Technologic Innovations for the Prevention of Catheter-Related Bloodstream Infection

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Objectives

• Recognize the significance of Catheter Related Bloodstream Infection (CR-BSI) and understand that knowledge of pathogenesis drives prevention efforts
• Describe evidence-based measures to prevent CR-BSI by limiting intraluminal and extraluminal catheter contamination
• Be able to introduce technologic innovations for the prevention of Catheter Related Bloodstream Infection (CR-BSI)
Clinical Significance of CLA-BSI
**Clinical Significance of CLA-BSI**

- 50% reduction in CLA-BSI between 2008 and 2014 in acute care hospitals in the United States

- CLA-BSI rate in critical care units ranges from 0.0 – 2.9/1000 CVC d

- 30,389 CLA-BSI reported by 3710 hospitals to CDC NHSN in 2021. 12,219 from ICUs, 14,328 Wards, 3,842 NICU.

- CLA-BSI are associated with increased mortality (OR 2.75, CI 1.86-4.07), and attributable cost of $45,814 (CI, $30,919-$65,245)

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## COVID-19: Reversal of Trends

<table>
<thead>
<tr>
<th>Category</th>
<th>2020 Q1</th>
<th>2020 Q2</th>
<th>2020 Q3</th>
<th>2020 Q4</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLABSI</td>
<td>-11.8%</td>
<td>27.9%</td>
<td>46.4%</td>
<td>47.0%</td>
</tr>
<tr>
<td>CAUTI</td>
<td>-21.3%</td>
<td>No Change¹</td>
<td>12.7%</td>
<td>18.8%</td>
</tr>
<tr>
<td>VAE</td>
<td>11.3%</td>
<td>33.7%</td>
<td>29.0%</td>
<td>44.8%</td>
</tr>
<tr>
<td>SSI: Colon surgery</td>
<td>-9.1%</td>
<td>No Change¹</td>
<td>-6.9%</td>
<td>-8.3%</td>
</tr>
<tr>
<td>SSI: Abdominal hysterectomy</td>
<td>-16.0%</td>
<td>No Change¹</td>
<td>No Change¹</td>
<td>-13.1%</td>
</tr>
<tr>
<td>Laboratory-identified MRSA bacteremia</td>
<td>-7.2%</td>
<td>12.2%</td>
<td>22.5%</td>
<td>33.8%</td>
</tr>
<tr>
<td>Laboratory-identified CDI</td>
<td>-17.5%</td>
<td>-10.3%</td>
<td>-8.8%</td>
<td>-5.5%</td>
</tr>
</tbody>
</table>

Weiner-Lastinger, et al. ICHE 2021
Pathogenesis of CVC-Associated BSI
Pathogenesis of CVC-Associated BSI

Hands of Medical Personnel or Patient

Hub Colonization
Contaminated Infusate

Skin Microflora

Exit Site

Conditioning Film / Fibrin Sheath

Subcutaneous Tract

Hematogenous Seeding

**Biofilms: Complex and Dynamic Environment**

Microbial “Community”

**Biofilm: Structure & Function**
Prevention of CR-BSI

Pre and Peri-CVC Insertion
**CR-BSI Prevention Pre and Peri-insertion**

**Education**
- Indications for vascular catheters
- Sterile technique (Sim lab training)

**Staffing & personnel**

**Insertion bundle**
- Maximal sterile barriers
- Chlorhexidine + Alcohol skin prep
- Checklist
CR-BSI Prevention Pre and Peri-insertion

Surgical ICU

- 10-page self-study module for ICU nurses

Overall BSI rate

- Pre: 10.8/1000 CVC d
- Post: 3.7/1000 CVC d

CR-BSI Prevention: Catheter Selection Algorithm

Algorithm used at Nebraska Medicine to guide catheter selection decision.

