



UNIVERSITY OF CENTRAL FLORIDA

Infectious Disease Update: Managing Common Infections in the Nephrology Patient

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Infection and Renal Disease

- ID in the Nephrology Patient:
 - Patients with CKD and end stage renal disease (ESRD) receiving dialysis have a higher rate of infection than individuals without kidney disease
 - Higher rates of pneumonia and sepsis than individuals without CKD

Infection and Renal Disease

- ID in the Nephrology Patient (Ctd):
 - An incident cohort of patients beginning dialysis was found to have a 1-year incidence of infection related hospitalization of 32% if receiving hemodialysis and 24% if receiving peritoneal dialysis
 - Risk seems to increase with time on dialysis

Infection and Renal Disease

- Catheter-related infections account for 250,000 serious infections every year
 - Of these, 31,000 infections result in death
- Hospitals are required to publicly report preventable infections and infection related deaths
- Hemodialysis clinics are not required to publicly report their infection rates

Infection and Renal Disease

- At present, only evidence of surveillance and quality improvement initiatives is required by the Centers for Medicare and Medicaid (CMS) Conditions for ESRD Coverage
- Public reporting of catheter-related infection rates to the National Healthcare Safety Network (NHSN) is voluntary
- Only a small percentage of hemodialysis facilities participate in the NHSN program

Infection and Renal Disease

- State surveyors and ESRD networks that monitor hemodialysis facilities approximately every three years review infection incidence surveillance reports
- Public reporting on the CMS Dialysis Facility Compare Web site is limited to only three quality performance measures: a) anemia, b) dialysis adequacy, and c) patient survival, but it does not include infection rates

Infection and Renal Disease

- Infection is the second leading cause of death in patients on hemodialysis; and for the majority of those infections, **the access is usually implicated as the source for the infection**



Dialysis Access Infection

- Avoiding catheter-related bacteremia should be the highest priority for hemodialysis facilities
- New guidelines to reduce catheter-related bloodstream infections were published April 1, 2011 (CDC, 2011)
- Use of these guidelines has proven to be effective in reducing catheter-related blood stream infections within hospital based intensive care units by 58% from 2001 to 2009

Dialysis Access Infection

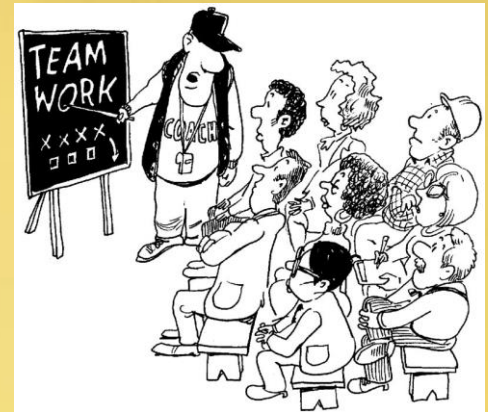
- The Agency for Healthcare Research and Quality (AHRQ) estimates that this reduction saved an estimated 6,000 lives and approximately \$414 million in extra costs
- But could these measures work in hemodialysis facilities?
 - Hemodialysis facilities are very different from intensive care units (such as staffing ratios, environment, and structure)
 - Structural barriers need to be recognized and discussed openly to direct change

Epidemiology

- In the United States, 15 million central vascular catheter (CVC) days (i.e., the total number of days of exposure to CVCs among all patients in the selected population during the selected time period) occur in intensive care units (ICUs) each year
- Catheter related bloodstream infections (CRBSIs) independently increase hospital costs and length of stay, but have not generally been shown to independently increase mortality
- While 80,000 CRBSIs occur in ICUs each year, a total of 250,000 cases of BSIs have been estimated to occur annually

Purpose of Reducing CRBSIs

- The effort to reduce CRBSIs should be multidisciplinary, involving healthcare professionals who order the insertion and removal of CVCs, those personnel who insert and maintain intravascular catheters, infection control personnel, healthcare managers including the chief executive officer (CEO) and those who allocate resources, and patients who are capable of assisting in the care of their catheters



Objective of Prevention Program

- The goal of an effective prevention program should be the elimination of CRBSI from all patient-care areas
- Although this is challenging, programs have demonstrated success
- Sustained elimination requires continued effort
- The goal is to reduce the rate to as low as feasible given the specific patient population being served, the universal presence of microorganisms in the human environment, and the limitations of current strategies and technologies



CDC Guidelines

- Intended to provide evidence-based recommendations for preventing intravascular catheter-related infections
- Major areas of emphasis include:
 - 1) educating and training healthcare personnel who insert and maintain catheters;
 - 2) using maximal sterile barrier precautions during central venous catheter insertion;
 - 3) using a $> 0.5\%$ chlorhexidine skin preparation with alcohol for antisepsis;
 - 4) avoiding routine replacement of central venous catheters as a strategy to prevent infection; and
 - 5) using antiseptic/antibiotic impregnated short-term central venous catheters and chlorhexidine impregnated sponge dressings

