Big Challenges for Small Patients: Update on the Management of Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Pediatrics

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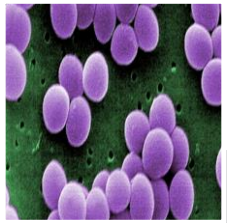
Learning Objectives

- Evaluate the impact of infection-specific characteristics and transmission prevention practices on outcomes in pediatric patients with or at risk for MRSA infections.
- Recommend evidence-based therapies and monitoring for invasive MRSA infections.
- Develop a therapeutic strategy for prevention or treatment of MRSA infection in a pediatric patient taking into consideration patient characteristics.

Disclosure

- All planners, presenters, and reviewers of this session report no financial relationships relevant to this activity.

Methicillin Resistant *Staphylococcus aureus (MRSA)*



Community - associated (CA- MRSA)

- SCC $_{mec}$ types IV, V, VII
- Clonal variations geographically
  - USA 300
    - Carry plasmid-mediated resistance
- Increased production of toxins
  - Panton-Valentine leukocidin (PVL)
  - Increased inflammatory response on presentation
- Varied susceptibility patterns

Hospital- associated (HA-MRSA)

- SCC $_{mec}$ types I, II, III
  - Enhanced multi-drug resistant (MDR) strains
- Leading cause of increased morbidity
  - Increased lengths of stay
  - Poor outcomes
  - Higher inoculum
- Varied susceptibility patterns
- Associated with necrotizing features

Clinical manifestations

- **Skin and soft tissue infections**
- **Respiratory tract infections**
- **Bloodstream infections**
- Urinary tract infections
- Brain abscesses
- Surgical site infections
- Endocarditis
- Musculoskeletal infections

Gould IM et al. *Int J Antimicrob Agents*. 2012;39(2):96-104.

Ritz N et al. *Pediatr Infect Dis J.* 2012:31(5):514-518.

