Pharmacokinetics of Antibiotic Agents

Alireza Hayatshahi, PharmD, BCPS
American Board Certified Pharmacotherapy Specialist
Faculty of Pharmacotherapy, Tehran University of Medical Sciences
Outlines

• Pharmacokinetics (ADME)
  – Vancomycin
  – Gentamicin
  – Linezolid
  – Fluconazole
  – Amphotericin B
Vancomycin

• Poor oral bioavailability
• IV
  – Distributed widely to body tissues and fluids except CSF
    • Inflamed BBB
      – 20% TO 30% of serum concentration
    • Uninflamed BBB
      – Minimal
Vancomycin

• Half life
  – Adults
    • 5-11 hours
  – Renal impairment will prolong the half life
    • ESRD
      – Over 200 hours
Vancomycin

• Excretion
  – 80% to 90% renal
  – If use oral vancomycin
    • Excreted by feces

• Time to peak
  – Right after the end of infusion
Vancomycin

- Using PK calculations or protocols to schedule the doses
  - 15-20 mg/kg
    - Q8H, Q12H, Q24H, Q48H,...
  - Patient’s weight (actual)
  - Renal function
    - Serum creatinine
    - GFR
Vancomycin

• In hemodialysis patients
  – Depends on the HD filter
    • Conventional
      – 0 to 5% removal
    • High flux
      – Higher rates of clearance after each HD
      – Requires dose replacement post HD
  • All patients need loading dose regardless of the type of the filter (15-20mg/kg)
Vancomycin

• Levels
  – Peak
    • 30 minutes after the end of infusion
  – Trough
    • Right before the next dose
    • 1st trough usually before the forth dose
  – It is recommended to use trough level NOT peak
Vancomycin

• Based on the indications
  – Skin and soft tissue infections
    • Trough between 10-15 mcg/ml
  – Bacterial meningitis, bacteremia, endocarditis, osteomyelitis, pneumonia
    • Trough between 15-20 mcg/ml
• Always keep trough levels above 10 mcg/ml to avoid resistance and treatment failure
Gentamicin

• IM, IV
• Poor penetration to CSF even with inflammation
• Highly hydrophilic
• Renal excretion
  – Depends on the renal function
Gentamicin

• Half life
  – 1.5-3 hours
  – 2-3 days in renal impairment
  – Removed by HD
  • May need dosing replacement
  • Get levels post HD
  • Depends on the HD filter type
Gentamicin

• Dosing (use ideal body weight)
  – Conventional
    • 2.5mg/kg/dose
    • Q8H, Q12H, Q24H
    • Depends on renal function
    • Adjust the interval by monitoring the peak and trough levels
  – Once daily dose
    • 7mg/kg/day
    • Adjust the interval based on the random levels
Gentamicin

• Levels
  – Peak
    • 30 minutes after the end of infusion
  – Trough
    • Right before the next dose
  – Random
    • Between the intervals
    • In once daily schedule
Gentamicin

- **Peak:**
  - Serious infections: 6-8 mcg/mL
  - Life-threatening infections: 8-10 mcg/mL
  - Urinary tract infections: 4-6 mcg/mL
  - Synergy against gram-positive organisms: 3-5 mcg/mL

- **Trough:**
  - Serious infections: 0.5-1 mcg/mL
  - Life-threatening infections: 1-2 mcg/ml
Linezolid

- Oral bioavailability 100%
- PO and IV exchangeable
- No renal dose adjustment needed
  - 30% in the urine as unchanged
  - Non renal clearance about 65%
- No dose adjustment in mild to moderate hepatic insufficiency
Linezolid

- **Dosing**
  - **PO**
    - Regardless of food intake
    - Q12H
  - **IV**
    - Q12H
  - **If HD**
    - Give the dose post HD
Fluconazole

• PO bioavailability over 90%
• Widely distributed in all body tissues including CSF
• Excreted renally 80%
• Half life with normal kidney function about 30 hours
Fluconazole

• Dose adjustment needed based on the renal function
• Depends on the HD filter type, may be cleared up to 50%
  – Give the whole daily dose after HD
• PO dose may be taken regardless of the meal
Amphotericin B

- IV infusion over 4 hours
- **Poor penetration** to many body fluids and tissues including CSF
- Half life:
  - Takes days to be cleared totally from the body after discontinuation
- Renally excretion
Amphotericin B

- Once daily dosing
- 0.05–1.5 mg/kg/day
- Dose adjustment needed in renal insufficiency