Epidemiology and Microbiology

- The most commonly reported causative pathogens remain coagulase-negative staphylococci, *Staphylococcus aureus*, enterococci, and *Candida*
- Gram negative bacilli accounted for 19% and 21% of CLABSIs reported to CDC and the Surveillance and Control of Pathogens of Epidemiological Importance (SCOPE) database, respectively



Pathophysiology

- There are four recognized routes for contamination of catheters:
 - Migration of skin organisms at the insertion site into the cutaneous catheter tract and along the surface of the catheter with colonization of the catheter tip; **this is the most common route of infection for short-term catheters**
 - Direct contamination of the catheter or catheter hub by contact with hands or contaminated fluids or devices;
 - Less commonly, catheters might become hematogenously seeded from another focus of infection; and
 - Rarely, infusate contamination might lead to CRBSI

Pathophysiology: CRBSI Considerations

- Some catheter materials also have surface irregularities that enhance the microbial adherence of certain species (e.g., *S. epidermidis* and *C. albicans*)
- Catheters made of these materials are especially vulnerable to microbial colonization and subsequent infection
- Due to the formation of the fibrin sheath, silastic catheters are associated with higher risk of catheter infections than polyurethane catheters
- On the other hand, biofilm formation by *C. albicans* occurs more readily on silicone elastomer catheter surfaces than polyurethane catheters
- Modification of the biomaterial surface properties has been shown to influence the ability of *C. albicans* to form biofilm

Pathophysiology: CRBSI Considerations

- *S. aureus* can adhere to host proteins (e.g., fibrinogen, fibronectin) commonly present on catheters by expressing clumping factors (ClfA and ClfB) that bind to the protein adhesins
- Adherence is enhanced through the production by microbial organisms, such as coagulase negative staphylococci, *S. aureus*, *Pseudomonas aeruginosa*, and *Candida* species of an extracellular polymeric substance (EPS) consisting mostly of an exopolysaccharide that forms a microbial biofilm layer
- This biofilm matrix is enriched by divalent metallic cations, such as calcium, magnesium and iron, which make it a solid enclave in which microbial organisms can embed themselves

Pathophysiology: CRBSI Considerations

- Such a biofilm potentiates the pathogenicity of various microbes by allowing them to withstand host defense mechanisms (e.g., acting as a barrier to engulfment and killing by polymorphonuclear leukocytes) or by making them less susceptible to antimicrobial agents (e.g., forming a matrix that binds antimicrobials before their contact with the organism cell wall or providing for a population of antimicrobial tolerant "persister" cells)



Infection Prevention with Antimicrobials

- **Do not administer systemic antimicrobial prophylaxis routinely before insertion or during use of an intravascular catheter to prevent catheter colonization or CRBSI**
 - Efficacy data are largely conflicting
 - Some studies have indicated decreases in infections while others have not
 - 35% of patients in a study assessing oral prophylaxis with rifampin and novobiocin discontinued treatment due to toxicity
 - Heterogeneity in these studies precludes making any conclusion regarding efficacy

Infection Prevention with Antimicrobials

- Use povidone iodine antiseptic ointment or bacitracin/ gramicidin*/polymyxin B 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

* - US containing preparations do not include gramicidin

Infection Prevention with Antimicrobials

- The application of bacitracin/gramicidin/polymyxin B ointment at the catheter insertion site was compared with placebo in 169 hemodialysis patients. Infections were observed in more patients in the placebo group than in the bacitracin/gramicidin/polymyxin B group (34 versus 12%; relative risk, 0.35; 95% CI, .18 to .68)
- The number of infections per 1,000 catheter days (4.10 versus 1.02; $P < .0001$) and the number of bacteremias per 1,000 catheter days (2.48 versus .63; $P = .0004$) were also greater in the placebo group

Infection Prevention with Antimicrobials

- Within the 6-month study period, there were 13 deaths in the placebo group as compared with three deaths in the bacitracin/gramicidin/ polymyxin B group ($P = .004$)
- Thus, there is evidence from one study in hemodialysis patients that bacitracin/gramicidin/ polymyxin B ointment can improve outcome, but no similar data exist for use in other patient populations
- Outside of the US, this is essentially Polysporin® (US Polysporin® does not contain gramicidin)

Infection Prevention with Antimicrobials

- **Use prophylactic antimicrobial lock solution in patients with long term catheters who have a history of multiple CRBSI despite optimal maximal adherence to aseptic technique**
 - To prevent CRBSI, a wide variety of antibiotic and antiseptic solutions have been used to flush or lock catheter lumens



Infection Prevention with Antimicrobials

- Catheter lock is a technique by which an antimicrobial solution is used to fill a catheter lumen and then allowed to dwell for a period of time while the catheter is idle
- Antibiotics of various concentrations that have been used either alone (when directed at a specific organism) or in combination (to achieve broad empiric coverage) to prophylactically flush or lock central venous catheters include vancomycin, gentamicin, ciprofloxacin, minocycline, amikacin, cefazolin, cefotaxime, and ceftazidime; while antiseptics have included alcohol, taurolidine, trisodium citrate.

