Vancomycin and Rifampin

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Vancomycin

I. CLASSIFICATION
   A. Glycopeptide antibiotic
      1. Vancomycin (Vancocin®)
      2. Teichoplanin (not commercially available in U.S.)
      3. Ristocetin (not available)

   Note: Remaining discussion is for vancomycin only.

II. MAIN INDICATIONS
   A. Infections (osseous and soft tissue) secondary to methicillin - resistant *Staphylococcus aureus* (MRSA) and methicillin - resistant *Staphylococcus epidermidis.* (MRSE)
   B. Enterococcal infections (usually administered in combination with other agents such as aminoglycosides)
   C. Gram positive infections of patients allergic to B-lactam antibiotics
   D. Orthopedic surgical prophylaxis if patient is allergic to B-lactam antibiotic or if surgery is performed at a medical center where MRSA and/or MRSE are problem pathogens
   E. *Clostridium difficile* colitis (oral administration only)

   CLINICAL NOTE: Controversy exist over vancomycin's usage empirically to curtail possible MRSA and MRSE infections. Caution should be taken with this method of treatment as overusage may increase resistance and subsequently eliminate an available antibiotic for MRSE and MRSA infections.

III. MAIN PROPERTIES/ADVANTAGES
   A. Spectrum of activity - Aerobic and anaerobic gram (+) organisms
      1. Bactericidal against most strains of staphylococci and non-enterococcal streptococci
      2. Bacteriostatic against most strains of enterococci. (Use with an aminoglycoside is synergistic and bacteriocidal)
   B. 75-90% excreted by glomerular filtration
   C. Long 1/2 life
      1. Normal renal function - 6 hours
      2. Anuric patient - 7 1/2 days
   D. Minimal toxicity with improved purification
   E. True allergy is rare
   F. Minimal development of resistance
   G. Good tissue distribution and penetration

IV. DISADVANTAGES
   A. Route of administration - IV only
      1. Oral administration not absorbed. Used for treatment of *C. difficile* colitis only
      2. IM administration is severely painful
   B. Requires slow infusion
   C. No gram negative activity

V. ADVERSE REACTIONS
   A. Red Man Syndrome
      1. Related to speed of infusion
      2. Secondary to nonimmunologically mediated release of histamine from mast cells
      3. Not a true allergy
      4. Clinical presentation:
         a. erythematous rash of face, neck and upper torso
         b. flush hot feeling
         c. pruritus
         d. if severe, hypotension
      5. Self limiting after termination of infusion
      6. Relieve symptoms with anti-histamine
   B. Pain and Spasm Syndrome
      1. Infusion related syndrome
      2. Throbbing pain and/or muscle spasms in chest and back without evidence of an acute MI
      3. Self limiting after termination of infusion

C. Ototoxicity
   1. Auditory nerve damage
   2. Tinnitus and high pitch hearing loss frequently precede deafness
   3. Usually irreversible
   4. Associated with serum levels > 30 ug/ml
   5. Rare
   6. Enhanced risk with concomitant use of an aminoglycoside or other ototoxic drug

D. Nephrotoxicity
   1. Rare since development of improved purified preparations of vancomycin
   2. Enhanced risk with concomitant use of aminoglycoside
   3. Reversible
   4. Monitor renal function
   5. Associated with elevated serum levels

E. Neutropenia
   1. Rare
   2. Occurs after prolonged use
   3. Reversible

F. Chemical Thrombophlebitis
   1. Occurs in 13% of patients with peripheral venous cannulas

VI. Guidelines for clinical usage/monitoring

A. Peak and trough serum levels
   1. 1st levels around 3rd dose
   2. Therapeutic range
      a. Peak value - 20-30 ug/ml
      b. Trough value - 5-10 ug/ml
   3. Timing for levels
      a. Peak - two hours after the one hour infusion is completed
      b. Trough - just prior to administration of next dose
   4. Important for adjusting dosage
   5. Elderly and renal impaired patients should be monitored closely

