When are Oral Antibiotics a Safe and Effective Choice for Bacterial Bloodstream Infections? An Evidence-Based Narrative Review

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Bacterial bloodstream infections (BSIs) are a major cause of morbidity and mortality in the United States. Traditionally, BSIs have been managed with intravenous antimicrobials. However, whether intravenous antimicrobials are necessary for the entirety of the treatment course in BSIs, especially for uncomplicated episodes, is a more controversial matter. Patients that are clinically stable, without signs of shock, or have been stabilized after an initial septic presentation, may be appropriate candidates for treatment of BSIs with oral antimicrobials. There are risks and costs associated with extended courses of intravenous agents, such as the necessity for long-term intravenous catheters, which entail risks for procedural complications, secondary infections, and thrombosis. Oral antimicrobial therapy for bacterial BSIs offers several potential benefits. When selected appropriately, oral antibiotics offer lower cost, fewer side effects, promote antimicrobial stewardship, and are easier for patients. The decision to use oral versus intravenous antibiotics must consider the characteristics of the pathogen, the patient, and the drug. In this narrative review, the authors highlight areas where oral therapy is a safe and effective choice to treat bloodstream infection, and offer guidance and cautions to clinicians managing patients experiencing BSI. *Journal of Hospital Medicine* 2018;13:XXX-XXX. © 2018 Society of Hospital Medicine

Bacterial bloodstream infections (BSIs) are a major cause of morbidity and mortality in the United States. Approximately 600,000 BSI cases occur annually, resulting in 85,000 deaths,[1] at a cost exceeding $1 billion.[2] Traditionally, BSIs have been managed with intravenous antimicrobials, which rapidly achieve therapeutic blood concentrations, and are viewed as more potent than oral alternatives. Indeed, for acutely ill patients with bacteremia and sepsis, timely intravenous antimicrobials are lifesaving.[3]

However, whether intravenous antimicrobials are essential for the entire treatment course in BSIs, particularly for uncomplicated episodes, is controversial. Patients that are clinically stable or have been stabilized after an initial septic presentation may be appropriate candidates for treatment with oral antimicrobials. There are costs and risks associated with extended courses of intravenous agents, such as the necessity for long-term intravenous catheters, which entail risks for procedural complications, secondary infections, and thrombosis. A prospective study of 192 peripherally inserted central catheter (PICC) episodes reported an overall complication rate of 30.2%, including central line-associated BSIs (CLABSI) or venous thrombosis.[4] Other studies also identified high rates of thrombosis[5] and PICC-related CLABSI, particularly in patients with malignancy, where sepsis-related complications approach 25%.[6] Additionally, appropriate care of indwelling catheters requires significant financial and healthcare resources.

Oral antimicrobial therapy for bacterial BSIs offers several potential benefits. Direct economic and healthcare workforce savings are expected to be significant, and procedural and catheter-related complications would be eliminated.[7] Moreover, oral therapy provides antimicrobial stewardship by reducing the use of broad-spectrum intravenous agents.[8] Recent infectious disease "Choosing Wisely" initiatives recommend clinicians "prefer oral formulations of highly bioavailable antimicrobials whenever possible",[9] and this approach is supported by the Centers for Disease Control and Prevention antibiotic stewardship program.[10] However, the expected savings and benefits of oral therapy would be lost should they be less effective and result in treatment failure or relapse of the primary BSI. Pathogen susceptibility, gastrointestinal absorption, oral bioavailability, patient tolerability, and adherence with therapy need to be carefully considered before choosing oral antimicrobials. Thus, oral antimicrobial therapy for BSI should be utilized in carefully selected circumstances.

