

Prevention of Intravascular Catheter Infections – Insights and Prospects for Hemodialysis Catheters

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Hemodialysis catheters have become an invaluable device in management of patients with acute renal failure and they are being used with increased frequency in patients with chronic renal failure. One in five new hemodialysis patients in the United States are dialyzed with tunneled, cuffed catheters and 13% are dialyzed through the same catheter 60 days after starting dialysis.¹ The increased use of these devices is not without risk of serious infectious complications. For example, a recent meta-analysis of prospective studies found 16.2% of non-cuffed hemodialysis catheters were associated with catheter-related bloodstream infection.²

Strategies aimed at prevention of hemodialysis catheter-related bloodstream infections should be based on an understanding of the pathogenesis of such infections. In general, intravascular catheters become infected by microbes migrating down the length of the catheter from colonized catheter hubs or from colonization of the skin at the skin-catheter interface.³ For hemodialysis catheters, the catheter hub appears to be main reservoir from which microbes migrate into the bloodstream causing serious infection. This is supported by at least one prospective study of hemodialysis catheter-related bloodstream infections in which 100% of the episodes had the same of microbe isolated from the catheter hub whereas only 36% of the cases had the same microbe at the catheter insertion site.⁴

Prevention is ever more important when one realizes that catheter salvage in patients with hemodialysis catheter-related bloodstream infections is often unsuccessful and associated with complications. For example, in one prospective study, the success rate in 38 episodes of attempted catheter salvage was 32%.⁵ Notably, the risk of recurrent bacteremia was significantly greater if catheter salvage was attempted (OR 4.1, CI 1.6-10.3).

There are numerous evidence-based strategies that are effective in prevention of intravascular catheter-related bloodstream infections⁶ and guidelines specific to hemodialysis already exist.⁷ Cutaneous antisepsis of catheter insertion sites with chlorhexidine-based preparations has been associated with a significant reduction in catheter colonization in three of four randomized, controlled trials.⁸⁻¹¹ There were non-significant reductions in catheter-related bloodstream infections in three of these studies. Although none of these studies involved hemodialysis catheters, this data suggests that chlorhexidine-based antiseptics, particularly those that are alcohol-based, are the antiseptics of choice for preparing the insertion site of hemodialysis catheters. It should also be noted that tincture of iodine is a more effective cutaneous antiseptic than povidone-iodine,^{12,13} yet there are no published studies of this antiseptic in preparing the skin for hemodialysis catheter insertion.

In a prospective, randomized trial, maximal barrier precautions during central venous catheter insertion (sterile gloves, long-sleeved sterile gown, mask, cap, and large sterile sheet drape) significantly reduced the incidence of catheter-related bloodstream infection compared with standard (sterile gloves and small drape) precautions (0.08 /1000 vs. 0.3 /1000 catheter days, respectively, $p = 0.02$).¹⁴ These results are supported by the findings of a prospective, observational study of pulmonary artery catheters.³ Similar studies of hemodialysis catheters are unavailable. However, based on this data, maximal barrier precautions should be the standard of care during hemodialysis catheter insertion.

There are no adequately powered, randomized studies of the impact of subcutaneous tunneling of hemodialysis catheters on the risk of catheter-related infection. A review of studies carried out to date¹⁵ found the incidence of hemodialysis catheter-related bloodstream infections to be 4/1000 catheter days in patients with non-tunneled, non-cuffed catheters, 1.9/1000 catheter days in patients with tunneled, non-cuffed catheters, and 1.8/1000 catheter days in patients with tunneled, cuffed catheters. Based on this data, it would appear that subcutaneously tunneled hemodialysis catheters should be carried out in an effort to reduce the risk of infection. Ideally, future prospective, randomized studies of tunneling and use of cuffed catheters will lead to more definitive recommendations.

Use of povidone-iodine ointment on the insertion site of hemodialysis catheters has been shown to reduce the incidence of catheter-related bloodstream infection from 4.6/1000 catheter days to 0.4/1000 catheter days ($p < 0.01$) in one prospective, randomized study.¹⁶ Of note, none of the nasal *S. aureus* carriers in the povidone-iodine group developed catheter-related bloodstream infection, whereas 29% did in the control group ($p < 0.05$). The results of this study have been confirmed by other investigators.¹⁷ Based on the available literature, povidone-iodine ointment should be applied to the insertion site of hemodialysis catheters.

