Wake Forest Baptist Medical Center

Center for Antimicrobial Utilization, Stewardship, and Epidemiology

Adult guidelines for monitoring aminoglycoside concentrations

I. Why obtain concentrations of aminoglycosides?

- A. To optimize dosing based on the indication
- B. To monitor for drug accumulation if renal function declines
- C. To ensure the aminoglycoside is still therapeutic if renal function improves

II. What is the most appropriate timing to obtain an aminoglycoside concentration?

- A. Both peaks and troughs should be obtained for most infections requiring aminoglycoside therapy, except with extended interval dosing (see below)
  1. Achieving a target peak ensures adequate microbiologic activity
  2. Achieving a target trough minimizes risk of toxicity
- B. Optimal peaks are obtained 30-60 minutes after the end of the infusion
- C. Optimal troughs are obtained within 30 minutes before the next dose
- D. Acceptable peaks are obtained 60-120 minutes after the end of the infusion
- E. Acceptable troughs are obtained 30-60 minutes before the next dose
- F. If measuring concentrations with an initial or new dosing regimen, the trough should be obtained prior to the 4^{th} dose and the peak should be obtained after the 4^{th} dose

III. What is the target trough for gentamicin and tobramycin?

- A. Pneumonia, bacteremia, abdominal infection: 0.5-2mg/L (around 1mg/L is preferred)
- B. All other infections: 0.5-1mg/L

IV. What is the target trough for amikacin?

- A. All infections: 2-4mg/L

V. What is the target peak for gentamicin and tobramycin?

- A. UTI: 3-5mg/L
- B. Pneumonia: 8-10mg/L
- C. Bacteremia and abdominal infection: 6-8mg/L
- D. Cellulitis and sepsis from urinary source: 5-7mg/L

E. Gram positive synergy, e.g. endocarditis: 3-4mg/L

VI. What is the target peak for amikacin?

A. UTI: 15-20mg/L

B. Pneumonia: 27-30mg/L

C. Bacteremia, abdominal infection, and cellulitis: 25-30mg/L

E. Sepsis from urinary source: 20-25mg/L

VII. How often should aminoglycoside concentrations be obtained?

A. If an aminoglycoside will be part of ongoing therapy, a steady-state peak and trough should be documented to support definitive dosing

B. Concentrations should be obtained if renal function changes (better or worse) or if there is suspicion of aminoglycoside toxicity

C. Concentrations should be obtained after a dose change to document appropriateness of the new dose

D. If a long duration of therapy is expected (e.g. 3-6 weeks) and all clinical parameters are stable, a peak and trough should be obtained once weekly

VIII. Extended Interval Dosing of Aminoglycosides, a.k.a. "Once Daily Aminoglycoside Dosing"

A. Peaks and troughs should not be obtained

B. A random concentration approximately 10 hours after the start of the first extended interval dose should be obtained

C. A random concentration obtained within 6 – 14 hours after the start of the first extended interval dose is acceptable

D. The random concentration should be plotted on the appropriate nomogram specific for the drug and dose prescribed (see WFBH Antimicrobial Dosing Guide)

E. If the plotted concentration falls below the line, the dose is validated and the patient should continue to receive the drug as prescribed

F. If the plotted concentration falls above the line, the patient's aminoglycoside should be converted to traditional dosing

G. If a long duration of therapy is expected (e.g. 3-6 weeks) and all clinical parameters are stable, a random concentration at 6 – 14 hours after the start of the infusion should be

obtained every week. This concentration should be plotted on the appropriate nomogram to determine ongoing use of extended interval dosing

H. Extended interval dosing using gentamicin 3mg/kg Q24h is an option only for gram positive synergy, e.g. streptococcal endocarditis. A nomogram for this dose does not exist. Monitoring troughs to document absence of accumulation is reasonable in this setting

I. When using extended interval dosing, if a Q24h dose is not validated by the nomogram, changing the interval to Q36h or Q48h is not preferred due to a relative paucity of data supporting these intervals compared with Q24h

VIII. Measuring concentrations among patients receiving renal replacement therapy

A. Intermittent hemodialysis (HD)

1. A "standard" hemodialysis session will remove approximately 50% of the pre-dialysis aminoglycoside concentration

2. For patients receiving a standard HD session, obtaining a pre-HD concentration is preferred in order to avoid distributional effects of HD

3. If post-HD concentrations are required, the sample should be obtained at least 30 minutes after the end of HD to allow for re-distribution

4. In order to maintain consistently therapeutic concentrations, a post-HD trough of approximately 2mcg/mL (gentamicin or tobramycin) or 6-8mcg/mL (amikacin) is acceptable

B. Continuous renal replacement therapy (CRRT)

1. CRRT results in aminoglycoside elimination that is equivalent to a creatinine clearance of 30-40mL/min

2. Obtaining a random concentration 24 hours after a dose is reasonable until a dosing pattern is established; often times, the required dosing interval will be every 24-48 hours

3. Frequent interruptions in CRRT of more than 2 hours may produce an inconsistent pattern of concentrations, resulting in the need for erratic dosing

IX. Monitoring for toxicity

A. If the anticipated duration of aminoglycoside therapy is >2 weeks, audiometry should be performed at baseline and every 1-2 weeks during therapy

B. A basic metabolic panel or comprehensive metabolic panel should be obtained at least 2-3 times per week to assess renal function

X. Caveats about monitoring aminoglycoside concentrations

A. Concentrations may be falsely elevated if the sample is drawn inappropriately

1. When the sample is drawn through the same line used to infuse the aminoglycoside

2. When the sample is drawn "downstream" from the infusion site

3. When the sample is drawn too soon after the end of the infusion, i.e. before the drug has had time to distribute

B. Concentrations must be interpreted carefully among patients with extreme fluid shifts or rapidly changing renal function, e.g. severe sepsis

1. Initial concentrations may be low due to a large volume of distribution (not due to rapid clearance)

2. After therapeutic concentrations are achieved, elimination may be slower than expected due to impaired renal function

3. If pharmacokinetic indices are unreliable based on standard estimates, it is acceptable to obtain two concentrations after the first dose to determine the subsequent dosing strategy (a.k.a. "first dose kinetics", see below)

C. First dose kinetics

1. Determine an appropriate loading dose based on the patient's expected volume of distribution

2. Obtain a peak concentration 1-2 hours after the end of the loading dose infusion

3. Obtain a random concentration 8-12 hours after the peak

4. Use the two concentrations to calculate patient-specific pharmacokinetic parameters and determine an appropriate dosing strategy