In this narrative review, we highlight areas where oral therapy is safe and effective in treating bloodstream infections, as well

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TABLE 1. **Penetration of Select Oral Antimicrobials to Tissue Sites**[7,44]

Antimicrobial	Bloodstream bioavailability	Lung	Liver	Urinary Tract	Prostate	Bone	GI	Skin	Bile	CSF	Synovial
Ciprofloxacin	70%	++	+++	+++	+++	+++	+++	+++	+++	+	+++
Levofloxacin	99%	+++	+++	+++	+++	+++	+++	+++	+++	+	+++
Moxifloxacin	90%	+++	+++	+++	+++	+++	+++	+++	+++	+	+++
Trimethoprim-Sulfamethoxazole	90%	++	++	+++	++	++	++	+++	++	+	++
Doxycycline	95%	++	++	++	++	++	++	++	++	+	++
Minocycline	95%	++	++	++	++	++	++	++	++	+	++
Linezolid	99%	+++	++	+++	++	++	++	+++	++	++	++
Metronidazole	90%	++	+++	++	++	++	++	++	++	++	++
Clindamycin	90%	++	++	++	++	++	++	++	++	+	++
Ampicillin	50%	+	++	++	+	++	++	++	++	++	+
Penicillin V	50%	++	++	++	+	++	++	++	++	++	+
Amoxicillin	85%	+	++	++	+	++	++	++	++	++	+
Cephalexin	60%	++	++	++	++	++	++	++	++	+	++

+++ Tissue concentrations equal to or higher than serum concentrations

++ Tissue concentrations at least 50% of the serum concentrations

+ Tissue concentrations less than 50% of the serum concentrations

Bioavailability represents the percentage of the dose that reaches systemic circulation. Tissue penetration reflects the drug movement from the vascular to the interstitial and intracellular compartments of a particular body site. Drugs passively diffuse through fenestrated capillaries into the interstitial compartment of most tissues. However, some tissue sites (eg, the brain and prostate) contain nonfenestrated capillaries and/or active transport pumps that prevent entry or remove the drug. Tissue concentrations are methodologically dependent on the various techniques used in their quantification, and, in some body sites, are influenced by the presence or absence of inflammation (eg, brain tissue). Thus, the values presented here are best approximations.

as offer guidance to clinicians managing patients experiencing BSI. Given the lack of robust clinical trials on this subject, the evidence for performing a systematic review was insufficient. Thus, the articles and recommendations cited in this review were selected based on the authors' experiences to represent the best available evidence.

INFECTION SOURCE CONTROL

Diagnosing the source of a patient's BSI is vital to successful treatment for 2 reasons. First, without achieving source control, antimicrobial therapy of any sort is more likely to fail.[7] For example, patients with *Staphylococcus aureus* abscess and persistently positive blood cultures despite intravenous antimicrobials require drainage. Similarly, patients with a CLABSI typically benefit from removal of the foreign body.[11] Second, particular oral antibiotics have different penetration levels into various tissues (Table 1).[12] For instance, if a patient has meningitis due to *Streptococcus pneumoniae* with concurrent BSI, doxycycline would be an inferior choice, despite having good bioavailability and achieving high blood concentrations, because it poorly penetrates the central nervous system. An oral regimen must adequately penetrate the source of infection.

PATHOGEN AND ANTIMICROBIAL FACTORS

Several important factors regarding the BSI pathogen should be considered when deciding on oral versus intravenous therapy, as follows: 1) organism speciation and susceptibilities should be available; 2) the pathogen should be susceptible to an oral antimicrobial with high bioavailability that achieves adequate blood and source-tissue concentrations; 3) the candidate antibiotic should have a high barrier to acquired resistance for the pathogen. For example, although *S. aureus* is often susceptible to rifampin, it has a low genetic barrier to resistance; thus, rifampin monotherapy is not recommended; and 4) the selected agent should generally be well-tolerated and have an acceptable safety profile. Table 2 summarizes the characteristics of several key antibiotics.