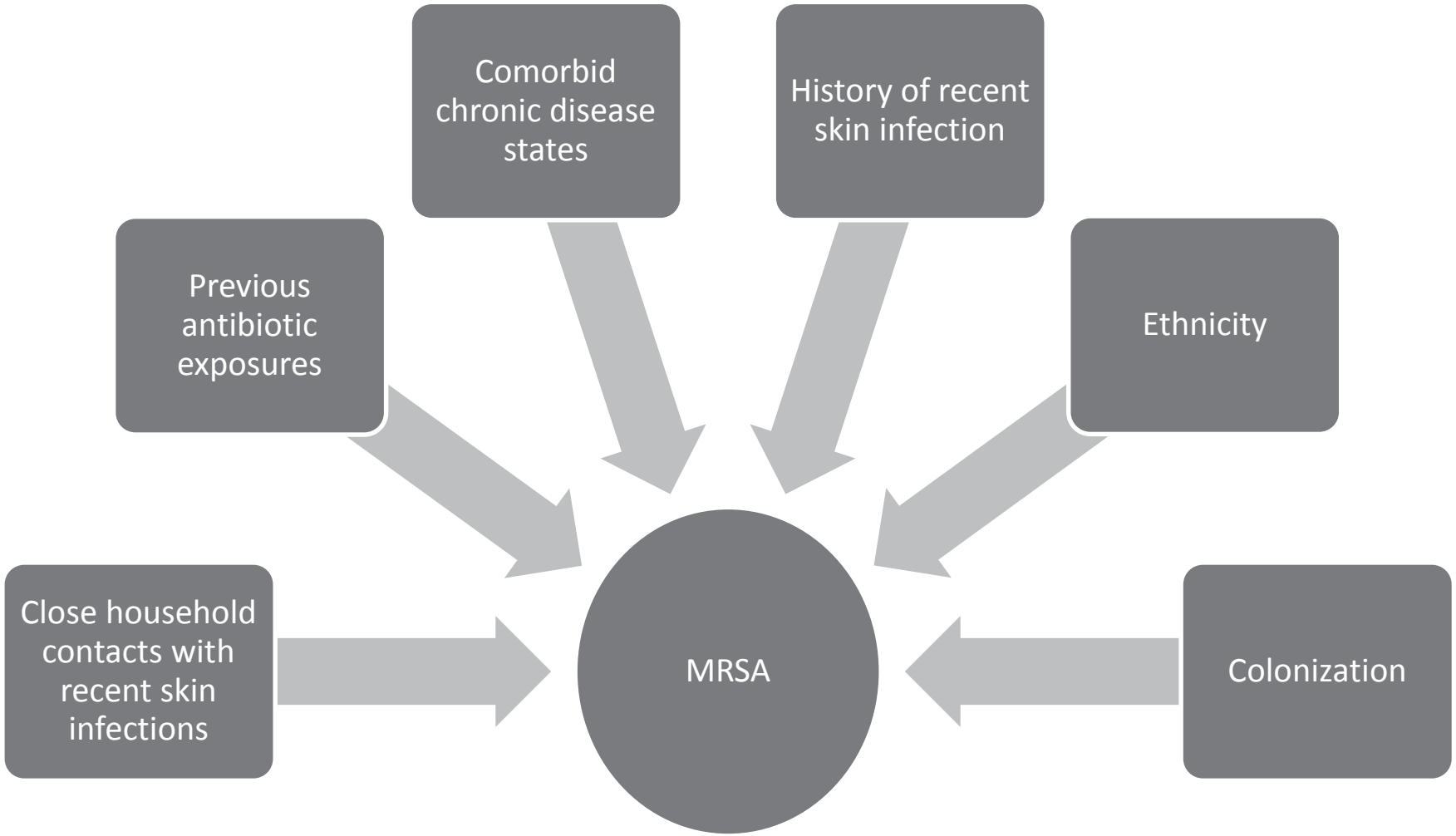
Preventing the Spread of MRSA

Centers for Disease Control & Prevention (CDC)	• Ongoing Tracking and Surveillance • National Healthcare Safety Network (NHSN) • Health and Human Services Action Plan to prevent healthcare-associated infections • Emerging Infections Program (EIP)
Laboratory Collaboration	• Collaboration with laboratory staff for accurate identification • Clinical and Laboratory Standards Institute (CLSI) methods for identification and appropriate susceptibility testing • Cefoxitin disk testing – best inducer of *mecA* gene → better reproducibility
Infection Prevention & Control – Facility Level	• Standard precautions • Contact precautions • Active surveillance and reporting to the NHSN • Appropriate personal protective equipment (PPE)

Centers for Disease Control and Prevention. Methicillin-resistant Staphylococcus aureus (MRSA). https://www.cdc.gov/mrsa/index.html. (accessed 2017 Aug 18).

Milstone AM et al. *Clin Infect Dis*. 2011; 53(9):853-859.

Risk Factors for Invasive Disease



Le J et al. *Pharmacotherapy.* 2012;26(12):1758-1770.

JW 8 y/o M presents to the ED with a self reported “spider bite” and associated abscess with no significant past medical history. Which of the following considerations should be made prior to initiation of antibiotic therapy?

A. JW may have a CA – MRSA infection which will most likely be susceptible to any antibiotic that is not a β - lactam antibiotic.

B. Contact precautions should be initiated and the patient should be isolated from other patients in the area per the facility policy.

C. JW most likely has CA – MRSA and should be directly admitted to the ICU as PVL toxin may cause rapid decompensation for which advanced care may be needed.

D. Infection prevention and control should be contacted for surveillance cultures to be obtained via nasal swab to determine risk for invasive infection.

