Preventing Hemodialysis Catheter-Related Infections: Where do Antimicrobial Locks Stand?
Speakers

Anju Oommen, MD
Division of Renal Medicine
Emory University School of Medicine
Financial Disclosures: Consulting for 11TEN innovations

Ibironke Apata, MD
Division of Renal Medicine
Emory University School of Medicine
Financial Disclosures: None
Definitions before we get started……..

• Bloodstream Infection (BSI)
  • Bacteremia or fungemia confirmed with a positive blood culture, typically accompanied with clinical symptoms or signs

• Catheter-related BSI (CRBSI)
  • A clinical definition, in which a central venous catheter is identified as the source of the BSI

• Central-line associated BSI (CLABSI)
  • A surveillance definition, BSI in a patient with catheter, and not related to an alternate source

• Dialysis Access-Related BSI
  • A surveillance definition, BSI secondary to dialysis vascular access

https://academic.oup.com/cid/article/49/1/1/369414
https://www.cdc.gov/infectioncontrol/guidelines/bsi/background/terminology.html
Learning Objectives

• Highlight the burden of CRBSI in hemodialysis
• Discuss CDC’s core interventions for preventing BSI in outpatient dialysis facilities
• Explore Antimicrobial Locks for preventing CRBSI
• Highlight some catheter devices for preventing BSI
Clinical Scenario

You are the medical director of Dialysis Facility O. The nurse manager is concerned about an increased rate of CLABSI over the past 6 months. She reviewed results of infection control audits including hand hygiene, catheter connection and disconnection, and catheter exit site dressing care. Based on the audits, she identified areas for education and training. She asks you if antibiotic locks should be implemented for all catheters.

Catheter care procedures for Facility O:
• Catheter hub disinfection: scrub the hub with sterile alcohol pad every time catheter is accessed, disconnected, cap removed, cap replaced
• Catheter exit site care: disinfect exit-site with alcohol swab, apply chlorhexidine-impregnated transparent dressing, change dressing once a week and when visibly wet/soiled
• Catheter lumen: heparin lock

In addition to performing staff education/trainings, consider what you would recommend?
Catheter-Related Infections and Hemodialysis

• Central venous catheters (catheters) have the highest risk of bloodstream infection (BSI) compared to grafts (AVG) and fistulas (AVF)
  • From 2014-2018, **50,000 BSIs** (or **70%** of dialysis access related BSIs) occurred in patients with catheters

**Attributable Mortality** from CLABSI: **12-25%**

**Estimated Costs** per CLABSI episode: **3,700-45,000 dollars**

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1. National Healthcare Safety Network (NHSN) Unpublished Data
2. CDC. MMWR 2011; 60(08);243-248
How do Catheter-Related BSIs Occur?

• Bacteria migration from skin/exit site to catheter
• Direct contact of catheter, or catheter hub with contaminated hands, fluids or devices
• Hematogenous seeding from other focus of infection
• Infusate contamination

Bacterial contamination leads to formation of extracellular matrix that adheres to catheter surface, called biofilm
Core Interventions for Dialysis BSI Prevention

- Introduced in 2011
- Studies have shown the effectiveness of Core Interventions in decreasing BSIs\(^1,2,3\)
  - 54\% reduction in dialysis access-related BSIs\(^1\)
  - Decrease in IV antibiotic starts\(^3\)
  - Decrease in sepsis-related hospitalizations\(^3\)


More can be done! You can play a role in decreasing BSIs
Surveillance and feedback

CDC Approach to BSI Prevention in Dialysis Facilities
(i.e., the Core Interventions for Dialysis Bloodstream Infection (BSI) Prevention)

1. Surveillance and feedback using NHSN
Conduct monthly surveillance for BSIs and other dialysis events using CDC’s National Healthcare Safety Network (NHSN). Calculate facility rates and compare to rates in other NHSN facilities. Actively share results with front-line clinical staff.

