Antimicrobial Stewardship News

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Management of *Staphylococcus aureus* bacteremia in community hospitals

Introduction

Staphylococcus aureus is a leading cause of community-acquired and healthcare-associated bacteremia.[4,5] The 30-day all-cause mortality of *S. aureus* bacteremia (SAB) is 20%. In addition, SAB can lead to complex complications that could end in surgery, endocarditis, joint infections, and significant morbidity.[6] Appropriate management of SAB is complex, and infectious diseases (ID) consultation has been shown to improve clinical outcomes.[7-10] However, ID consultants are not readily available in all community hospitals.

A recent retrospective study compared SAB management at community hospitals to management at academic hospitals. Compliance with quality-of-care indicators, which have been shown to improve clinical outcomes, was lower in the community hospital setting (Table 1).[11] This newsletter describes key principles of SAB management, which can be applied by antimicrobial stewardship programs in community hospitals to improve patient care.

Table 1. Compliance with quality-of-care indicators for SAB by hospital setting

Variable	Academic Hospital (n=53)	Community Hospital (n=245)	p value
Remove central catheters	65%	46%	0.04
Follow-up blood cultures	96%	70%	< 0.001
TEE obtained	70%	13%	< 0.001
≥ 28 days of therapy if complicated	87%	62%	0.001
Met all criteria	91%	41%	< 0.001

TEE, transesophageal echocardiogram

***S. aureus* isolated from a blood culture should never be considered a contaminant**

Initial management of *Staphylococcus aureus* bacteremia (SAB)

Staphylococcus aureus isolated from a blood culture is never considered a contaminant, even if present in only one of two bottles. Failure to identify the primary source of infection and/or promptly administer effective therapy is associated with serious complications.[12] Therefore, all patients with SAB should undergo a thorough workup to rule out potential foci of infection and identify the primary source of bacteremia. Addressing the primary source or ongoing foci of infection is a critical component of SAB management, also known as "source control." Source control may require surgical intervention and/or device removal, which can involve risks but are essential for cure of infection and clearance of bacteremia. Stewardship programs are uniquely positioned to direct evidence-based management of SAB. Multiple studies have demonstrated improved compliance with quality-of-care indicators following implementation of a stewardship "bundle" or "checklist."[13-15] DASON encourages stewardship programs to adopt the following checklist (Table 2) as a tool to guide management of patients with SAB. Where available, early ID consultation is also recommended.

Table 2. Checklist for management of SAB

IDSA-recommended quality-of-care indicators[16]
▪ Intravenous vancomycin for MRSA ▪ Intravenous beta-lactam for MSSA
▪ Follow-up blood cultures every 2-4 days until documented clearance
▪ Early source control (i.e., draining abscess or removing infected prosthetic material)
▪ Echocardiography
▪ At least 2-4 weeks of intravenous therapy (based on complexity of infection, see Table 4)

MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*

When is endocarditis "ruled out"?

Because the diagnosis of infective endocarditis determines prognosis, monitoring, and treatment, the presence of infective endocarditis should be considered in all patients with SAB.[17] To "rule out" endocarditis, all patients with SAB should undergo echocardiography. The question of whether to pursue a transthoracic (TTE) or transesophageal echocardiogram (TEE) is an area of ongoing research. In general, TEE is preferred for most patients because of the better detection rates for infective endocarditis. However, a subgroup of patients at low risk for endocarditis demonstrate certain clinical features, as identified by Holland et al in a recent review. These clinical features are: 1) no permanent intracardiac device; 2) sterile follow-up blood cultures within 4 days after the initial set; 3) no hemodialysis; 4) nosocomial acquisition of SAB; and 5) no clinical signs of infective endocarditis.[17] TTE may be adequate for patients with all of these factors.

ALL patients with SAB should have a thorough work up to identify:
1. The primary source of *S. aureus*
2. Evidence of metastatic foci

What is the optimal therapy for SAB?

Appropriate agents for empiric treatment of invasive MRSA include vancomycin (preferred) and daptomycin (alternative for severe vancomycin allergy).[16] Once susceptibility results are available, if the isolate is MSSA, therapy should be de-escalated to a beta-lactam agent (nafcillin, oxacillin, or cefazolin).[16] Vancomycin is inferior to beta-lactams for treatment of MSSA.[1-3] Any penicillin allergy history should be carefully confirmed in order to optimize therapy choice for patients with MSSA bacteremia. Cefazolin challenge may be appropriate; see our June 2017 DASON Newsletter.