B. CBC
   1. Monitor for neutropenia
   2. Order prior to therapy and then once weekly

C. Serum creatinine and BUN
   1. Monitor kidney function
   2. Order prior to therapy and then weekly
   3. 0.4 mg/dl change of creatinine indicates likely renal dysfunction

D. Evaluate IV site frequently

E. Subjective evaluation for tinnitus

VII. DOSAGE SCHEDULE

A. Infuse slowly over at least a 60 minute period

B. Normal renal function
   1. 1 gram Q 12 IV (30 mg/kg/day)
   2. 500 mg Q 6 IV

C. Impaired renal function
   1. 15 mg/kg IV loading dose
   2. For estimate of daily parenteral dose use formula: 150 + (15 x creatinine clearance in ml/min) = mg vancomycin
   3. Nomogram may be used to calculate dosage
   4. 1 gram IV may yield effective concentrations for 7-14 days in anuric patients
   5. Monitor levels closely
   6. Hemodialysis does not remove Vancomycin

D. Prophylaxis for orthopedic surgery
   1. 1 gram IV beginning 60 minutes prior to surgery and infused slowly over 1 hour
   2. If post-op dose required, then 500 mg to 1 gm can be given 12 hours after surgery in a patient with normal renal function

RIFAMPIN

I. CLASSIFICATION

A. Rifamycins
   1. Rifampin (Rifadin®)
   2. Rifapentine
   3. Rifabutin

Note: Remaining discussion is for Rifampin only

II. MAIN INDICATIONS

A. Combination therapy with vancomycin, ciprofloxacin or trimethoprim/sulfamethoxazole for treatment of MRSE or MRSA infections

B. Treatment with other antistaphylococcal antibiotics (nafcillin) against tolerant staphylococci. The combination therapy leads to improved serum bactericidal levels against tolerant staphylococcal species

C. Combination therapy with other antistaphylococcal antibiotics for treatment of chronic staphylococcal osteomyelitis

D. Treatment of lower extremity mycobacterial infections in combination with other agents

III. MAIN PROPERTIES/ADVANTAGES
- A. Spectrum of activity
  1. Excellent activity against staphylococci and streptococci
  2. Active against all mycobacteria
  3. Some gram negative activity especially *neisseria* and *Hemophilus*
- B. Bactericidal
- C. Absorbed from GI tract - oral administration available
- D. Good 1/2 life
  1. 2-5 hours initially
  2. May decrease 40% during 1st two weeks of therapy
- E. Good tissue distribution and penetration
  1. Penetrates abscess fluids better than most other antibiotics with similar antimicrobial activity

IV. DISADVANTAGES
- *A. Rapidly develops resistance
- B. Requires combination therapy
- C. Enhanced hepatic metabolism
  1. Decreased 1/2 life and effectiveness of medications that are detoxified by the liver (ie. Warfarin, Digoxin and Birth control pills)

V. ADVERSE REACTIONS
- A. Orange-red discoloration of body fluids
- B. Permanently stained soft contact lenses
- C. Flu-like symptoms with high, prolonged dosages
- D. Maculopapular rash
- E. Liver disease
  1. Mild transient elevation of transaminase-common
  2. Severe hepatotoxicity - 0.6% of patient taking the drug

VI. GUIDELINES FOR CLINICAL USAGE/ MONITORING
- A. Periodic liver function test
- B. Inform patient not to wear contact lenses due to staining
- C. Inform patient of decreases effectiveness of birth control pills

VII. DOSAGE SCHEDULE
- A. Adult - 600 mg p.o. Q 24 hr
- B. Pediatric - 10-20 mg/kg/day Q 12-24 hr
- C. Minimal or no adjustments necessary with renal impairment
- D. Hepatic failure requires dosing adjustments
- E. Para-aminosalicylic acid interferes with absorption