PATIENT FACTORS

Although the causative pathogen may be susceptible to an oral antibiotic with favorable pharmacokinetics, several patient factors need to be considered. The patient should: 1) have no allergies or intolerances to the selected agent; 2) be physically able to swallow the medication or have a working gastric or jejunal tube in place, as well as have no significant impairment in gastrointestinal absorption; 3) have a history of adherence to oral therapy, particularly if the regimen is dosed multiple times per day, and should be appropriately educated and able to demonstrate understanding of the importance of adherence; 4) take no other medications that may significantly interact with the antibiotic; and 5) be able to immediately access the oral agent upon discharge from the hospital. Some medical facilities are able to provide new medications to the patient before discharge, ensuring availability of oral antibiotic therapy as an

TABLE 2. **Selected Oral Antibiotics**

Antibiotic	Typical Oral Dose[a]	Dietary Interaction	Notable Side Effects	Approx. Cost per Day[b]
Ciprofloxacin	500–750 mg BID	Decreased by concurrent calcium/magnesium/aluminum intake. Take 2 hours before or 6 hours after intake of antacids, dairy, or calcium-fortified food.	Black Box Warning: potentially irreversible serious adverse reactions include tendinitis, tendon rupture, peripheral neuropathy, and CNS effects QTc interval prolongation Hypoglycemia	$10.90
Levofloxacin	500–750 mg daily			$24.61
Moxifloxacin	400 mg daily	No recommendations		$26.77
Linezolid	600 mg BID	Concurrent ingestion of foods rich in certain amino acids (eg, tyramine) such as red wine or aged cheese can precipitate hypertensive crisis	Myelosuppression Serotonin syndrome (avoid other proserotonergic drugs) Peripheral/optic neuropathy	$366.00
Metronidazole	500 mg TID	No recommendations	Black Box Warning: possibly carcinogenic (based on animal data) Disulfiram reaction with alcohol use Neurotoxicity	$4.02
Trimethoprim-sulfamethoxazole	160 mg/800 mg (DS tablet) 1–2 tablets BID	No recommendations	Hypersensitivity to sulfa-drugs Blood dyscrasias Severe dermatologic reactions Hyperkalemia	$2.18
Clindamycin	300–450 mg QID	Take with food	Black Box Warning: Risk for severe *C. difficile* infection Gastrointestinal upset Large pill with unpleasant taste	$9.52
Doxycycline	100 mg BID	Decreased by concurrent calcium and/or high-fat foods and high gastric pH. Avoid taking with antacids, dairy, or calcium-fortified food.	Photosensitivity Esophagitis if not taken with water	$12.30
Minocycline		No recommendations	Photosensitivity Esophagitis if not taken with water Autoimmune syndromes Hyperpigmentation Vertigo	$6.79
Most β-lactams such as ampicillin or dicloxacillin	Not typically recommended for BSI	Penicillin should be taken on an empty stomach	N/A	N/A
Amoxicillin	1g TID	No recommendations	Hypersensitivity Rash	$2.98
Cephalexin	Not typically recommended for BSI	N/A	N/A	N/A

White denotes best evidence for treating select BSIs.

Light yellow denotes antimicrobials with a good bioavailability profile, but minimal data for use in BSI.

Dark yellow denotes antimicrobials with a poor bioavailability profile; these are included to highlight the risks of using such agents for BSI.

[a]Assuming normal renal function. Unless bioavailability is 100%, the doses recommended here, in the context of treating BSI, are often higher than for other indications, given the need to achieve adequate blood concentrations. Doses adapted from reference 44.

[b]Cost per day based on the 2017 average wholesale price (AWP). AWP refers to the average price pharmacies pay for drugs from their wholesale distributors. The price that patients pay will vary depending upon prescription markups and insurance coverage, although in most instances, AWP would be the bare minimum.

outpatient.[13] 6) Finally, the patient should be available for close follow-up. Table 3 summarizes the patient factors to consider.

