AMINOGLYCOSIDES

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I. CLASSIFICATION OF DRUGS
   A. Streptomycin
   B. Kanamycin (Kantrex®, Klebcil®)
   C. Netilmicin (Netromycin®)
   D. Neomycin-D (Mycifradin®)
   E. Gentamicin (Garamycin®)
   F. Tobramycin (Nebcin®)
   G. Amikacin (Amikin®)
   H. Sisomycin

II. MAIN INDICATIONS
   A. Serious gram-negative rod infections or sepsis
   B. *Pseudomonas aeruginosa* (usually in combination with a third generation cephalosporin or an anti-pseudomonal penicillin)
   C. Severe enterococcal infection (combined with ampicillin)
   D. Initial or definitive therapy for suspected/proven gram-negative rod infections with multiple organisms (especially if *Serratia sp.*, *Enterobacter sp.*, and *Pseudomonas aeruginosa*)
   E. Mixed surgical infections (usually combined with other drugs for appropriate coverage of gram-positive and anaerobic organisms)
   F. Antibiotic-impregnated PMMA beads
   G. Surgical irrigation solution (although this usage can be debated)
   CLINICAL NOTE: In situations where organisms are known to be sensitive to a cephalosporin, strong consideration should be given to utilizing one of those drugs (e.g., ceftazidime). This is particularly true in individuals with known renal impairment.

III. MAIN PROPERTIES/ADVANTAGES
   A. Bactericidal
   B. Good half-life (approximately 2 hours)
   C. Good tissue distribution and penetration
   D. Negligible protein binding
   E. Primarily renal excretion
   F. Thermostabile

IV. DISADVANTAGES
   A. Potential risk for severe toxicity
      1. Renal failure
      2. Vestibular/cochlear damage
   B. Limited to parenteral (IV/IM) use only
   C. No activity against anaerobes

V. ADVERSE EFFECTS
   A. Vestibular toxicity
   B. Auditory toxicity
   C. Renal toxicity
      1. Gentamicin probably more so than tobramycin
      2. Amikacin probably less than gentamicin and tobramycin
   D. Potential neuromuscular blockade (when used with general anesthesia)
   E. Skin rash
   F. Drug-induced fever

VI. PREDISPOSING FACTORS FOR NEPHROTOXICITY
   A. Advanced age
   B. Pre-existing renal disease
   C. Previous administration of aminoglycosides
   D. Prolonged administration of aminoglycosides
   E. Low blood volume
   F. Septicemia
   G. Concurrent nephrotoxic drug usage
   H. Concurrent loop diuretics used (especially in older patients)
   I. Concurrent high dose cephalosporins
   J. High "trough" value is more important than high "peak" value for monitoring

VII. PREDISPOSING FACTORS FOR OTOTOXICITY
   A. Advanced age
   B. Pre-existing hearing loss
   C. Previous administration of aminoglycosides
   D. Prolonged administration of aminoglycosides

E. Pre-existing renal impairment
F. Concurrent ototoxic drug usage
G. Renal dialysis patients
H. High "trough" value is more important than high "peak" value for monitoring, although ototoxicity is less dependent on serum concentration than nephrotoxicity

VIII. GUIDELINES FOR CLINICAL USAGE AND MONITORING

A. Peak and trough values are critical
1. Begin with second or third dose
2. Used as indicator for modification of dosage or administration time interval
3. Gentamicin and tobramycin
a. Peak value: 6-10 ug/ml
b. Trough value: less than 2 ug/ml
4. Amikacin
a. Peak value: 18-30 ug/ml
b. Trough value: less than 10 ug/ml
5. "Peak" values/levels
a. 15-30 minutes after IV infusion
b. 60 minutes after IM injection
6. "Trough" values/levels
a. Should be drawn just prior to administration of next dose

B. Serum creatinine
1. Order before therapy then roughly every other day
2. 0.4 mg/dl change indicates likely renal impairment

C. Serum blood urea nitrogen (BUN)
1. Secondary test
2. Less specific for renal function than creatinine

D. Urinalysis
1. Order before therapy than everyday or every other day
2. Change in specific gravity most important
3. Proteinuria
4. Casts
5. Lab variability and lack of specificity make this test generally less valuable than creatinine

E. Audiometry
1. If available
2. Baseline should be obtained prior to therapy if monitoring is to be employed

IX. DOSAGE SCHEDULE

A. Gentamicin and tobramycin
1. Loading dose: 1-2 mg/kg
2. Maintenance dose: 3-5 mg/kg/day at 8 to 24 hour intervals

B. Amikacin
1. Loading dose: 5.0-7.5 mg/kg
2. Maintenance dose: 15 mg/kg/day at 8 to 24 hour intervals

C. Adjust maintenance dose based upon creatinine clearance
(140 - age) x weight (in kg)
1. Creatinine clearance =
serum creatinine x 72
a. Use "lean" body weight
b. In women multiply above result by 0.85
c. "Normal" creatinine clearance is around 100 ml/min or greater
2. May also estimate the creatinine clearance with a dosing nomogram
3. If the creatinine clearance is less than 100, maintenance dose should be a calculated as above divided by 100 and multiplied by the creatinine clearance (e.g., if the creatinine clearance is 50 ml/min, 50% of the standard maintenance dose would be given)

X. DOSAGE ADJUSTMENTS

A. Based on "peak" and "trough" levels
B. Increased "peak", normal "trough" = decrease amount of aminoglycoside
C. Decreased "peak", normal "trough" = increase amount of aminoglycoside
D. Normal "peak", increased "trough" = increase dosage interval
E. Increased "peak", increased "trough" = decrease amount of aminoglycoside and increase dosage interval
F. Decrease amount of aminoglycoside
1. Difficult to determine quantity of change
2. Requires more frequent peak and trough values to assess effectiveness
G. Increase dosage interval
1. Determine serum creatinine value
2. Multiply serum creatinine value by 8 (e.g., if serum creatinine is 1.5 mg/dl, then 1.5 x 8 = 12.0. Therefore, dose is administered at 12 hour intervals)
3. Commonly employed and easy to structure and monitor