Meet Amber: HPI

- A.D. is an 8 – year - old (27 kg) Caucasian female presenting to the emergency department with a 2 - day history of left leg pain and subjective fever as reported by parents and decreased oral intake
- Parents report Amber “fell pretty hard” off the trampoline in the backyard about a week ago when playing with friends with no apparent trauma
- IV access has been established for initiation of fluids because patient is mildly dehydrated
- Imaging study (CT) has been performed

Meet A.D.: Clinical Status

Vitals	Pertinent Laboratory Results	Radiologic Findings
HR: 132 beats/minute	WBC: 39.4 thousand/mm^3	CT Impression: 1) Complex left hip effusions and complex collections along the anterior aspect of the left proximal shaft 2) Signal abnormality of the proximal left femur consistent with osteomyelitis 3) Extensive myositis within the medial and anterior compartments of the left lower extremity
RR: 28 breaths/minute	SCr: 0.4 mg/dL	
BP: 97/70 mm Hg	ESR : 145 mm/hr	
T_{max}: 38 °C	CRP: 24 mg/dL	
O_2 : 98% room air	Microbiology: Blood culture (peripheral) + Gram positive cocci in clusters; abundant growth on gram stain only; culture pending	

Which of the following agents should be used as the empiric agent of choice for management of AD's suspected MRSA musculoskeletal infection at this time?

A. Vancomycin 30 mg/kg/dose as a load, then 15 mg/kg/dose IV every 6 hours

B. Daptomycin 6 mg/kg/dose IV every 24 hours

C. Clindamycin 10 mg/kg/dose IV every 8 hours

D. Trimethoprim/Sulfamethoxazole 4 mg/kg/dose IV every 12 hours

Vancomycin

- Glycopeptide cell wall active agent
- AUC:MIC ≥ 400 mg-hr/L
- Requires serum drug level monitoring
- Increased doses and durations →increased risk of nephrotoxicity
- Poor outcomes with higher minimum inhibitory concentrations (MIC)
- Altered pharmacokinetic profile in pediatric patients

Efficacy

- Mainstay of therapy
- Known outcomes with adequate dosing (based on mg/kg/day)

Safety

- Red man syndrome can be managed by reducing infusion rate
- Nephrotoxicity risks somewhat known
- Serum drug monitoring may aid in management
- DRESS in limited cases

Clinical Pearls

- Slowly bactericidal activity further exacerbated by higher inoculums of *Staphylococcus aureus*
- Increased risk of treatment failure with certain sites of infection

Walraven CJ et al. *J Antimicrob Chemother.* 2011;66(10):2386-2392.
McKamy S et al. *J Pediatr.* 2011;158(3):422-426.
Stevens DL et al. *Clin Infect Dis.* 2014;59(2):e10-e52.
Liu C et al. *Clin Infect Dis.* 2011;52(3):e18-e55.

Clindamycin

- Lincosamide ribosomal targeted agent
- Increasing community resistance rates (> 20%)
- Bacteriostatic activity
- Utility in toxin-mediated processes
  - No clinical difference in PVL (+) versus (-) MRSA infections
- Not effective for invasive disease and/or active bacteremia

Efficacy

- Limited effectiveness in invasive disease
- Drug of choice in the absence of bacteremia and intravascular focus

Safety

- Well tolerated at 30 – 40 mg/kg/day
- Monitoring of transaminases with prolonged therapy
- Pseudomembranous colitis risk

Clinical Pearls

- CA – MRSA infections are likely to be susceptible but geographic differences in susceptibility exist
- Potential for inducible resistance while on therapy leading to clinical failure and/or relapse

Hussain FM et al. *Pediatr Infect Dis J.* 2000;19(12):1163-1166.
Frank A et al. *Pediatr Infect Dis J*. 2002;21(6):530-534.
Ochoa TJ et al. *Emerg Infect Dis.* 2005:966.

Case Update

- Vancomycin 15 mg/kg/dose IV every 6 hours
  - Initial serum trough level obtained at steady state = 15 mg/dL
- Blood cultures remain (+); on day 7 of therapy s/p surgical drai
  - Re
- Mic
  - Bl
  - Fluid obtained from hip effusion

Culture & Susceptibility

STAPHYLOCOCCUS AUREUS, MRSA

Antibiotic	Sensitivity	Result	Method	Status
Clindamycin	Susceptible	<0.25	MIC	Final
Gentamicin	Susceptible	<1	MIC	Final
Comment:	*For Staphylococci that test susceptible, aminoglycosides are used only in combination with other active agents that test susceptible.*			
Oxacillin	Resistant	>2	MIC	Final
Trimethoprim/Sulfamethoxazole	Susceptible	<0.5/9.5	MIC	Final
Vancomycin	Susceptible	1	MIC	Final

Based on the updated blood culture results which of the following regimens would be most appropriate?