EVIDENCE REGARDING BLOODSTREAM INFECTIONS DUE TO GRAM-NEGATIVE RODS

BSIs due to gram-negative rods (GNRs) are common and cause significant morbidity and mortality. GNRs represent a broad and diverse array of pathogens. We focus on the *Enterobacteriaceae* family and *Pseudomonas aeruginosa*, because they are frequently encountered in clinical practice.[1]

Gram-Negative Rods, *Enterobacteriaceae* Family

The *Enterobacteriaceae* family includes *Escherichia coli*, *Klebsiella*, *Salmonella*, *Proteus*, *Enterobacter*, *Serratia*, and *Citrobacter* species. The range of illnesses caused by *Enterobacteriaceae* is as diverse as the family, encompassing most body sites.

TABLE 3. **Checklist for Using an Oral Antibiotic for Bloodstream Infection**

Bacterial/Antimicrobial Factors	
[ ]	Speciation and susceptibilities are available
[ ]	Susceptibilities indicate an oral antibiotic is effective against the pathogen
[ ]	Oral agent is highly bioavailable
[ ]	Oral agent has a low acquired-resistance potential for the given pathogen
[ ]	Oral agent is well-tolerated and has an acceptable safety profile for the patient (Table 2)
[ ]	No serious drug–drug interactions between the selected agent and other medications
Patient Factors	
[ ]	No allergies or intolerances to the selected agent
[ ]	No impaired gastrointestinal absorption
[ ]	Hemodynamically stable
[ ]	Minimal compliance concerns
[ ]	Patient has received appropriate education and demonstrated understanding regarding importance of compliance
[ ]	Dietary interactions considered (Table 2)
[ ]	Underlying source of bloodstream infection identified and controlled
[ ]	Upon discharge, patient has access to the oral agent
[ ]	• The pharmacy has the agent available
[ ]	• The patient is able to get medication from pharmacy before the next dose is due
[ ]	• Medication copay at the pharmacy is affordable
[ ]	Available for follow-up

Although most *Enterobacteriaceae* are intrinsically susceptible to antibiotics, there is potential for significant multi-drug resistance. Of particular recent concern has been the emergence of *Enterobacteriaceae* that produce extended-spectrum β-lactamases (ESBL) and even carbapenem-resistant strains.[14]

However, *Enterobacteriaceae* species susceptible to oral antimicrobials are often suitable candidates for oral BSI therapy. Among 106 patients with GNR BSI treated with a highly bioavailable oral antibiotic (eg, levofloxacin), the treatment failure rate was only 2% (versus 14% when an antimicrobial with only moderate or low bioavailability was selected).[15] Oral treatment of *Enterobacteriaceae* BSIs secondary to urinary tract infection has been best studied. A prospective randomized, controlled trial evaluated oral versus intravenous ciprofloxacin amongst 141 patients with severe pyelonephritis or complicated urinary tract infections, in which the rate of bacteremia was 38%.[16] Notably, patients with obstruction or renal abscess were excluded from the trial. No significant differences in microbiological failure or unsatisfactory clinical responses were found between the IV and oral treatment groups. Additionally, a Cochrane review reported that oral antibiotic therapy is no less effective than intravenous therapy for severe UTI, although data on BSI frequency were not provided.[17]

Resistance to fluoroquinolones such as ciprofloxacin has been identified as a risk factor for GNR BSI oral treatment failure, highlighting the importance of confirming susceptibilities before committing to an oral treatment plan.[18,19] Even ESBL *Enterobacteriaceae* can be considered for treatment with fluoroquinolones if susceptibilities allow.[20]

The ideal duration of therapy for GNR BSI is an area of active research. A recent retrospective trial showed no difference in all-cause mortality or recurrent BSI in GNR BSI treated for 8 versus 15 days.[21] A recent meta-analysis suggested that 7 days of therapy was noninferior to a longer duration therapy (10–14 days) for pyelonephritis, in which a subset was bacteremic.[22] However, another trial reported that short course therapy for GNR BSI (<7 days) is associated with higher risk of treatment failure.[22] Further data are needed.

