd Generation Cephalosporin resistance
- OR death if bacteraemic = 2
- Prevalence 10% UK, 50% Turkey, 60% Asia, 50% SA
- Carbapenem use
- Carbapenemase production (esp Greece – 40%, Isreal – 20%)
- Rare in Enterobacteriaceae, common in Acinetobacter
Macrolide Resistance in Pneumococci

- Efflux pump – MEF A/MEF B
- Or Ribosomal methylase (ERM B)

- Erythromycin resistance may emerge within therapy of individual patient

- Therefore combine macrolide with B-lactam antibiotic

- Most traits of H’flu resistant to macrolides

Cough Mixtures, Decongestants and Mucolytics
Antibiotic Use

Correct Antibiotic Use
- Correct antibiotic selection
- Correct dosage
- Correct dosing interval
- Correct duration of therapy
- Appropriate de-escalation

Resistance of microbes

Infection Cure

Decontaminate

- Hand washing – the most effective strategy to prevent resistance
- All personal and parents must hand wash
- Use notices and wall mounted sprays
- Anti-inflammatory strategies of Macrolides/Linezolid