Nurse Ratio and Staffing Levels

Outbreak of CVC BSI associated with higher patient to nurse ratio in an SICU⁷

Maximal Sterile Barrier Precautions

Cap, Mask, Sterile Gown, Sterile Gloves, Head-to-toe Sterile Sheet
An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU

Intervention in 108 ICUs:

• Daily Goals Sheet
• Hand Hygiene
• Full Sterile Barrier Precautions
• Chlorhexidine Antiseptic
• Avoidance of the Femoral Site
• Removal of CVCs as soon as possible

(P<0.002)

Prevention of CR-BSI

Post Insertion Interventions
Post Insertion CVC Care

- Perform hand hygiene before manipulating the CVC
- Maintain clean and intact dressing
  - CHG impregnated dressing
- “Scrub the Hub” every time the catheter is accessed
  - Passive port protector
- Bathe patients with CHG
- Remove the CVC as soon as it is not needed

Prevention of CR-BSI

Technologic Innovations
Behavioral Change vs. Technology

“If you can choose between education and influencing human behavior or introduction of a gizmo, choose the gizmo every time.”

-Bob Weinstein
“It is impossible to make anything foolproof because fools are so ingenious”

-Anonymous
Commercially Available Antimicrobial Central Venous Catheters

- CHG / SS Chlorhexidine - Silver Sulfadiazine
- Minocycline – Rifampicin
- Silver / Platinum / Carbon
- Miconazole / Rifampicin
- Benzalkonium
- Benzalkonium + Heparin
Compounds used in Coated Catheters\textsuperscript{11}

- Chlorhexidine – cationic polybiguanide disinfectant, disrupts cell membranes
- Silver – disinfectant, deactivates enzymes and membrane transport by binding to thiol groups
- Sulfadiazine – antibiotic, inhibits dihydropteroate synthetase
- Rifampin – antibiotic, inhibits bacterial DNA-dependent RNA polymerase
- Minocycline – broad spectrum tetracycline antibiotic, inhibits bacterial protein synthesis

No correlation between in vitro/in vivo testing methods and clinical outcomes have currently been ascertained.

Spectrum and Duration of Activity of Antimicrobial Catheters¹²

No correlation between in vitro/in vivo testing methods and clinical outcomes have currently been ascertained.

Spectrum and Duration of Activity of Antimicrobial Catheters\textsuperscript{12}

No correlation between in vitro/in vivo testing methods and clinical outcomes have currently been ascertained.

Chlorhexidine treated PICC prevents bacterial adherence and biofilm formation over 24 hour exposure to *GFP-S aureus* in flow cell experiment.

Duration of Activity CH/SS CVC^14,15

S. aureus
1st & 2nd generation CH/SS CVCs

S. epidermidis
2nd generation CH/SS CVC


Do antimicrobial-coated catheters prevent BSI?

CSS Catheters

First Generation CSS
Control CVC Infection Rate 4.2%

Second Generation CSS
Control CVC Infection Rate 2.3%

0.68 x 1000 days

0.47 x 1000 days

Do antimicrobial-coated catheters prevent BSI?

M/R Catheters

Minocycline – Rifampicin
Control CVC Infection Rate 5.9%

0.29 x 1000 days

Raad 1997
Marik 1999
Chatzinikolaou 2003
Leon 2004
Hanna 2004
Total (FEM)

Effectiveness of antimicrobial-coated central venous catheters for preventing catheter-related blood-stream infections with the implementation of bundles: a systematic review and network meta-analysis

25 RCTs reported
CRBSI/1000 CVC days

CH/SS vs. CSC OR 0.64
AC vs. CSC OR 0.53
OVS vs. CSC OR 0.70

Are antimicrobial peripherally inserted central catheters associated with reduction in central line-associated bloodstream infection? A systematic review and meta-analysis


<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>Weight (%)</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armstrong</td>
<td>2012</td>
<td>49</td>
<td>7.90</td>
<td>0.03 (0.00, 0.17)</td>
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<tr>
<td>Rutkoff</td>
<td>2014</td>
<td>517</td>
<td>11.06</td>
<td>0.12 (0.02, 0.98)</td>
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<tr>
<td>Baskin</td>
<td>2014</td>
<td>146</td>
<td>15.00</td>
<td>0.26 (0.06, 1.06)</td>
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<tr>
<td>Tavianiini</td>
<td>2014</td>
<td>436</td>
<td>7.75</td>
<td>0.11 (0.01, 1.79)</td>
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<tr>
<td>Yousif</td>
<td>2015</td>
<td>159</td>
<td>7.50</td>
<td>0.13 (0.01, 2.33)</td>
</tr>
<tr>
<td>Storey</td>
<td>2016</td>
<td>167</td>
<td>9.50</td>
<td>2.17 (0.20, 23.53)</td>
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<tr>
<td>Subtotal</td>
<td></td>
<td></td>
<td>58.75</td>
<td>0.21 (0.06, 0.74)</td>
</tr>
</tbody>
</table>