Gram-Negative Rods, *Pseudomonas aeruginosa*

Pseudomonas aeruginosa is a common pathogen, intrinsically resistant to many antimicrobials, and readily develops antimicrobial resistance during therapy. Fluoroquinolones (such as ciprofloxacin, levofloxacin, and delafloxacin) are the only currently available oral agents with antipseudomonal activity. However, fluoroquinolones may not achieve blood concentrations appropriate for *P. aeruginosa* treatment at standard doses, while higher dose regimens may be associated with increased risk for undesirable side effects.[24,25] Currently, given the minimal trial data comparing oral versus intravenous therapy for *P. aeruginosa* BSIs, and multiple studies indicating increased mortality when *P. aeruginosa* is treated inappropriately,[26,27] we prefer a conservative approach and consider oral therapy a less-preferred option.

EVIDENCE REGARDING BLOODSTREAM INFECTIONS DUE TO GRAM-POSITIVE COCCI

The majority of bloodstream infections in the United States, and the resultant morbidity and mortality, are from gram-positive cocci (GPCs) such as *Staphylococcus*, *Streptococcus*, and *Enterococcus* species.[1]

Gram-Positive Cocci, *Streptococcus pneumoniae*

Of the approximately 900,000 annual cases of *S. pneumoniae* infection in the United States, approximately 40,000 are complicated by BSI, with 70% of those cases being secondary to pneumococcal pneumonia.[28] In studies on patients with pneumococcal pneumonia, bacteremic cases generally fare worse than those without bacteremia.[29,30] However, several trials demonstrated comparable outcomes in the setting of bacteremic pneumococcal pneumonia when switched early (within 3 days) from intravenous to oral antibiotics to complete a 7-day course.[31,32] Before pneumococcal penicillin resistance became widespread, oral penicillin was shown to be effective, and remains an option for susceptible strains.[33] It is worth noting, however, that other trials have shown a mortality benefit from treating bacteremic pneumococcal pneumonia initially with dual-therapy including a β-lactam and macrolide such as azithromycin. This observation highlights the importance

of knowing the final susceptibility data prior to consolidating to monotherapy with an oral agent, and that macrolides may have beneficial anti-inflammatory effects, though further research is needed.[34,35]

Although the evidence for treating bacteremic pneumococcal pneumonia using a highly active and absorbable oral agent is fairly robust, *S. pneumoniae* BSI secondary to other sites of infection sites is less well studied and may require a more conservative approach.

Gram-Positive Cocci, β-hemolytic Streptococcus species

β-Hemolytic *Streptococci* include groups A to H, of which groups A (*S. pyogenes*) and B (*S. agalactiae*) are the most commonly implicated in BSIs.[36] Group A *Streptococcus* (GAS) is classically associated with streptococcal pharyngitis and Group B *Streptococcus* (GBS) is associated with postpartum endometritis and neonatal meningitis, though both are virulent organisms with a potential to cause invasive infection throughout the body and in all age-groups. Up to 14% of GAS and 41% GBS BSIs have no clear source;[37,38] given these are skin pathogens, such scenarios likely represent invasion via microabrasion. As β-hemolytic streptococcal BSI is often observed in the context of necrotizing skin and soft tissue infections, surgical source control is particularly important.[39] GAS remains exquisitely susceptible to penicillin, and intravenous penicillin remains the mainstay for invasive disease; GBS has higher penicillin resistance rates than GAS.[40] Clindamycin should be added when there is concern for severe disease or toxic shock.[41] Unfortunately, oral penicillin is poorly bioavailable (approximately 50%), and there has been recent concern regarding inducible clindamycin resistance in GAS.[42] Thus, oral penicillin V and/or clindamycin is a potentially risky strategy, with no clinical trials supporting this approach; however, they may be reasonable options in selected patients with source control and stable hemodynamics. Amoxicillin has high bioavailability (85%) and may be effective; however, there is lack of supporting data. Highly bioavailable agents such as levofloxacin and linezolid have GAS and GBS activity[43] and might be expected to produce satisfactory outcomes. Because no clinical trials have compared these agents with intravenous therapy for BSI, caution is advised. Although bacteriostatic against *Staphylococcus*, linezolid is bactericidal against *Streptococcus*.[44] Fluoroquinolone resistance amongst β-hemolytic *Streptococcus* is rare (approximately 0.5%) but does occur.[45]