2. Hand hygiene observations
Perform observations of hand hygiene opportunities monthly and share results with clinical staff.

3. Catheter/vascular access care observations
Perform observations of vascular access care and catheter accessing quarterly. Assess staff adherence to aseptic technique when connecting and disconnecting catheters and during dressing changes. Share results with clinical staff.

4. Staff education and competency
Train staff on infection control topics, including access care and aseptic technique. Perform competency evaluation for skills such as catheter care and accessing every 6-12 months and upon hire.

5. Patient education engagement
Provide standardized education to all patients on infection prevention topics including vascular access care, hand hygiene, risks related to catheter use, recognizing signs of infection, and instructions for access management when away from the dialysis unit.

6. Catheter reduction
Incorporate efforts (e.g., through patient education, vascular access coordinator) to reduce catheters by identifying and addressing barriers to permanent vascular access placement and catheter removal.

7. Chlorhexidine for skin antisepsis
Use an alcohol-based chlorhexidine (>0.5%) solution as the first line skin antiseptic agent for central line insertion and during dressing changes.*

8. Catheter hub disinfection
Scrub catheter hubs with an appropriate antiseptic after cap is removed and before accessing. Perform every time catheter is accessed or disconnected.**

9. Antimicrobial ointment
Apply antibiotic ointment or povidone-iodine ointment to catheter exit sites during dressing change.***
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Catheter care

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• Catheter lumen: heparin lock

In addition to performing staff education/trainings, what do you recommend?
A) Institute gentamicin locks for all catheters
B) Replace alcohol swab with >0.5% alcohol-based chlorhexidine solution for catheter exit site disinfection
C) Add antimicrobial mupirocin ointment to exit site during dressing change
D) Continue current procedures without change
Catheter Lumen- Antimicrobial Locks
Antimicrobial Locks for Preventing CRBSI

Antimicrobial 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.

The antimicrobial agent is usually combined with a compound acting as an anticoagulant (heparin/citrate).

Discussing antimicrobial locks for preventing CRBSI (Not locks for treatment of CRBSI or catheter salvage)
Ideal Antimicrobial Lock Solution Properties

• Spectrum of activity should include common or targeted pathogens
• Ability to penetrate or disrupt a biofilm
• Compatibility with anticoagulants
• Prolonged stability
• Low risk of toxicity and adverse events
• Low potential for resistance
• Cost-effective

Antimicrobial Locks

Antibiotic Locks
- Gentamicin
- Other antibiotics
- Taurolidine

Non-Antibiotic Locks
- Ethanol
- Methylene blue/parabens
- Citrate
**Antibiotic Locks**

- **Gentamicin Locks**
  - Most studied antibiotic lock
  - Has been combined with vancomycin, cefazolin
  - Associated with decreased CRBSI rates
  - Concern for systemic absorption, ototoxicity, and gentamicin resistance

*Other antibiotics:* minocycline, linezolid, cefotaxime, vancomycin, cefazolin, ciprofloxacin, etc.

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Most studied- and combined with vanc/cefazolin Yahav et al. Clinical Infectious Diseases 47: 83-93, 2008
Gentamicin Lock Studies

Gentamicin (4mg/mL) + Heparin Lock

*Landry et al. CJASN 2010.*

- Retrospective chart review
- 1,410 patients over a 4-year study period
- Catheter care:
  - Hubs soaked in Povidone Iodine (PI)
  - Exit site cleansed with PI
  - Exit site dressing- Mupirocin ointment/dry gauze

CRBSI rates: 17.0 → 0.83/1,000 catheter days, in 1 year

Gentamicin resistance – 26%, discontinued use
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Gentamicin (0.32mg/mL in 4% Citrate) vs. Heparin *Moore et al, CJASN 2014*

- Prospective, observational cohort study
- 555 patients over 3 years (crossover from heparin to Gent lock)
- Catheter Care:
  - Hubs soaked in Chlorine (Alcavis)
  - Exit site cleansed with chlorhexidine (3.15%)
  - Exit site dressing - Triple antibiotic ointment (bacitracin, neomycin, and polymyxin B)/dry gauze

