Catheter-Related Bloodstream Infections

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ABSTRACT

Tunneled, cuffed, double-lumen catheters are commonly used for long-term venous access in hemodialysis patients. Complications of these catheters, including catheter-related infection, are a major cause of morbidity and resource utilization in the hemodialysis population. Treatment of catheter-related bloodstream infections includes the use of antibiotics and evaluation of the need for catheter removal or exchange. Measures to prevent catheter-related infections include use of an aseptic technique and antiseptic cleaning solution, elimination of *Staphylococcus aureus* nasal carriage, topical exit site application of antibiotics, use of antibiotic lock solutions, and use of catheters and cuffs coated or impregnated with antimicrobial or antiseptic agents. This review article will provide an update on the prevalence, diagnosis, treatment, and prevention of catheter-related infections in the hemodialysis population.

KEYWORDS: Hemodialysis catheters, catheter-related infection, antibiotic prophylaxis

Objectives: Upon completion of this article, the reader should know about the prevention, diagnosis, and management of catheter-related bloodstream infections.

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Tunneled, cuffed, double-lumen catheters are commonly used for long-term venous access in hemodialysis patients despite recommendations of professional organizations to limit such use.¹ From 1995 to 1999 the use of these catheters increased from 12.7% to 22.2%.² Complications of these catheters, including catheter-related infection, are a major cause of morbidity and resource utilization in the hemodialysis population. The epidemiology, cost, diagnosis, treatment, and prevention of such infections will be discussed in this article.

There are various types of catheter-related infections including localized infections, exit site infections, tunneled infections, pocket infections, and bloodstream infections (Table 1).³ The risk of infection with catheters

is much higher than with arteriovenous (AV) fistulas with a relative risk for bacteremia in patients with hemodialysis catheters almost 10-fold the risk.⁴ A prospective study of 101 hemodialysis patients with venous catheters followed over a 24-month period found that the risk of bacteremia with tunneled cuffed venous catheters averaged 5.5 episodes per 1000 catheter days.⁵ Rates as low as 1 episode per 1000 catheter days have been achieved with strict catheter protocols.⁶

There is a large economic and clinical impact of catheter-related infections in hemodialysis patients which has been quantified by various studies. One study looked at the average cost for male patients on hemodialysis at a VA hospital studied over a 12-month period

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Table 1 Various Types of Catheter-Related Infections

Type of Infection	Description
Localized infection	>15 CFU cultured from the catheter tip or subcutaneous segment of catheter, or catheter hub
Exit site infection	Erythema or induration within 2 cm of exit site in the presence or absence of coexistent bloodstream infection
Tunneled infection	Tenderness, erythema, or induration >2 cm from exit site along subcutaneous tract of the tunnel with or without evidence of blood stream infection
Pocket infection	Infected fluid in the subcutaneous pocket of a totally implantable intravascular device
Catheter-related bloodstream infection	Bacteremia in a patient with intravascular device without other obvious source

CFU, colony forming units.
Adapted from Ref.3.

with catheter-related infection. The cost was estimated at \$23,451 per hospitalization.⁷ Other studies have examined the clinical impact of catheter-related infections in hemodialysis patients including the risk of metastatic complications, prolonged hospitalization, and mortality. A retrospective cohort study of 22,130 hospitalizations of dialysis patients with septicemia showed an overall death rate of 34% at 12-week follow-up.⁸ Another study reported a 21% complication rate in patients with *Staphylococcus aureus* (*S. aureus*) bacteremia with an average hospital stay of 13 days.⁹

Gram-positive organisms are the most common cause of catheter-related infections, with both coagulase negative staphylococcus and *S. aureus* accounting for the majority of cases. The remaining infections are due to enterococci, aerobic gram-negative rods, and fungal species.¹⁰ Methods available to diagnose catheter-related infections include culture of the catheter tip, quantitative blood cultures, and time to positivity of cultures taken from the catheter and a peripheral site. Clinical findings, including fever, redness, or tenderness at catheter site are unreliable for the diagnosis of catheter-related infection due to poor sensitivity and specificity.¹¹ Two sets of blood cultures (one from the catheter and one from a peripheral site) should be drawn on all patients with suspected catheter-related infection.³ Paired quantitative blood cultures from the catheter site and peripheral site are the most accurate test for diagnosis of bloodstream infection based upon a 2005 meta-analysis.¹² With this method, when the blood obtained from the central venous catheter yields a colony count 5- to 10-fold

greater than the peripheral sample it is predictive of catheter-related bloodstream infection.¹³ If quantitative blood cultures are not performed in the laboratory evaluating the time it takes blood cultures from the catheter and peripheral site to turn positive can also be useful in aiding diagnosis. Catheter-related bacteremia is likely when the sample taken from the catheter reveals earlier growth than the sample taken from the peripheral vein. One retrospective study showed that a catheter blood culture that turned positive at least 2 hours prior to a peripheral blood culture has a sensitivity of 91% and specificity of 94% in identifying catheter-related bloodstream infection.¹⁴ Catheter tips can also be submitted to the laboratory for evaluation in the diagnosis of catheter-related infection. A catheter tip culture is considered to be significant for bacterial colonization if semiquantitative culture yields >15 colony forming units (CFU).¹⁵ The clinical usefulness of catheter tip cultures in the hemodialysis population, however, has come into question with a recent study showing that catheter tip cultures did not alter management in the treatment of presumed tunneled hemodialysis catheter infections.¹⁶