A Vancomycin 15 mg/kg/dose IV every 6 hours

B Daptomycin 10 mg/kg/dose IV every 24 hours

C Clindamycin 10 mg/kg/dose IV every 8 hours

D Trimethoprim/Sulfamethoxazole 4 mg/kg/dose IV every 12 hours

Battle of the Bactericidal Agents

- To continue vancomycin or not?
  - Consideration of PK/PD parameters
    - Is it adequately reflected by serum trough levels?
  - Adequate source control? **Guidelines endorse achievement of adequate source control as more important than choice of antimicrobial agent**
    - Any new drainable sites?
    - Any extended involvement in other areas?
- To switch therapy…role for daptomycin?

Liu C et al. *Clin Infect Dis.* 2011;52(3):e18-e55.

Daptomycin

- Cyclic lipopeptide
- Rapidly bactericidal
- Concentration dependent activity
- Clinically significant post antibiotic effect
- Inactivated by pulmonary surfactant
- Decreased half - life in pediatric patients < 6 y/o
- Increased clearance in infants and young children

Efficacy

- Increasing data for pediatric osteomyelitis with improved or similar outcomes to vancomycin therapy
- Optimal dosing by age may be higher than initially recommended in the 2011 MRSA guidelines

Safety

- Requires creatine phosphokinase (CPK/CK) monitoring and renal dosage adjustments
- CPK changes seem to be transient in pediatric patients and not associated with clinical rhabdomyolysis

Clinical Considerations

- Diminished inflammatory response
- Improved activity with higher inoculum *Staphylococcus aureus*
- Resistance concerns already apparent, can be overcome with higher doses
- Compatibility issues with dextrose - containing fluids

Bradley JS et al. *Pediatr Infect Dis J.* 2014;33(9):936-939.

Bradley JS et al. *Pediatrics.* 2017;139(3):pii: e20162477.

Liu C et al. *Clin Infect Dis.* 2011;52(3):e18-e55.

Syriopoulou V et al. *Pediatr Infect Dis J.* 2016;35(5):511.

Effective Combinations for Consideration

- Criteria for consideration
  - High inoculum
  - Higher MICs within the susceptible range
- Potential mechanisms
  - "Seesaw" effect
    - As glyco- and lipopeptide susceptibility decreases, increased observed susceptibility to β - lactam antibiotics
      - Majority of studies look at combinations of vancomycin + oxacillin or nafcillin
  - Decreased virulence
    - β- lactam - mediated decrease in expression of key virulence factors
  - Synergy
    - Increased cellular binding - mostly demonstrated with daptomycin

Berti AD et al. *Antimicrob Agents Chemother*. 2013;57(10):5005-5012.
Ortwine JK et al. *Drug Resist Updat*. 2013;16(3):73-79.

Case Update

- Deep vein thrombus identified on repeat imaging
  - Transitioned to daptomycin 10 mg/kg/dose IV every 24 hours to complete 4 weeks for osteomyelitis with intravascular focus
- Transferred to the ICU for increased respiratory support
  - Chest X-ray demonstrates pleural effusions with opacity in the left lower lobe
  - Bronchoscopy yields MRSA from sample
- Now what?
  - Will daptomycin therapy be sufficient if HA-MRSA is the culprit of Amber's newly developed pneumonia?

Case Update

- How do we cover her pneumonia + prolonged bacteremia + osteomyelitis?
  - Think outside the box …
    - Tetracyclines
      - Doxycycline
      - Minocycline
    - Trimethoprim/Sulfamethoxazole (TMP/SMX)
    - Fluoroquinolones (FQs)
      - Ciprofloxacin
      - Levofloxacin
  - Switch agents?