Gram-Positive Cocci, *Staphylococcus* Species

Staphylococcus species include *S. aureus* (including methicillin susceptible and resistant strains: MSSA and MRSA, respectively) and coagulase-negative species, which include organisms such as *S. epidermidis*. *S. aureus* is the most common cause of BSI mortality in the United States,[1] with mortality rates estimated at 20%–40% per episode.[46] Infectious disease consultation has been associated with decreased mortality and is recommended.[47] The guidelines of the Infectious Diseases Society of America for the treatment of MRSA recommend the use of parenteral agents for BSI.[48] It is important to consider if a patient with *S. aureus* BSI has infective endocarditis.

Oral antibiotic therapy for *S. aureus* BSI is not currently standard practice. Although trimethoprim-sulfamethoxazole (TMP-SMX) has favorable pharmacokinetics and case series of using it successfully for BSI exist,[49] TMP-SMX showed inferior outcomes in a randomized trial comparing oral TMP-SMX with intravenous vancomycin in a series of 101 *S. aureus* infections.[50] This observation has been replicated.[51] Data on doxycycline or clindamycin for *S. aureus* BSI are limited, and IDSA guidelines advise against their use in this setting because they are predominantly bacteriostatic.[48] Linezolid has favorable pharmacokinetics, with approximately 100% bioavailability, and *S. aureus* resistance to linezolid is rare.[52] Several randomized trials have compared oral linezolid with intravenous vancomycin for *S. aureus* BSI; for instance, Stevens et al. randomized 460 patients with *S. aureus* infection (of whom 18% had BSI) to linezolid versus vancomycin and observed similar clinical cure rates.[53] A pooled analysis showed oral linezolid was noninferior to vancomycin specifically for *S. aureus* BSI.[54] However, long-term use is often limited by hematologic toxicity, peripheral or optic neuropathy (which can be permanent), and induced serotonin syndrome. Additionally, linezolid is bacteriostatic, not bactericidal against *S. aureus*. Using oral linezolid as a first-line option for *S. aureus* BSI would not be recommended; however, it may be used as a second-line treatment option in selected cases. Tedizolid has similar pharmacokinetics and spectrum of activity with fewer side effects; however, clinical data on its use for *S. aureus* BSI are lacking.[55] Fluoroquinolones such as levofloxacin and the newer agent delafloxacin have activity against *S. aureus*, including MRSA, but on-treatment emergence of fluoroquinolone resistance is a concern, and data on delafloxacin for BSI are lacking.[56,57] Older literature suggested the combination of ciprofloxacin and rifampin was effective against right-sided *S. aureus* endocarditis,[58] and other oral fluoroquinolone-rifamycin combinations have also been found to be effective[59] However, this approach is currently not a standard therapy, nor is it widely used. Decisions on the duration of therapy for *S. aureus* BSI should be made in conjunction with an infectious diseases specialist; 14 days is currently regarded as a minimum.[47,48]

Published data regarding oral treatment of coagulase-negative *Staphylococcus* (CoNS) BSI are limited. Most CoNS bacteremia and up to 80% *Staphylococcus epidermidis* bacteremia represent blood culture contamination, though true infection from CoNS is not uncommon, particularly in patients with indwelling catheters.[60] An exception is the CoNS species *Staphylococcus lugdunensis*, which is more virulent, and bacteremia with this organism usually warrants antibiotics. Oral antimicrobial therapy is currently not a standard treatment practice for CoNS BSI that is felt to represent true infection; however, linezolid has been successfully used in case series.[61]