Infection Prevention with Antimicrobials

- Although most studies indicate a beneficial effect of the antimicrobial flush or lock solution in terms of prevention of catheter-related infection, this must be balanced by the potential for side effects, toxicity, allergic reactions, or emergence of resistance associated with the antimicrobial agent
- The wide variety of compounds used, the heterogeneity of the patient populations studied, and limitations in the size or design of studies preclude a general recommendation for use.
- In addition, there are no FDA approved formulations approved for marketing, and most formulations have been prepared in hospital pharmacies

Infection Prevention with Antimicrobials

- Do not routinely use anticoagulant therapy to reduce the risk of catheter-related infection in general patient populations
- In a meta-analysis evaluating the benefit of heparin prophylaxis (3 units/mL in parenteral nutrition, 5,000 units every 6 or 12 hours flush or 2,500 units low molecular weight heparin subcutaneously) in patients with short-term CVCs, the risk for catheter-related central venous thrombosis was reduced with the use of prophylactic heparin. However, no substantial difference in the rate of CRBSI was observed.
- Because the majority of heparin solutions contain preservatives with antimicrobial activity, whether any decrease in the rate of CRBSI is a result of the reduced thrombus formation, the preservative, or both is unclear

Infection Prevention with Antimicrobials

- **Do not routinely replace CVCs, PICCs, hemodialysis catheters, or pulmonary artery catheters to prevent catheter-related infections**
- **Do not remove CVCs or PICCs on the basis of fever alone:**
 - **Use clinical judgment regarding the appropriateness of removing the catheter if infection is evidenced elsewhere or if a noninfectious cause of fever is suspected**

Infection Prevention with Antimicrobials

- **Do not use guidewire exchanges routinely for non-tunneled catheters to prevent infection**
- **Do not use guidewire exchanges to replace a non-tunneled catheter suspected of infection**
- **Use a guidewire exchange to replace a malfunctioning non-tunneled catheter if no evidence of infection is present**
- **Use new sterile gloves before handling the new catheter when guidewire exchanges are performed**

Infection Prevention with Antimicrobials

- ***Hemodialysis Catheters:***

- The use of catheters for hemodialysis is the most common factor contributing to bacteremia in dialysis patients
- The relative risk for bacteremia in patients with dialysis catheters is sevenfold the risk for patients with arteriovenous (AV) fistulas
- AV fistulas and grafts are preferred over hemodialysis catheters in patients with chronic renal failure, due to their lower associated risk of infection
- If temporary access is needed for dialysis, a tunneled cuffed catheter is preferable to a non-cuffed catheter, even in the ICU setting, if the catheter is expected to stay in place for >3weeks



Infection Prevention with Antimicrobials

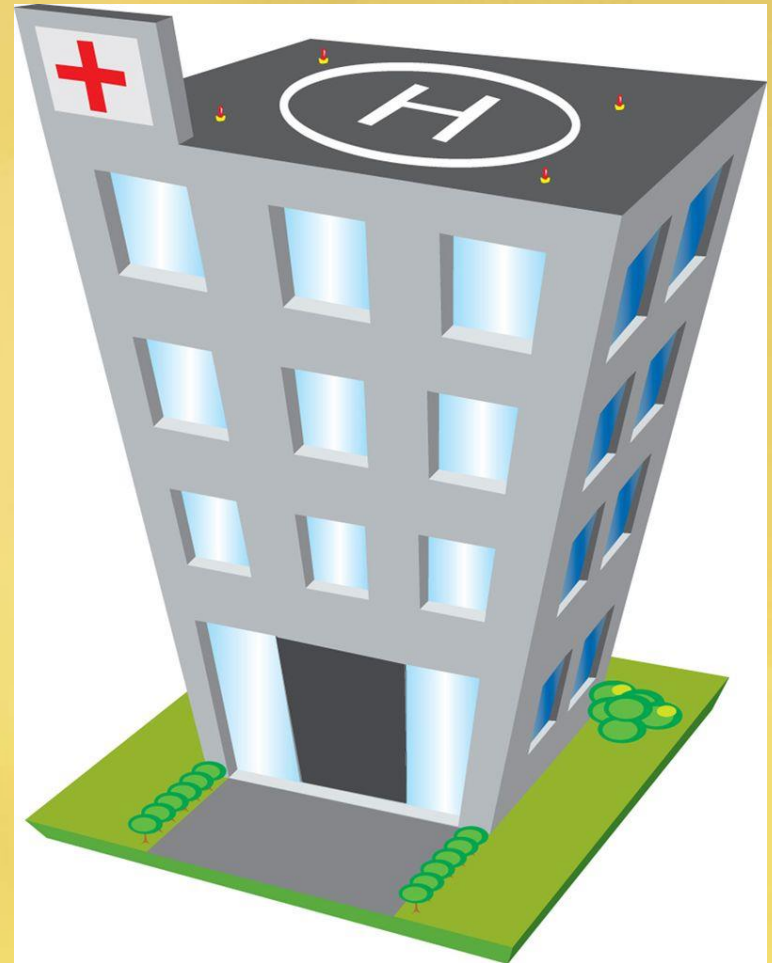
- **Remove and do not replace umbilical artery catheters if any signs of CRBSI, vascular insufficiency in the lower extremities, or thrombosis are present**
- **Remove and do not replace umbilical venous catheters if any signs of CRBSI or thrombosis are present**
- **No recommendation can be made regarding attempts to salvage an umbilical catheter by administering antibiotic treatment through the catheter**