AUC_{24}:MIC Associated with Efficacy & Toxicity

AUC_{24}:MIC ≥ 400 mg-hr/L improves clinical outcomes	• AUC:MIC "breakpoint" of 211 - 578 • Mortality, composite treatment failure, bacteremia persistence
Higher AUC_{24} associated with nephrotoxicity	• AUCs of > 800 - 1300 for increased risk • Toxicity also associated with elevated troughs
Limited available data in pediatrics	• Minimal assessment of AUC:MIC vs. outcomes • 36 patients evaluated; non-significant decrease in length of stay and time to first negative blood culture

Rybak M et al. *Am J Health-Syst Pharm.* 2009; 66:82-98.

Doxycycline

- Inhibits protein synthesis
- Guideline endorsed empiric agent for moderate skin and soft tissue infections
- Alternative agent for consideration in the management of pneumonia
- High enteral bioavailability
- Bacteriostatic activity against MRSA

Efficacy

- Limited clinical data for MRSA outside of the cystic fibrosis patient population

Safety

- Relative contraindication in patients less than 8 years of age due to calcium binding and tooth discoloration
- Hepatic and renal dysfunction and photosensitivity risk

Clinical Pearls

- Useful when bacteremia has cleared and other sites of infection persist
- Great penetration into pleural space and lung parenchyma
- Minimal resistance concerns

Newland JG et al. *Paediatr Drugs.* 2008;10(6):367-378.
Stevens DL et al. *Clin Infect Dis.* 2014;59(2):e10-e52.

Trimethoprim/Sulfamethoxazole

- Successful use in CA – MRSA associated skin and soft tissue infections
- Typically used as " step down" therapy option
- Expanded coverage of other clinically relevant species (gram negative organisms)
- Excellent tissue penetration

Efficacy

- Limited data in pediatrics in invasive infections
- Guideline endorsed option in empiric management of skin and soft tissue infection

Safety

- Long term therapy can result in neutropenia
- Dermatologic manifestations may occur (SJS)
- Monitoring of hepatic transaminases needed

Clinical Pearls

- Great option in areas where clindamycin susceptibilities are low
- Can provide coverage if polymicrobial infection including MRSA
- Inexpensive with high enteral bioavailability

Messina AF et al. *Pediatr Infect Dis J*. 2011;30(12):1019-1021.
Paul M et al. *BMJ.* 2015;350:h2219.

Ciprofloxacin/Levofloxacin

- Geographic variation in MRSA susceptibility patterns to various agents
- Excellent tissue penetration
- High enteral bioavailability
- Low barrier for the development of resistance
- Limited outcome data for use in MRSA infections
- Not a guideline endorsed option

Efficacy

Safety

- Ever evolving black box warnings
- Unclear incidence of side effect distribution in pediatric patients

Clinical Pearls

- Exposure increases risk for VRE* and MDR gram negatives
- Last resort, newer FQs may have greater utility

*Vancomycin-resistant *enterococci*

Optimizing Vancomycin Dosing via Pharmacokinetic Monitoring

For vancomycin, which pharmacokinetic parameter has been best associated with efficacy?

A AUC:MIC

B C_{max}:MIC

C % Time>MIC

D $T_{1/2}$:MIC

Vancomycin Trough Monitoring

	Trough Predictive of AUC:MIC > 400 (MIC = 1 mg/L)
Adults	• ~60% of patients who achieve ≥ 400 have trough < 15 mg/L • ½ of patients with trough 10-20 mg/L may achieve goal AUC:MIC
Children	• Variability depending on frequency of administration & other factors • 7-13 mg/L

Lanke S et al. *J Clin Pharmacol*. 2017;57(1):77-84.
Hale CM et al. *J Pharm Prac*. 2017;30(3):329-335.
Kishk OA et al. *J Pediatr Pharmacol Ther*. 2017;22(1)41-47.
Rybak M et al. *Am J Health-Syst Pharm.* 2009; 66:82-98.