Significant risk factors for bacteremic episodes in hemodialysis patients with long-term tunneled catheters include diabetes, peripheral atherosclerosis, a previous history of bacteremia, nasal carriage of *S. aureus*, longer catheter use duration, more frequent urokinase catheter infusion, higher total intravenous iron dose, and local infection.¹⁷ Treatment of catheter-related infections includes the use of antibiotics and evaluating the need for catheter removal. Initial empiric therapy is based upon the severity of disease, risk factors for infection, and the likely pathogens. Vancomycin is recommended as first-line therapy in those hospitals with an increased incidence of methicillin-resistant staphylococci.³ Additional empiric coverage for gram-negative organisms with an aminoglycoside or cephalosporin may be needed in patients who are severely ill. Medications should be adjusted after culture and sensitivity results are known. Use of vancomycin for methicillin-susceptible *S. aureus* is not recommended due to higher failure rates and increasing incidence of infections with vancomycin-resistant enterococci. In cases of infection with known methicillin-susceptible gram-positive organisms antibiotics should be changed to cefazolin or nafcillin. There is no compelling data regarding specific recommendations for duration of treatment. In clinical practice patients with uncomplicated infections are commonly treated with a 2-week course of antibiotics; those patients with infections complicated by metastatic disease or persistent bacteremia can be treated with courses ranging from 4 to 8 weeks.³ There is no adequate data to aid clinicians in the decision of when to place a new long-term catheter in patients whose catheter has been removed for catheter-related bloodstream infection. Factors affecting whether or not a dialysis catheter should be removed

in the face of catheter-related infection include location of the infection, clinical response to treatment, presence of metastatic complications, and infecting agent. Dialysis catheters should be removed in patients who remain febrile after 48 hours of appropriate treatment, who have persistently positive blood cultures while on appropriate antibiotic therapy, have evidence of a tunnel infection, have evidence of an infected thrombus, or have evidence of metastatic complications including endocarditis and osteomyelitis.³ Infection with certain organisms, such as *Candida* species, gram-negative organisms, and *S. aureus* should also prompt evaluation for catheter removal, as higher treatment failure rates are likely if the catheter is left in place.^{18,19} Patients who do not meet these criteria can have a trial of catheter salvage or exchange.

Options for catheter site salvage include treatment with intravenous antibiotics alone, systemic antibiotics in addition to an antibiotic lock solution, and catheter exchange over a guide wire. Many studies have evaluated attempted catheter salvage using intravenous (IV) antibiotics alone and have shown varying success rates. In patients with evidence of intraluminal infection, the addition of high concentrations of antibiotics into the catheter lumen may increase catheter salvage success rates.²⁰ This method can be considered in patients who are afebrile within 48 hours and who are clinically stable.² However, some organisms may be difficult to eradicate even with using the antibiotic lock solution. One study looking specifically at catheter salvage in hemodialysis patients with *S. aureus* bacteremia showed treatment failure in 59% of patients and increased risk of serious complications in patients with persistent fever.¹⁹ Catheter exchange over a guide wire in addition to systemic antibiotics is another option that has been evaluated in patients with hemodialysis catheter related bacteremia. Studies that have included patients who are afebrile after 48 hour of antibiotic therapy, clinically stable, and have no evidence of tunnel tract involvement, have shown infection-free catheter survival in 80% of patients at 90 days.²¹⁻²³ Catheter retention or exchange should not be attempted in patients with catheter-related candidemia as retention of the catheter has been shown to lead to prolonged periods of candidemia and poorer clinical outcomes.²⁴

The formal guidelines from the Infectious Disease Society of America, which were prepared in part by representatives from the Society of Interventional Radiology, recommend the following approach to the management of hemodialysis catheter-related bloodstream infections.^{3,25}

- Antibiotic lock therapy is recommended when the hemodialysis catheter is retained and should be used for 2 weeks with standard systemic therapy for uncomplicated catheter infections.