Infection Prevention with Antimicrobials

- Cleanse the umbilical insertion site with an antiseptic before catheter insertion
 - Avoid tincture of iodine because of the potential effect on the neonatal thyroid
 - Other iodine-containing products (e.g., povidone iodine) can be used
- Do not use topical antibiotic ointment or creams on umbilical catheter insertion sites because of the potential to promote fungal infections and antimicrobial resistance
- Add low-doses of heparin (0.25–1.0 U/ml) to the fluid infused through umbilical arterial catheters

Performance Improvement

- Use hospital-specific or collaborative-based performance improvement initiatives in which multifaceted strategies are "bundled" together to improve compliance with evidence-based recommended practices



Performance Improvement

- Clinical decision makers, healthcare payers, and patient safety advocates emphasize the importance of translating research findings into everyday practice
- Rigorous evaluations of CRBSI preventive practices using study designs with high internal validity and including study populations that optimize external validity remain necessary
- Once practices have been determined to be effective and economically efficient, the next step is to implement these evidence-based practices so they become part of routine clinical care
- Unfortunately, implementation of evidence- based CRBSI preventive practices in U.S. hospitals has been suboptimal

Performance Improvement

- In a national survey conducted in March 2005 of over 700 U.S. hospitals, approximately one quarter of U.S. hospitals indicated that either maximal sterile barrier precautions during central line insertion or chlorhexidine gluconate as site disinfectant, two practices widely recommended in the guidelines published in 2002, were not being used routinely
- Approximately 15% of U.S. hospitals reported routinely changing CVCs to prevent infection despite evidence that this practice should no longer be used

Performance Improvement

- Numerous quality improvement studies have been published during the past several years that have used various methods, such as education of healthcare personnel, audit and feedback, organizational change, and clinical reminders
- The educational interventions primarily targeted hand hygiene, use of maximal sterile barriers during insertion, appropriate insertion site selection, proper site care using chlorhexidine gluconate, and prompt removal of unnecessary catheters

Performance Improvement

- While a large number of before-and-after studies with a few using concurrent control groups have been published, no randomized, controlled trial evaluating a quality improvement strategy to prevent CRBSI has been reported
- The vast majority of before-and-after studies reported statistically significant decreases in CRBSI rates after a quality improvement strategy was implemented

Performance Improvement

- In addition to educating clinicians about CRBSI prevention, evidence-based interventions include:
 - 1) a central venous catheter cart that contains all the necessary supplies
 - 2) a checklist to ensure adherence to proper practices;
 - 3) stoppage of procedures in non-emergent situations, if evidence- based practices were not being followed;
 - 4) prompt removal of unnecessary central catheters identified during daily patient rounds;

Performance Improvement

- 5) feedback to the clinical teams regarding the number of CRBSI episodes and overall rates; and
 - 6) buy-in from the chief executive officers of the participating hospitals that chlorhexidine gluconate products/solutions would be stocked
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- Using an interrupted time series analysis and multivariable regression, the investigators reported a statistically significant 66% decrease in CRBSI rates approximately 18 months after the intervention began and sustained reductions over time

Performance Improvement

- Specific process and outcome measures for tracking and feedback (i.e rate of central line infections, proportion of central lines placed with all or individual bundle elements performed AND documented) should be identified in individual institutions based on areas that have been identified for performance improvement

Performance Improvement

- Finally, emphasis on the care and maintenance of catheters once they are in place should be a focus of performance improvement and quality assurance in all programs
- In one study:
 - Dressings (not intact) and caps (incorrectly placed) were identified as the major lapses in CVC care with 158 and 156 breaches per 1000 catheter days, respectively.
- Interventions to improve reliability of care should focus on making the implementation of best practice easier to achieve



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