Which equation for estimation of AUC was validated in a study performed by Le and colleagues?

A Ke x Vd

B Ke x CL

C Dose (daily) ÷ Vd

D Dose (daily) ÷ CL

Estimating the AUC

Bayesian software

1 or 2 concentrations

Trough only + population values

1. Trapezoidal method with population ke to back-extrapolate peak

2. AUC = Dose/CL; CL estimate per Le et al

$CL\ (L/hr) = 0.248 * wt^{0.75} * (0.48/SCr)^{0.361} * [ln(age)/7.8]^{0.995}$

Two concentration estimations

1. Trapezoidal method

2. $AUC = Dose_{24}/CL$

$CL = Vd * ke$

Use traditional Sawchuk-Zaske equations for estimation of ke and Vd

Kishk OA et al. *J Pediatr Pharmacol Ther*. 2017;22(1)41-47.
Le J et al. *Pediatr Infect Dis J*. 2013;32($):e155-163.

TD: a 19.4 kg, 6 yo female with acute osteomyelitis

Vancomycin 320 mg IV every 6 hours
8th dose administered at 0811 over 1 hour

1020: 23.6 mg/L 1355: 9.8 mg/L

$$AUC = \frac{\text{Dose (24°)}}{CL}$$

$$K_e = \frac{\ln(C_1/C_2)}{\Delta t} = \frac{\ln(23.6/9.8)}{3.6} = 0.24\ hr^{-1}$$

$$\text{true peak} = 23.6 \div e^{-0.24 hr^{-1} \times 1.2 hr} = 31.5\ mg/L$$

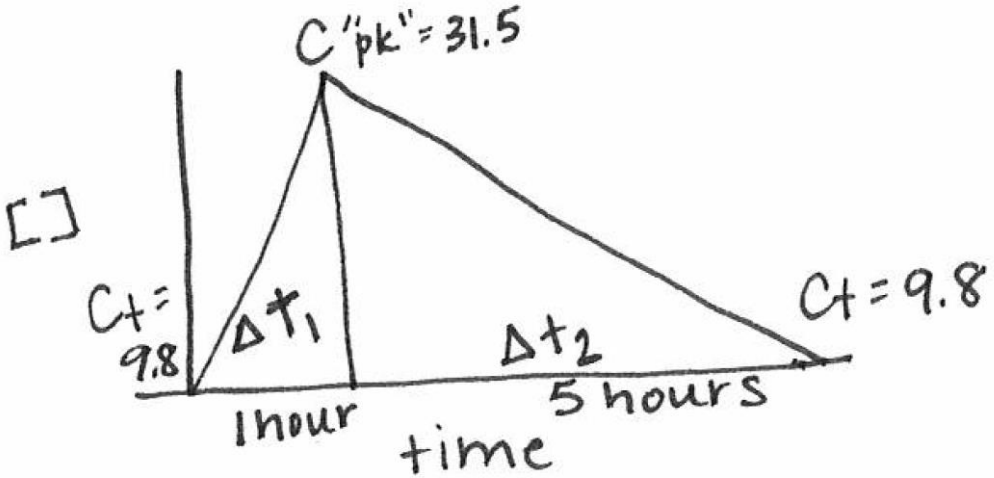
$$Vd = \frac{\text{Dose}}{K_e \times C_{pk\,x+inf}} \times \frac{(1 - e^{-K_e \times inf})}{(1 - e^{-K_e \times Tau})} = 11.8\ L = 0.614\ kg$$

$$AUC_{24} = \frac{320\ mg \times 4}{0.24 hr^{-1} \times 11.8\ L} \quad (CL = K_e \times Vd)$$

$$AUC = 452\ mg \cdot hr/L$$

Trapezoidal (will slightly under-predict)

using Ke & end of infusion concentration that we calculated for the other method:



$$AUC = \frac{C_t + C_{pk}}{2} \times \Delta t_1 + \frac{C_{pk} - C_t}{K_e}$$

$$= \frac{9.8 + 31.5}{2} \times 1 + \frac{31.5 - 9.8}{0.24}$$

$$= 20.7 \text{ mg·hr/L} + 90.4 \text{ mg·hr/L}$$

$$= \sim 111 \text{ mg·hr/L per dose}$$

$$\frac{111 \text{ mg·hr/L}}{\text{dose}} \times \frac{4 \text{ doses}}{\text{day}} = \sim 445 \text{ mg·hr/L}$$