Oral stepdown therapy is not recommended for SAB. Fluoroquinolones, sulfamethoxazole-trimethoprim, and tigecycline should never be used as monotherapy. Preferred intravenous agents are shown in Table 3.

Vancomycin is INFERIOR to beta-lactams for treatment of MSSA.[1-3]

Table 3. Treatment options for *S. aureus* Bacteremia[16]

Organism	Drug	Dose*
MRSA	Vancomycin IV	Dose for trough level 15-20 mg/dL
	Daptomycin[1]	6-10 mg/kg IV daily
MSSA	Cefazolin	2 g IV q8h
	Nafcillin[2]	2 g IV q4h
	Oxacillin[2]	2 g IV q4h

*Doses listed are based on normal renal function
[1]Reserved for severe vancomycin allergy. Do not use for bacteremia associated with pneumonia.
[2]May be administered as a continuous infusion

What if the isolate has an MIC of 1.5 to 2 mcg/mL to vancomycin?

Vancomycin MICs of 1.5 to 2.0 are still within the susceptible range; however, some clinicians may be concerned about risks for vancomycin failure.[16,18,19] This scenario is directly addressed in the IDSA MRSA guidelines.[16] In general, the decision to switch to an alternative regimen should be guided by clinical response rather than the MIC result alone. For example, patients responding to vancomycin should not necessarily be switched to an alternative regimen on the basis of an MIC of 1.5 or 2. Alternatively, patients failing to respond to vancomycin (that is appropriately dosed) in the setting of adequate source control should be considered for an alternative regimen, regardless of the MIC. In the setting of treatment failure, consultation with an ID expert to select an alternative regimen is recommended.

When is it appropriate to use rifampin or an aminoglycoside?

There is no role for routine use of rifampin or an aminoglycoside in combination with antistaphylococcal penicillins or vancomycin for the treatment of SAB due to increased rates of toxicity. The combination of nafcillin and gentamicin has been associated with nephrotoxicity, and rifampin has been associated with hepatic adverse effects, drug interactions, and emergence of

resistance.[20-23] Combination therapy, however, may be useful in the presence of prosthetic material.

How long should patients with SAB be treated?

The optimal duration of therapy for SAB depends on management of the primary source and complexity of infection. In order to differentiate patients with uncomplicated bacteremia (who can be successfully managed with 2 weeks of therapy) from patients with complicated bacteremia (who require at least 4-6 weeks of therapy), a thorough workup must be performed.[16] In general, a patient may be presumed to have uncomplicated bacteremia if all of the criteria shown in Table 4 are met. Patients with SAB that do not meet all of these criteria should be presumed to have a deep focus of infection, warranting treatment for at least 4-6 weeks from the day of first negative blood cultures. A longer, diagnosis-directed duration may be necessary for some patients (e.g. osteomyelitis or endocarditis with *S. aureus* require a 6-week duration).

Table 4. Complicated versus uncomplicated SAB[16]

	Uncomplicated (ALL criteria must be met)	**Complicated**
Criteria	▪ Endocarditis ruled out ▪ No implanted prosthesis ▪ Cultures obtained 2-4 days after initial set are negative ▪ Defervescence within 72 hours of effective therapy ▪ No evidence of metastatic infection	▪ All cases not fulfilling criteria for uncomplicated SAB
Duration	▪ Minimum 2 weeks of IV therapy	▪ Minimum 4-6 weeks of IV therapy

Take Home Points:

- *Staphylococcus aureus* isolated from a blood culture should never be considered a contaminant.
- Management of SAB is complex and often requires a multidisciplinary approach.
- All patients with SAB should have a thorough work up to identify:
    1. The primary source of *S. aureus*
    2. Evidence of metastatic foci
- Stewardship programs are encouraged to implement an automatic infectious diseases consult and/or a SAB checklist to improve compliance with IDSA-recommended quality-of-care indicators (Table 2) and patient outcomes.
- Vancomycin is recommended first line for empiric treatment while susceptibilities are pending and for documented MRSA bacteremia.
- Nafcillin, oxacillin, and cefazolin are superior to vancomycin for MSSA bacteremia.
- Duration of treatment is determined by the primary source of *S. aureus* and if the patient meets criteria for uncomplicated SAB.

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