Pharmacokinetics of Antibiotic Agents

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Outlines

- Pharmacokinetics (ADME)
  - **Vancomycin**
  - **Gentamicin**
  - **Linezolid**
  - **Fluconazole**
  - **Amphotericin B**

Vancomycin

- Poor oral bioavailbility
- 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