CRBSI rate: 0.45 (gent) vs 1.68 (heparin) episodes/1,000 catheter days (p =0.001)

- No emergence of gentamicin resistance
- Antibiotic lock was associated with a mortality reduction (hazard ratio 0.36; 95% CI, 0.22 to 0.58 in unadjusted analyses)
Non-Antibiotic Locks

**Taurolidine Locks**
- Considered promising non-antibiotic lock
  - May mitigate issue of antibiotic resistance
- Broad spectrum activity
- No resistance reported
- Multiple studies showing associated with decreased CRBSI
- No reported side effects

A Meta-Analysis of Antimicrobial Lock Solutions for Hemodialysis Catheters

Methods: Included 26 randomized control studies comparing antimicrobial locks (i.e., antibiotic and non-antibiotic locks) to heparin (control group)

Results: Compared to heparin, antimicrobial locks associated with 30% lower incidence of CRBSI.

- **Antibiotic lock** led to decreased risk of CRBSI episodes by 28% compared to heparin
- **Non-antibiotic** lock led to decreased risk of CRBSI episode by 32%

Limitations: few studies, low sample size of individual studies

Salim SA et al. ASAO Journal. 2021
Antimicrobial Locks Considerations

- Ideal antimicrobial lock for preventing CRBSI among is yet to be decided

- No FDA approved formulations approved for marketing
  - No pre-mixed antimicrobial locks in the market, in the USA
  - How and where will the lock be prepared
  - If mixed dialysis staff, mixing locks, will require training and quality checks

- Cost- Center for Medicare and Medicaid Services does not provide reimbursement for antimicrobial locks
So...Where Do Antimicrobial Locks Stand?

• Evidence supports antimicrobial locks effectiveness in reducing CRBSIs
  • Gentamicin well-studied, lower dose did not appear to lead to antibiotic resistance
  • Tauroldidine may be promising solution to antibiotic resistance

• In most studies, CDC Core Interventions for preventing BSI were not used
  • Opportunities for decreasing CRBSI without locks, given high rates of CRBSI in some studies
  • Studies are needed to determine if there is additional benefit of antimicrobial locks when the Core Interventions are followed

• No antimicrobial lock has been approved by FDA
  • Several considerations to ensure patient safety and preventing dosage errors or contamination if locks are prepared by dialysis staff
CDC’s Recommendations on Antimicrobial Locks, 2011

CDC recommends **against** routine use of antimicrobial locks for prevention of CRBSIs

“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.**”

https://www.cdc.gov/infectioncontrol/guidelines/bsi/recommendations.html#rec9
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Catheter Lumen- ClearGuard
ClearGuard™HD

Antimicrobial agent remains in desired region due to the existing clamps

Coated with chlorhexidine a broad-spectrum antimicrobial agent
ClearGuard versus Tego + Curos

Favored ClearGuard:
• Decreased positive blood culture
• Decreased IV antibiotic starts

Brunelli SM et al. JASN 2018
Wrapping Up…

• The best way to prevent CRBSI, is to avoid catheter use
• Remember CDC Core Interventions to prevent BSI
• Your patient, with multiple CRBSI episodes in spite of adhering to optimal maximal aseptic techniques, may benefit from an antimicrobial lock
• Stay tuned for innovations (e.g., FDA approved locks, devices) to prevent CRBSI

You have an important role to play in promoting patient safety by decreasing BSI

Important Resources
Thank you
A Meta-analysis of Antimicrobial Lock Solutions for Hemodialysis Catheters

Methods: Included 7 prospective randomized control studies comparing antimicrobial lock solution (i.e., antibiotic and non-antibiotic locks) with heparin

Results: Catheter-related infections were 7.72 times less likely when using antimicrobial lock solutions compared to heparin

Limitations: relatively short duration of follow-up of the included studies