Antibiotic Treatment of Community Acquired Methicillin Resistant Staphylococcus Aureus
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I) Introduction to CA-MRSA
A) Microbiology of CA-MRSA
   i) Coag+, Gram+ cocci in clusters
   ii) mecA gene expresses PBP2a, preventing binding of β-lactam antibiotics
B) CA-MRSA Infection
   i) Rapid rise in incidence from 1999-2006 (3.6% to 28.2% of patients)(1)
   ii) MRSA related infections plateaued from 2005-2009 (16.31 to 17.68/1,000 hospitalizations P=0.22)(2)
   iii) Primarily SSTI: 80% of CA-MRSA infections in 2006(1)
   iv) Risk factors: immunosuppression, antibiotic use, IVDA, close proximity(3)
   v) Prevention: antibiotic restriction, hand hygiene(3)

II) Antibiotic Treatment of CA-MRSA
A) IDSA Treatment Guidelines(3)
   i) I&D primary treatment for simple abscess/boil
   ii) Collect drainage for culture
   iii) Add antibiotics if: severe/extensive disease, evidence of systemic illness, immunosuppressed patient, extremes of age, difficulty draining, lack of response
   iv) Empiric treatment for CA-MRSA recommended for purulent cellulitis or nonpurulent cellulitis nonresponsive to β-lactams
B) Vancomycin
   i) Binds D-Ala-D-Ala, preventing polymerization of cell wall components NAM and NAG, preventing cell wall cross-linking, allowing bactericidal activity
   ii) Dosed per nomogram at U-M with goal trough 10-15(4)
   iii) First line inpatient option for complicated infections(3)
   iv) Lack of oral bioavailability makes unsuitable for outpatient
C) Trimethoprim/sulfamethoxazole
   i) Synergistic dual enzyme inhibition of folate synthesis allowing bactericidal activity
   ii) Recommended dose at U-M: 1 DS po BID-TID(4)
      (1) High dose (≥4 DS tab/day) increased adverse reactions(5)
      (2) Clinical resolution: 73% 1 DS po BID vs. 75% 2 DS po BID P=0.79(6)
      (3) Renal dosing: CrCl 15-30 halve dose, CrCl <15 use not recommended(7)
   iii) First line option for uncomplicated infections (95-100% in vitro susceptibility)(3,8)
   iv) Boston study shows increased use of TMP/SMX from 2001-2010 without reduced CA-MRSA susceptibility(9)
   v) Recent in vitro study suggests TMP/SMX can increase the production of cytotoxic Panton-Valentine leukocidin (PVL) from CA-MRSA strains(10)
   vi) High risk of hyperkalemia in patients on ACEi/ARB (AOR 6.7; CI95% 4.5-10.0)(11)
   vii) Pregnancy category C, avoid per mfr. in 3rd trimester possible kernicterus(7)
D) Clindamycin
   i) Binds 50S ribosomal subunit and prevents translocation allowing bacteriostatic activity (not recommended for endocarditis/thrombophlebitis)(3)
   ii) Recommended dose at U-M: 300-450 po TID(4)
   iii) Covers both CA-MRSA and β-hemolytic strep when desired(3)
   iv) Geographic variability in susceptibility (83-96% susceptible in MI in 2005)(8)
   v) Limited national data suggests a rise in resistance from 2002-2005 (13 to 25% resist strains)(8)
   vi) Inducible resistance: D-test for MLS\textsubscript{B} if erythromycin R and clinda S
   vii) 20% incidence diarrhea, higher risk of C. difficile colitis than other antibiotics (absolute risk +3% P<0.05)(12,13)
   viii) Pregnancy Category B(12)

E) Tetracyclines
   i) Bind 30S ribosomal subunit and prevents peptide elongation allowing bacteriostatic activity (not recommended for complicated infection)(3)
   ii) Doxycycline recommended at U-M dosed 100 mg BID(4)
   iii) Maintained >90% in vitro susceptibility from 2005-2008(14)
   iv) \textit{tetK} gene confers tetracycline resistance, inducible doxycycline resistance, but spares minocycline susceptibility(15,16)
   v) \textit{tetM} gene confers class-wide resistance(15)
   vi) Evidence of treatment failures when used for non-SSTI(17)
   vii) Pregnancy category D and not to be used in children <8 years of age due to possible tooth discoloration and decreased bone growth(18)

F) Other Options(3)
   i) Reserved for hospitalized patients with complicated infections that have failed other therapeutic options
   ii) Include linezolid, daptomycin, and telavancin
   iii) Wide geographic variation in susceptibility, but fluoroquinolones generally not first line options(8)

III) Summary
   A) CA-MRSA infections have rapidly grown in incidence through the early 2000s
   B) For non-complicated SSTI that require antibiotic treatment, TMP/SMX, clindamycin, and tetracyclines are considered first line \textit{empiric} agents
   C) For complicated infections, vancomycin is preferred agent
   D) Local \textit{susceptibilities} vary; consider local trends when selecting a patient’s therapy
   E) Important to tailor therapy to specific cultures and sensitivities and patient characteristics
References