Application of mupirocin ointment to temporary hemodialysis catheter insertion sites reduced catheter-related bloodstream infection in a prospective, randomized trial from 6.0/1000 catheter days to 0.4/1000 catheter days ($p < 0.01$).¹⁸ However, mupirocin ointment may impair the integrity of polyurethane catheters.¹⁹⁻²⁰ In addition, prolonged use of mupirocin ointment at catheter insertion sites leads to the development of mupirocin resistance.²¹ Therefore, mupirocin ointment should not be applied to catheter insertion sites.

As noted above, *S. aureus* carriage increases the risk of hemodialysis catheter-related bloodstream infection threefold.¹⁶

Two prospective, open trials^{22,23} have demonstrated that intranasal application of mupirocin ointment used to eradicate nasal *S. aureus* carriage (e.g. applied twice daily for five days) followed by once weekly application significantly reduced the incidence of *S. aureus* bacteremia compared to historical controls. The development of mupirocin resistance was not observed and has been rarely observed even after seven years of intranasal use in hemodialysis patients.²⁴ These studies included all hemodialysis patients and were not specific for patients hemodialyzed through intravascular catheters. Nevertheless, this data strongly suggests that intranasal carriers of *S. aureus* dialyzed through intravascular catheters will have a high risk of *S. aureus* bacteremia and this protocol should be considered for this patient population, in addition to monitoring for the development of mupirocin resistance.

As reviewed elsewhere,⁶ assuring adequate nurse to patient ratios and infection control education for nurses and physicians, including appropriate care of intravascular catheters, significantly reduces the risk of catheter-related infection. In one observational study specifically of patients dialyzed through intravascular catheters, a five-fold increase in septic episodes was noted when patients were cared for by nurses with less professional experience.²⁵ *In toto*, these data suggest that adequate physician and nursing education, experience, and appropriate numbers of nurses caring for patients dialyzed through intravascular catheters, should reduce the risk of hemodialysis catheter-related infections. In this regard, institutional standards should be developed and reviewed periodically to assure that appropriate staffing and infection control education is maintained.

Prospective, randomized studies of central venous catheters impregnated on the outer surface with chlorhexidine-silver sulfadiazine *in situ* for an average of 11 days or less significantly reduces the incidence of catheter-related bloodstream infections (RR 0.4, 95%CI 0.2-0.8).⁶ However, no such studies with hemodialysis catheters have been published. Central venous catheters impregnated with minocycline and rifampin on the inner and outer surface reduced the risk of catheter-related bloodstream infection compared to the above-noted chlorhexidine-silver sulfadiazine impregnated catheters in a prospective, randomized trial (RR 0.1, 95% CI 0-0.6).²⁶ Yet, there are no published studies using these catheters in hemodialysis.

There are a number of hopeful technologies currently under study to reduce the risk of hemodialysis catheter-related infection. Preliminary studies suggest that hemodialysis catheters coated with silver may reduce the risk of such infections in the future.²⁷ Taurolidine (bis-(1,1-dioxoperhydro-1,2,4-thiabiazinyl-4) methane) is a unique antimicrobial agent which is a derivative of the aminosulfonic acid taurine. Taurolidine has broad-spectrum activity against Gram-positive bacteria,²⁸⁻³⁰ Gram-negative bacteria³⁰ and *Candida*.³¹ In one observational study, the use of taurolidine as an antimicrobial lock solution in patients hemodialyzed through intravascular catheters was associated with a low incidence of catheter-related bloodstream infections.³² In a prospective, clinical trial, hemodialysis catheters randomized to have the lumen flushed with a solution containing minocycline and EDTA had a significantly reduced incidence of bacterial catheter colonization compared with catheters flushed with standard heparin solution (8% and 69%, respectively, $p = 0.005$).³³ However, due to the risk of the development of resistance, this strategy is less appealing since it would involve widespread use of therapeutic antibiotics for the prevention of hemodialysis catheter-related infections.

Future strategies to prevent hemodialysis catheter-related infection will undoubtedly be based on a better understanding of the pathogenesis of these infections. At the present time, the following strategies should be undertaken: cutaneous antiseptics of catheter insertion sites with chlorhexidine-based preparations; maximal barrier precautions during catheter insertion; subcutaneous tunneling of catheters; application of povidone-iodine ointment on the insertion site; intranasal mupirocin ointment for *S. aureus* carriers; and institutional standards assuring appropriate staffing by nurses and infection control education of physicians and nurses.

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