Practical Considerations in AUC Estimation

- Sample timing
  - Post-distribution peak (consider venipuncture to avoid contamination)
  - Trough
- Increased # of samples?
  - Nursing education
  - Continue stewardship of monitoring
- All patients vs. selected patients: institution-specific
  - Patients with “low” initial trough
  - Complicated infection or expected long vancomycin duration
  - Process & education for practice change implementation
- No evidence yet for impact on outcomes when AUC monitoring is used

Pai MP et al. *Adv Drug Deliv Rev.* 2014;77:50-7.

Risks with Trough Concentrations < 10 mg/L

- 2009 Consensus Recommendations: "Moderate Evidence"
- In vitro evidence: MIC increases with
  - Exposure to 1 mg/L vs. 16 mg/L vancomycin
  - Pharmacodynamic model with troughs <10 mg/L and AUC <264
- Clinical evidence: trough evaluation only, no AUC
  - Dialysis patient case report
  - Initial trough <10 mg/L as predictor of heterogeneous vancomycin-intermediate *Staphylococcus* aureus (hVISA) (Gomes et al)
  - Patients with hVISA isolates and initial troughs <10 mg/L
    - Also high bacterial load

Gomes DM et al. *Pharmacotherapy*. 2015;35(4):424-432.
Rybak M et al. *Am J Health-Syst Pharm.* 2009; 66:82-98.
Sakoulas G et al. *J Infect Dis*. 2003;187(6):929-38.

Newer Options for Treatment of MRSA

Pharmacodynamics

AUC:MIC

T>MIC

C_{max}:MIC

AUC:MIC

Linezolid

PROS

- Antibiotic with most pediatric data
- HIGH enteral bioavailability
- Good tissue penetration
  - Including cerebrospinal fluid
  - Controversial whether superior to vancomycin for pneumonia
- Given orally or intravenously 2-3 times daily (age-dependent)

CONS

- Bacteriostatic
- Doesn't concentrate in blood
- Adverse effects more likely with long-term use (> 2 weeks)
  - Leukopenia, anemia, thrombocytopenia
  - Neuropathy
- Potential drug-drug interactions
  - Weak MAO-A inhibitor
- Cost/insurance considerations

Dotis J et al. *Int J Infect Dis*. 2010;14:e638-48.
Dryden MS. *J Antimicrob Chemother*. 2011;66(suppl 4):iv7-iv15.

When could linezolid therapy be considered?

A. Complicated MRSA pneumonia in a child who is not improving on vancomycin

B. Osteomyelitis in a child who developed acute kidney injury probably due to vancomycin

C. Pyomyositis with bacteremia caused by MRSA with a vancomycin MIC of 2 mg/L

D. All of the above

AUC:MIC

Tedizolid

PROS

- 91% orally bioavailable in adults
- Retains activity against certain linezolid resistance mechanisms
- Bactericidal in vivo
- Oral or intravenous
- Once daily administration
  - In adults

CONS

- No data in children to date
  - Adolescent exposure similar to adults (Phase 3 study underway)
  - Pediatric Phase I study ongoing
- Fewer gastrointestinal and myelosuppressive adverse effects than linezolid
- Retains risk for serotonergic drug-drug interactions

Bradley JS et al. *Pediatr Infect Dis J.* 201635(6):628-33.

Kisgen JJ et al. *Am J Health-Syst Pharm*. 2014;71:621-33.