Abstract Only

<table>
<thead>
<tr>
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<th>Year</th>
<th>N</th>
<th>Weight (%)</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stenz</td>
<td>2013</td>
<td>6031</td>
<td>20.40</td>
<td>1.15 (0.56, 2.24)</td>
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<tr>
<td>Kagan</td>
<td>2014</td>
<td>5372</td>
<td>20.35</td>
<td>0.18 (0.10, 0.33)</td>
</tr>
<tr>
<td>Subtotal</td>
<td></td>
<td></td>
<td>41.25</td>
<td>0.45 (0.56744)</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td>71.6%</td>
<td>0.20 (0.10, 0.78)</td>
</tr>
</tbody>
</table>

1476 patients. CLABSI: OR 0.21 (0.06, 0.74)

2.4/1000 PICC d vs 0.26/1000 PICC days (P = 0.014); NNT = 26

No difference between coating type: CHG = 0.31, R/M = 0.27; P= 0.93
Will antibiotic coated catheters lead to antibiotic resistance?
What about antiseptic coated catheters?

Technologic Innovations
Emergence of Resistance?

**In Vitro and in Vivo Efficacy of Catheters Impregnated with Antiseptics or Antibiotics: Evaluation of the Risk of Bacterial Resistance to the Antimicrobials in the Catheters**

- Serial passage experiments for *S. epidermidis* and *E. coli* in drug or antiseptic containing broth.
- Tested explanted catheters (from rats) in zone of inhibition tests against passaged strains.

**CONCLUSIONS:** Antiseptic and antibiotic catheters exhibit similar efficacy; however, when challenged with a rifampicin resistant strain, the antibiotic catheter appeared to be more susceptible to colonization than antiseptic device.

Emergence of Resistance?

In Vitro Exposure of Bacteria to Antimicrobial Impregnated – Central Venous Catheter Does Not Directly Lead to the Emergence of Antimicrobial Resistance

- In-vitro susceptibility testing of isolates of *S. epidermidis*, *S. aureus*, *E. faecalis*, and *E. coli* that had been grown next to CVC segments

CONCLUSIONS: Our in vitro data suggest that the exposure of Gram-positive cocci to either rifampicin or minocycline can lead to development of resistance. However, exposure of bacteria to these antibiotic in combinations does not directly lead to resistance. Clinical investigations will be required to determine the true risk and implications of the development of resistance.

Emergence of Resistance?

Clinical Effectiveness and risk of emerging resistance associated with prolonged use of antibiotic – impregnated catheters: More than 0.5 million catheters days and 7 years of clinical experience

- 9200 CVCs; 511,520 CVC days
- CLABSI decreased from 8.3 to 1.2/1000 CVC d
- Resistance of S aureus or CoNS to rifampin or tetracycline remained stable or decreased
- Long term use of R/M CVC not associated with clinical emergence of resistance

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Novel Antimicrobial Coatings

- 5-Fluorouracil
- Rifampin-Miconazole
- Silver Nanoparticles
- Chlorhexidine/Minocycline/Rifampin
- Gentian violet/ Chlorhexidine
- Surface Pattern

- Polymeric sulfobetaine (polySB)
- PolyHexaMethylene biguanide
- Gold, Silver, Palladium
- Antimicrobial peptides
- Auranofin
Additional to Catheter

Technologic Innovations
Chlorhexidine Impregnated CVC Dressings
**Meta-analysis and systematic reviews on use of CHG Dressings in Prevention of CRBSI**

- Ho, et al. J Antimicrob Chemother. 2006. 6 studies, 2446 catheters (OR 0.58)
- Safdar, et al. Crit Care Med. 2014. 9 RCTs, 10,481 catheters (RR 0.6)
- Ullman, et al. Cochrane Review. 2015. 22 studies, 7436 patients (RR 0.65)
- Xing, et al. Iran J Public Health. 2019. 13 RCTs, 7555 patients, 11,931 catheters (RR 0.55)
- Wei, et al. BMC Infect Dis. 2019. 12 RCTs, 6028 patients (OR 0.6)

6 meta-analyses all concluded that CHG dressings significantly reduced risk of CRBSI
Scrub the Hub!

