Bugs & Drugs: Did You Know?

September 2016

Topic: Infective Endocarditis: Enterococcus species

Key Points for BLactam and Aminoglycoside Susceptible Strains:

Enterococcus sp. is the 3rd leading cause of infective endocarditis (IE).
• E. faecalis is the most common species; ~ 97% of Enterococcus cases.
• Both native and prosthetic valves can be infected, and are treated similarly.
• Utilize a multidisciplinary approach including consultation from Infectious Disease, Cardiology, Cardiovascular Surgery and Pharmacy to optimize clinical outcomes. (Class I; Level of Evidence C)

Ampicillin and Penicillin (PCN) remain drugs of choice for all Enterococcus sp.
• PCN is advantageous for its more convenient, continuous infusion, dosing regimen, particularly when outpatient parenteral therapy is needed.
• Routine PCN minimum inhibitory concentration (MIC) susceptibility testing is recommended.

Combination therapy with an aminoglycoside or B-lactam is recommended for both native valve (NVE) and prosthetic valve endocarditis (PVE).
• The strength of recommendation is the same for both regimens. In cases of renal dysfunction, creatinine clearance (CrCl) < 50 mL/min, the double B-lactam is preferred.
• High-level resistance to gentamicin exists, therefore susceptibility testing is necessary. (Class I; Level of Evidence A)
• Ceftriaxone should not be used alone for Enterococcus IE due to lack of in vitro efficacy.

Key Points for Resistant Strains:

Vancomycin should be reserved for patients who cannot tolerate penicillin or ampicillin, or in cases of B-lactam resistance. Desensitization can be performed in patients with penicillin allergy. (Class I, Level of Evidence B)
• Combination therapy with an aminoglycoside is recommended, however renal function must be closely monitored (Class Ila, Level of Evidence B)
• Contact pharmacy for assistance with dosing.
• A loading dose of 25-30 mg/kg IV x 1, followed by a maintenance dose of 18 mg/kg IV every 12-24 hours based on renal function can be given to achieve therapeutic drug levels.
• Vancomycin trough levels should be maintained at 15-20 mg/L.

Aminoglycoside resistance
For treatment of gentamicin-resistant strains:
• Streptomycin sulfate 15 mg/kg IV q24h in two divided doses.
• Use caution in renal dysfunction, CrCl < 50 mL/min.
• Contact pharmacy for assistance with weight based dosing.

Vancomycin Resistance
For treatment of vancomycin-resistant Enterococcus sp (VRE), primary among Enterococcus faecium, several antimicrobials can be used:
• Although uncommon, ampicillin or penicillin may still be susceptible. If so, combination therapy as previously described is still encouraged.
• Linezolid and daptomycin are primary therapies for VRE isolates
  o Weekly CK monitoring should be performed in patients receiving daptomycin, particularly at high doses.
• Quinupristin-dalfopristin is rarely used due to severe side effects. Formulary status varies with institution.
• Tigecycline and tedizolid have minimal published data. Formulary status varies with institution.

B-lactam & Gentamicin-susceptible Enterococcus sp

All regimens Class IIa, Level of Evidence B

• Either
  • Ampicillin 2g intravenous (IV) Q4H x 4-6 weeks
  • 4 wk therapy: NVE with symptoms of illness < 3 months
  • 6 wk therapy: NVE symptoms > 3 months or PVE
• Or
  • Aqueous PCN G sodium 18-30 million units in 24 hours IV continuously or in 6 divided doses x 4-6 weeks
• Plus, combination therapy with:
  • Gentamicin 3 mg/kg ideal body weight in 2-3 divided doses x 4-6 weeks
  • A single 3 mg/kg IV q24h dose is not recommended for Enterococcus
  • Serum peak concentration goal 3 to 4 mg/mL
  • Serum trough concentration goal < 1 mg/mL
  • If pre-existing mild or severe renal failure, consider 2-3 week treatment or alternate regimen
• Or
  • Ceftriaxone 2g IV q12h x 6 weeks
  • When using double B-lactam therapy, ampicillin is preferred over PCN

B-Lactam & Aminoglycoside-resistant Enterococcus sp

• Linezolid 600mg IV q12h for at least 6 weeks
  • Bacteriostatic
  • Class Ila; Level of Evidence C
• Or
  • Daptomycin 10-12 mg/kg per dose > 6 weeks
  • Bacteriocidal
  • Class IIb; Level of Evidence C
• Consider combination therapy with ampicillin or ceftazoline (when Daptomycin MIC’s are high, 3 or 4 mg/L)

References:
2. Fernández-Hidalgo, N, et al. Ampicillin plus ceftriaxone is as effective as ampicillin plus gentamicin for treating Enterococcus faecalis infective endocarditis. CID 2013, cit052

This segment was brought to you by the Antimicrobial Stewardship Subcommittee KentuckyOne Health – Louisville Market.

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