Therapeutic Drug Monitoring of Aminoglycosides

Key concepts

- Aminoglycosides are **concentration-dependent**. Higher concentrations equal greater effect.
- **Aminoglycoside monotherapy** should generally be **avoided**, particularly in severe infections.
- Aminoglycosides are **nephrotoxic** and **ototoxic**. Close monitoring of creatinine, urine output, changes in hearing and vestibular function are important – particularly if patient is on other nephrotoxic (e.g. NSAID, ACEI/ARB, diuretics and vancomycin) and/or ototoxic (e.g. furosemide and vancomycin) medications.
    - Suggest baseline audiometry if patient frequently exposed and/or long duration (≥ 21 days) and PRN audiometry if suspicion of toxicity.
- **Extended dosing** (i.e. once-daily) is the **preferred** dosing strategy unless CNS (central nervous system) infections, severe CKD (CrCl < 10-20 mL/min), dialysis or burns (BSA > 20%); in these cases standard dosing is preferred
    - Best dosing strategy (extended or standard dosing) in **pregnant** women is **unkown**. Use clinical judgment.
- Patients should be **informed about risks and benefits** of aminoglycosides. If possible, **consent should be obtain** before prescribing this antibiotic class.
- For dosing, use actual body weight in non-obese patients and dosing body weight in obese patients (see formula below).
- For frequency of administration, use Cockcroft-Gault creatinine clearance formula.
- Amikacin is ID/resp restricted.
- Refer to **complete guide** on ASP web site for more information on aminoglycoside dosing and for references.

Non-cystic fibrosis (CF) high-dose extended-interval dosing (ED)

- Gentamicin/Tobramycin: 5-7 mg/kg IV q24h if CrCl > 60 mL/min
    - For severe infection (e.g. sepsis), prescribe 7 mg/kg
    - q36h for CrCl 40-59 mL/min and q48h for CrCl 20-39 mL/min
- Amikacin: 15 mg/kg IV q24h
    - q36h for CrCl 40-59 mL/min and q48h for CrCl 20-39 mL/min

CF high-dose extended-interval dosing

- Gentamicin/Tobramycin: 10 mg/kg IV q24h if CrCl > 50 mL/min
    - q36h for CrCl 30-49 mL/min and q48h for CrCl 20-29 mL/min
- Amikacin: 30 mg/kg IV q24h
    - q36h for CrCl 30-49 mL/min and q48h for CrCl 20-29 mL/min

Standard dosing

- Gentamicin/Tobramycin: 1-2.5 mg/kg IV q8h
    - q12h for CrCl 30-59 mL/min
    - For **CNS** and **severe infections** (e.g. sepsis): 2.5 mg/kg IV q8h
- Amikacin: 5-7.5 mg/kg IV q8h
    - q12h for CrCl 30-59 mL/min

Synergy dosing for specific gram-positive infections (infective endocarditis)

Consult Infectious Diseases

- Gentamicin 1 mg/kg IV q8h (consider 3 mg/kg IV q24h if viridans group streptococci, *S. gallolyticus* or gentamicin-susceptible *Enterococcus sp*)

Surgical prophylaxis

See Surgical Antibiotic Prophylaxis Guidelines for each type of surgery

- Tobramycin 5 mg/kg IV x 1 pre-op 30-60 minutes before incision (maximum 400 mg)
    - Follow renal function closely in post-operative context (e.g. creatinine every 2 days x 2 weeks or until discharge)
    - Reduce dose to Tobramycin 3 mg/kg IV x 1 if CrCl < 50 mL/min or renal replacement therapy
    - Reduce dose to Tobramycin 2 mg/kg IV x 1 for β-lactam allergic patient undergoing C-section

Timing of therapeutic drug levels

- If aminoglycoside are to be given for less than 48 hours, levels are not required
- **Extended dosing:** draw trough 15-30 minutes prior to 2nd dose (no need to wait for steady-state), draw peak 1 hour after the end of infusion
- **Standard dosing:** draw peak 30 minutes after the end of infusion of 3rd dose, draw trough prior to 4th dose
- Frequency of monitoring: draw levels after each dose adjustment and/or if patient's renal function or volume status changes. If stable, draw levels once weekly.

Monitoring for toxicity

- Renal function: at least 2 times a week (creatinine + urine output if possible)
- Ototoxicity: bedside monitoring of symptoms (e.g. hearing loss, nausea/vomiting, headache, dizziness, etc.), baseline audiometry if patient frequently exposed and/or long duration (≥ 21 days) and PRN audiometry if suspicion of toxicity.

Additional comments

- See **online calculator** for computation of individualized regimen
- Obesity: use dosing weight if actual body weight (ABW) is 20% greater than ideal body weight (IBW)
    - IBW male (kg) = 50 kg + 0.9 x (height (in cm) - 152 cm)
    - IBW female (kg) = 46 kg + 0.9 x (height (in cm) - 152 cm)
    - Dosing weight (kg) = IBW + 0.4 (ABW – IBW))
- Aminoglycoside dosing in patients on intermittent hemodialysis (IHD) is usually managed by Nephrology service
    - D8C (RVH) patients on IHD and aminoglycosides are NOT followed by Nephrology. Dose adjustments should be suggested by a pharmacist, or Nephrology should be consulted.

Suggested targets for peak and trough concentrations of aminoglycosides*

	Trough (pre dose)	Peak (post dose)
Amikacin (TB)	< 1.5 mg/L	35-45 mg/L
Amikacin (CF)	< 1.5 mg/L	40-60 mg/L
Amikacin (ED)	< 1.5 mg/L	35-50 mg/L
Amikacin (standard)	< 4 mg/L	20-35 mg/L
Gentamicin/Tobramycin (CF)	< 0.5 mg/L	15-30 mg/L
Gentamicin/Tobramycin (ED)	< 0.5 mg/L	15-25 mg/L
Gentamicin/Tobramycin (standard)	< 1-2 mg/L	CNS infection: 8-12 mg/L Sepsis/Pneumonia/Febrile neutropenia: 7-10 mg/L SSI/Osteomyelitis/Intra abdominal/ Pyelonephritis/Eye: 6-8 mg/L UTI: 4-6 mg/L
Gentamicin (synergy – IE)	q8h: < 0.5-1 mg/L q24h: < 1 mg/L	q8h: 3-4 mg/L q24h: 10-12 mg/L

*Peak and trough targets are based on expert opinion and usual practice, may be different in other references. Use clinical judgement to guide target levels (severity of infection, resistance profile, patient risk factors for toxicity, duration of treatment, etc.)

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