T>MIC

Ceftaroline

PROS

- Bactericidal with affinity for PBP-2a
- Well tolerated
- Pediatric data available
  - Pharmacokinetic data
  - Randomized trials: skin & skin structure infections, pneumonia
  - Case reports
- Given 2-3 times/day
  - Every 8 hours in younger patients, more severe infections, cystic fibrosis

CONS

- Intravenous only
- Broad spectrum
  - *E. coli*, *Klebsiella* spp., *Enterobacter* spp., *Citrobacter*
  - *Haemophilus influenzae* & *Moraxella*
- Coombs' test positivity
  - No increase in observed hemolytic anemia
- Possibility of hypersensitivity

Cannavino CR et al. *Pediatr Infect Dis J.* 2016;35:752-0.
Korczowski B et al. *Pediatr Infect Dis J.* 2016;35:e239-47.
Saravolatz LD et al. *Clin Infect Dis*. 2011;52(9):1156-63.

AUC:MIC & Cmax:MIC

Dalbavancin

PROS

- Weekly dosing
- Increased potency vs MRSA
- Retains activity when susceptibility to vancomycin is reduced
- Adolescent & child PK studies
  - Higher dose per weight in infants

CONS

- Intravenous only
- Most studies in skin & skin structure infections
- Very limited pediatric data
- Difficult to determine impact on resistance to vancomycin

Bradley JS et al. *Pediatr Infect Dis J.* 2015;34(7):748-52.
Gonzalez D et al. *Pediatr Infect Dis J*. 2017;36(7):645-53.
Roberts KD et al. *Pharmacotherapy*. 2015;35(10):935-48.

Cmax:MIC

Telavancin

- Once daily, intravenous lipoglycopeptide
- PK study active, enrolling 3 mos – 17 years
- Insomnia & taste disturbance
- Use limited by:
  - Interference with coagulation tests
    - Can't be used with unfractionated heparin
  - REMS due to risk of harm to fetus if used during pregnancy
  - Increased mortality observed in patients with CrCl < 50 mL/min

Gostelow M et al. *Expert Rev Clin Pharmacol*. 2014;7(3)327-40.

Cmax:MIC

Oritavancin

- Ongoing Phase 1 study in patients < 18 years
- One-time IV dose approved for adults with acute bacterial skin and skin structure infection
  - Half-life of 8-10 days
- Drug-drug interactions mediated by cytochrome P450 enzymes
  - Inhibitor: 2C9 & 2C19
  - Inducer: 3A4 & 2D6
- Interferes with coagulation studies (aPTT, ACT)

Roberts KD et al. *Pharmacotherapy*. 2015;35(10):935-48.

AUC:MIC

Delafloxacin

- Broad-spectrum fluoroquinolone
  - Approved in 2017 for treatment of acute skin infections
  - Likely carries class-based risks
    - Development of resistance
    - Collateral damage
    - Muscular & neurologic effects
- Active against MRSA/MSSA, *Enterobacteriaceae*, & *Pseudomonas aeruginosa*
- Not studied in pediatrics

Baxdela (delafloxacin) prescribing information. Lincolnshire, IL: Melinta Therapeutics, Inc; June 2017.

AUC:MIC

Tigecycline

PROS

- Good tissue concentrations
- Can have bactericidal activity at certain concentrations
- 2 pediatric PK studies & 1 phase 2 study available

CONS

- Low blood concentrations
- Bacteriostatic
- Broad-spectrum
- Intravenous only
- Increased mortality observed
  - Not in IDSA MRSA guidelines for this reason

Gostelow M et al. *Expert Rev Clin Pharmacol*. 2014;7(3)327-40.

Liu C et al. *Clin Infect Dis.* 2011;52(3):e18-e55.

Key Takeaways

- Choice of optimal targeted MRSA therapy must take into account patient-specific characteristics and PK/PD needs
- AUC:MIC is the pharmacodynamic parameter most closely associated with efficacy for vancomycin
- Pediatric pharmacists should be aware of newer anti-MRSA therapies, including oxazolidinones, lipoglycopeptides, ceftaroline, and delafloxacin

Questions?

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