- The catheter should be removed for complicated infections including metastatic disease, tunnel infection, and port abscess.
- The catheter should be removed for infections with *Candida* species and treatment with antifungal therapy should continue for 14 days after the last positive blood culture.
- Strong consideration should be given for catheter removal for infections with *S. aureus*, though catheter salvage may be attempted in certain circumstances.
- Strong consideration should be given for catheter removed for infections with gram negative organisms though catheter salvage can be attempted in certain circumstances.
- The catheter may be retained for infection with coagulase-negative staphylococcus.
- If catheter salvage is attempted, the catheter should be removed if there is clinical deterioration, relapsing, or persistently positive blood cultures.

The clinical practice recommendation from the 2006 Kidney Disease Outcomes Quality Initiative (K/DOQI) agree with the removal of catheters in patients with evidence of a tunnel infection or who are clinically unstable. The guidelines also support consideration of catheter salvage with the use of an antibiotic lock solution in patients who are afebrile within 48 hours and clinically stable.¹ In other patients it is recommended that catheter exchange occur within 72 hours of initiating antibiotic therapy.¹

Various methods have been used to try and decrease the rate of catheter-related infections in hemodialysis patients. Prophylactic antibiotics at the time of placement of a tunneled catheter in interventional radiology are commonly given as a regimen of one gram IV cefazolin though data are lacking and the benefit of this prophylaxis has never been validated in randomized controlled trials.²⁶ Other methods include the use of an aseptic technique and an antiseptic cleaning solution at the time of insertion of the catheter, elimination of *S. aureus* nasal carriage, topical exit site application of antibiotics, use of antibiotic lock solutions, and use of catheters and cuffs that are coated or impregnated with antimicrobial or antiseptic agents. Maximum sterile barrier precautions, including cap, mask, gown, gloves, and drape, should be used during the insertion of hemodialysis catheters to decrease the incidence of catheter-related bloodstream infections.¹⁰ An antiseptic should also be used for cleansing the catheter insertion sites. Povidone iodine is commonly used, though one study has shown the preparation of catheter sites with 2% aqueous chlorhexidine gluconate reduced bloodstream infection rates compared with the use of povidone iodine or 70% alcohol.²⁷ Antibiotic therapy to decrease nasal carriage of *S. aureus* has led to fewer access-related infections, though this strategy is limited

by increasing resistance of organisms to chronic antibiotic use.²⁸ Two recent meta-analyses showed that topical antibiotics or intraluminal antibiotics can decrease the rate of bacteremia and risk of catheter-related infections as well as decrease the need for catheter removal secondary to complications.^{29,30} Commonly used regimens include the topical use of Polysporin or mupirocin at catheter entrance sites or a gentamycin, minocycline, or cefotaxime lock solution. Long-term concerns with the use of prophylactic antibiotics include increasing antimicrobial resistance to topical or intraluminal antimicrobial agents and loss of efficacy over time. Another concern is that rates of catheter colonization with *Candida* species might be increased with the use of antibiotic ointments that have no fungicidal activity.^{31,32} The U.S. Food and Drug Administration (FDA) has not approved antibiotic lock solutions for the indication of prevention of catheter-related infections.

Multiple studies have shown that central venous catheters impregnated with antimicrobial or antiseptic solutions such as chlorhexidine/silver sulfadiazine and minocycline/rifampin can decrease the risk of catheter-related bloodstream infections, though these studies have been conducted only on patients with noncuffed, temporary catheters.^{33–35}

Based upon available data the formal recommendations for the management of tunneled venous catheter infections from the Centers for Disease Control Guidelines for the Prevention of Intravascular Catheter-Related Blood Stream Infections (CRBSI) are as follows:¹⁰

- Use a povidone-iodine antiseptic ointment at the hemodialysis catheter exit site after catheter insertion and at the end of each dialysis session only if this ointment does not interact with the material of the hemodialysis catheter per manufacturer's recommendation.
- Use an antimicrobial or antiseptic-impregnated central venous catheter (CVC) in adults whose catheter is expected to remain in place >5 days if, after implementing a comprehensive strategy to reduce rates of CRBSI, the CRBSI rate remains above the goal set by the individual institution. The comprehensive strategy should include the following three components: educating persons who insert and maintain catheters, use of maximal sterile barrier precautions, and a 2% chlorhexidine preparation for skin antisepsis during CVC insertion.
- Do not routinely use antibiotic lock solutions to prevent CRBSI. Use prophylactic antibiotic lock solution only in special circumstances (e.g., in treating a patient with a long-term cuffed or tunneled catheter or port that has a history of multiple CRBSIs despite optimal maximal adherence to aseptic technique).
- Hemodialysis catheters should be avoided in favor of arteriovenous fistulas and grafts; if temporary access is

needed for dialysis, a cuffed catheter is preferable to a noncuffed catheter.

Catheter-related infections remain a significant cause of morbidity and mortality in dialysis patients. Measures to prevent and adequately treat these infections in dialysis patients are important in decreasing costs and complications.

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