Gram-Positive Cocci, *Enterococcus*

E. faecium and *E. faecalis* are commonly implicated in BSI.[1] Similar to *S. aureus*, infective endocarditis must be ruled out when treating enterococcus BSI; a scoring system has been

proposed to assist in deciding if such patients require echocardiography.[62] Intravenous ampicillin is a preferred, highly effective agent for enterococci treatment when the organism is susceptible.[44] However, oral ampicillin has poor bioavailability (50%), and data for its use in BSI are lacking. For susceptible strains, amoxicillin has comparable efficacy for enterococci and enhanced bioavailability (85%); high dose oral amoxicillin could be considered, but there is minimal clinical trial data to support this approach. Fluoroquinolones exhibit only modest activity against enterococci and would be an inferior choice for BSI.[63] Although often sensitive to oral tetracyclines, data on their use in enterococcal BSI are insufficient. Nitrofurantoin can be used for susceptible enterococcal urinary tract infection; however, it does not achieve high blood concentrations and should not be used for BSI.

There is significant data comparing oral linezolid with intravenous daptomycin for vancomycin-resistant enterococci (VRE) BSI. In a systematic review including 10 trials using 30-day all-cause mortality as the primary outcome, patients treated with daptomycin demonstrated higher odds of death (OR 1.61, 95% CI 1.08–2.40) compared with those treated with linezolid.[64] However, more recent data suggested that higher daptomycin doses than those used in these earlier trials resulted in improved VRE BSI outcomes.[65] A subsequent study reported that VRE BSI treatment with linezolid is associated with significantly higher treatment failure and mortality compared with daptomycin therapy.[66] Further research is needed, but should the side-effect profile of linezolid be tolerable, it remains an effective option for oral treatment of enterococcal BSIs.

EVIDENCE REGARDING ANAEROBIC BACTERIAL BLOOD STREAM INFECTION

Anaerobic bacteria include *Bacteroides*, *Prevotella*, *Porphyromonas*, *Fusobacterium*, *Peptostreptococcus*, *Veillonella*, and *Clostridium*. Anaerobes account for approximately 4% of bacterial BSIs, and are often seen in the context of polymicrobial infection.[67] Given that anaerobes are difficult to recover, and that antimicrobial resistance testing is more labor intensive, antibiotic therapy choices are often made empirically.[67] Unfortunately, antibiotic resistance amongst anaerobes is increasing.[68] However, metronidazole remains highly active against a majority of anaerobes, with only a handful of treatment failures reported,[69] and has a highly favorable pharmacokinetic profile for oral treatment. Oral metronidazole remains an effective choice for many anaerobic BSIs. Considering the polymicrobial nature of many anaerobic infections, source control is important, and concomitant GNR infection must be ruled out before using metronidazole monotherapy.

Clindamycin has significant anaerobic activity, but *Bacteroides* resistance has increased significantly in recent years, as high as 26%-44%.[70] Amoxicillin-clavulanate has good anaerobic coverage, but bioavailability of clavulanate is limited (50%), making it inferior for BSI. Bioavailability is also limited for cephalosporins with anaerobic activity, such as cefuroxime. Moxifloxacin is a fluoroquinolone with some anaerobic coverage and a good oral pharmacokinetic profile, but *Bacteroides* resistance can be as high as 50%, making it a risky empiric choice.[68]

CONCLUSIONS

Bacterial BSIs are common and result in significant morbidity and mortality, with high associated healthcare costs. Although BSIs are traditionally treated with intravenous antimicrobials, many BSIs can be safely and effectively cured using oral antibiotics. When appropriately selected, oral antibiotics offer lower costs, fewer side effects, promote antimicrobial stewardship, and are easier for patients. Ultimately, the decision to use oral versus intravenous antibiotics must consider the characteristics of the pathogen, patient, and drug.

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