Not All Mechanical Valves are Created Equal

Negative Displacement Needleless Connector

Neutral Displacement Needleless Connector

Positive Displacement Needleless Connector
Antiseptic Caps Passive Port Protectors
**Scope of the Problem**

**What about Peripheral IVs??**

**Yearly Use of Peripheral IVs**

- 330 Million Peripheral IVs
- 1.7 Billion Peripheral IVs

Little systematic data regarding complications: infection, phlebitis, infiltration, extravasation

The Risk of Bloodstream Infection in Adults With Different Intravascular Devices: A Systematic Review of 200 Published Prospective Studies

- Review of 110 studies, 10,910 catheters
- 0.5 BSI (95% CI 0.2–0.7)/1000 device days
- 9 higher quality studies (microbial concordance between catheter and blood culture): 0.6 BSI/1000 device days
- 1 per 1000 devices x 330 Million/2.25 attempts per successful IV start = 146,000 episodes of BSI

Short-term Peripheral Venous Catheter-Related Bloodstream Infections: A Systematic Review

- BSI 0.18% amongst 85,063 PVCs
- PIVs responsible for 23% of catheter-related BSI


Observational cohort study at AMC in Switzerland from Jan 2016 to Mar 2020
- 412,631 PIVs in 164,331 pts
- Baseline: PIVs changed every 96 hours (27 mo);
- Intervention: PIVs changed as needed (18.5 mo); Reversion to baseline (5.5 mo)
- A significant increase in PIV BSI was observed (BSI/10,000 PIV d) 0.128 (baseline) vs 0.894 (intervention) vs 0.287 (reversion). Incidence rate ratio 7.2 (intervention vs baseline), 95% CI (3.65-14.22) vs 1.35 (reversion vs baseline), 95% CI (0.3-6.17).
What about Midlines?

A comparison of the incidence of midline catheter–associated bloodstream infections to that of central line–associated bloodstream infections in 5 acute care hospitals

- Multi-center retrospective review
- 165,166 CL-days and 26,063 ML-days among all 5 hospitals
- 23 MLABSIs for an overall MLABSI incidence of 0.88 per 1,000 ML-days
- 178 CLABSIs resulting in a CLABSI incidence of 1.10 per 1,000 CL-days
- MLABSI and CLABSI was not statistically significant ($P=0.37$)

Scope of the Problem

What about Arterial Catheters???

- Arterial catheters (AC) are associated with same risk for BSI as nontunneled CVCs. 1.7 BSI/1000 cath days.\(^{26}\)
- 8 Million ACs used per year in USA.\(^{31}\)
- Only 44% of institutions follow CDC recommendations for AC insertion precautions.\(^{32,33}\)
- ACs should be inserted and cared for with same level of respect as CVCs.\(^{26}\)

Infection Control – View for the Future

“There are known knowns. These are things we know that we know. There are known unknowns. That is to say, there are things that we know we don’t know. But there are also unknown unknowns. There are things we don’t know we don’t know.”

- Secretary of Defense Donald Rumsfeld

(PS: there are also things that we think we know, but we’re wrong)
Any Questions?
References


13. Real-time evaluation of Chlorhexidine-treated indwelling PICC in reducing bacterial attachment, colonization and biofilm formation Gupta & Haughton AVA 2019


References


References


Rx only

Contraindication: Clinical assessment of the patient must be completed to ensure no contraindications exist. Arrowgard Blue Advance® Catheters are contraindicated in the following areas:
• Patients with known hypersensitivity to chlorhexidine
• In presence of device related infections
• In presence of previous or current thrombosis in the intended vessel or along the catheterized vessel pathway.

No correlation between in vitro/in vivo testing methods and clinical outcomes have currently been ascertained.
Thank You