Strategies for the Treatment and Prevention of Central Venous Catheter Infections

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Objectives

1) To define central venous catheter (CVC) infection and strategies for treatment.

2) To discuss available evidence addressing strategies for prevention of central venous catheter infection during insertion.

3) To discuss available evidence addressing strategies for prevention of central venous catheter infection during catheter care.

4) To discuss combination strategies ("bundling") used by some institutions to minimize risk of central venous catheter infections.
Case discussion

24 month old with short bowel syndrome, on long-term TPN. Infant admitted for 3rd line infection over past 8 months…
Diagnosing CVC infection

- CVC cultures should be performed only when bloodstream infection is suspected.
- Blood samples should be obtained prior to initiation of antibiotic therapy.
- Skin preparation should be performed (alcohol, iodine, chlorhexidine) prior to blood draw.
- Two samples should be obtained:
  - Blood sample should be obtained through catheter (if catheter salvage planned) or catheter tip should be cultured (if removed)
  - Peripheral blood culture (blood sample through a second catheter lumen if not able to obtain peripheral sample)

Definition of CVC infection

- CRBSI (catheter-related bloodstream infection) = growth of the same organism from the catheter and the peripheral blood, meeting criteria for *quantitative blood cultures* or *differential time to positivity*

- Quantitative blood cultures = a catheter hub blood microbe colony count that is at least 3-fold greater than that generated from the peripheral blood

- Differential time to positivity = growth of microbes from catheter hub blood at least 2 hours before growth is detected from the peripheral blood

Common organisms

- Most CRBSI among children are caused by coagulase-negative staphylococci (CNS) (34%), followed by *S. aureus* (25%)
- In neonates, CNS (51%) is the most common, followed by *Candida* species, enterococci, and gram-negative bacilli
- Infants with short-gut syndrome are more likely to have CRBSI secondary to gram-negative bacilli

Empiric antibiotic coverage

- Gram positive and gram negative organisms should be covered in pediatric patients
- Consider an institution’s commonly isolated organisms and susceptibility patterns
- Vancomycin is recommended for empiric therapy
- Empiric coverage for gram-negative bacilli can be a third or fourth generation cephalosporin, carbapenem, or β-lactam/β-lactamase combination, with or without aminoglycoside
- In neutropenic patients, gram negative coverage should included *P. aeruginosa*

General treatment guidelines

- Remove CVC except in patients with uncomplicated coagulase-negative staphylococci or enterococci bacteremia
- Catheter salvage is an option in patients with uncomplicated CVC infection
- Uncomplicated - defined as:
  - Resolution of bloodstream infection and fever within 72 hours in a patient who:
    - Has no intravascular hardware
    - No endocarditis
    - No suppurative thrombophlebitis

Length of treatment

- Length of antimicrobial therapy:
  - **CNS**: may retain and treat 10 to 14 days
  - **Enterococcus**: may retain and treat 7 to 14 days
  - **S. aureus**: remove and treat 4 to 6 weeks
  - **Gram negative bacilli**: remove and treat 7 to 14 days; if salvaged, treat 10 to 14 days
  - **Candida species**: remove and treated for 14 days; difficult to eradicate without catheter removal

Antibiotic lock therapy

- Indicated in patients when catheter salvage is the goal
- Use in conjunction with systemic antimicrobial therapy
- Dwell times for antibiotic lock solutions should not exceed 48 hours
- Antibiotic concentrations must be increased (100 to 1000 times) to kill bacteria within a biofilm
- *S. aureus* and *Candida* species are less likely to respond to lock therapy

Treatment failure

- No clearance of bacteremia 72 hours after start of antimicrobial therapy or clinical deterioration
- If persistent fever or clinical signs of sepsis, consider work up for:
  - Endocarditis
  - Suppurative thrombophlebitis
  - Other metastatic infection

Prevention of CVC infection

1. Cutaneous antisepsis for CVC insertion and care
2. Chlorhexidine impregnated catheter dressing
3. Lock therapy
Is chlorhexidine (CH) a more effective cutaneous antiseptic agent than povidone-iodine (PI) for CVC insertion and care?

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Design</th>
<th>Population</th>
<th>N</th>
<th>Treatment</th>
<th>Outcome</th>
<th>Results (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mimoz, 2007</td>
<td>RCT</td>
<td>Adult</td>
<td>481 catheters</td>
<td>Biseptine</td>
<td>CC CRBSI</td>
<td>IR: Bs 11.6%, PI 22.2% IR: Bs 1.7%, PI 4.2%</td>
<td>P=0.002 P=0.09</td>
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<tr>
<td>Langgarter 2004</td>
<td>RCT</td>
<td>Adult</td>
<td>140 catheters</td>
<td>Skinsept + PI vs Skinsept vs PI</td>
<td>CC</td>
<td>IR: Sk+PI 4.7%, Sk 24.4%, PI 30.8%</td>
<td>P=0.006</td>
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<tr>
<td>Chaiyakun-apruk, 2002</td>
<td>Meta-analysis</td>
<td>8 RCTs, adult</td>
<td>4143 catheters</td>
<td>ChlorPrep, 0.5% CH, Biseptine</td>
<td>CC CRBSI</td>
<td>RR: 0.49 (0.31-0.71) RR: 0.49 (0.28-0.88)</td>
<td>--</td>
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<tr>
<td>Humar, 2000</td>
<td>RCT</td>
<td>Adult</td>
<td>242 patients</td>
<td>0.5% CH</td>
<td>CC CRBSI</td>
<td>RR: 1.33 (0.87-2.04) RR: 0.75 (0.20-2.75)</td>
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<tr>
<td>Mimoz, 1996</td>
<td>RCT</td>
<td>Adult</td>
<td>158 catheters</td>
<td>Biseptine</td>
<td>CC CRBSI</td>
<td>RR: 0.3 (0.1-1.0) RR: 0.3 (0.1-1.0)</td>
<td>P=0.03 P=0.02</td>
</tr>
<tr>
<td>Maki, 1991</td>
<td>RCT</td>
<td>Adult</td>
<td>144 catheters</td>
<td>2% CH</td>
<td>CC CRBSI</td>
<td>OR: 0.26 (0.07-0.91) OR: 0.23 (0.03-1.80)</td>
<td>P=0.02 P=0.18</td>
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<tr>
<td>Garland, 1995</td>
<td>PNT</td>
<td>Pediatric, NICU, PICC</td>
<td>826 catheters</td>
<td>0.5% CH + 70% isopropyl alcohol</td>
<td>CC</td>
<td>IR: CH 4.7%, PI 9.3%</td>
<td>P=0.01</td>
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Biseptine (Bs): 0.25% chlorhexidine, 0.025% benzalkonium chloride, 4% benzyl alcohol
Skinsept (Sk): 0.5% chlorhexidine, 70% isopropyl alcohol
ChlorPrep: 2% chlorhexidine, 70% isopropyl alcohol
Does the placement of a chlorhexidine-impregnated sponge (Biopatch®) at the CVC insertion site decrease the risk of CC and/or CRBSI?

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<td>Timsit, 2009</td>
<td>RCT</td>
<td>Adult</td>
<td>1636 patients, 3778 catheters</td>
<td></td>
<td>CC CRBSI</td>
<td>HR: 0.36 (0.28-0.46) HR: 0.24 (0.09-0.65)</td>
<td>P&lt;0.001 P=0.005</td>
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<tr>
<td>Ruschulte, 2009</td>
<td>RCT</td>
<td>Adult</td>
<td>601 patients</td>
<td></td>
<td>CRBSI</td>
<td>RR: 0.54 (0.31-0.94)</td>
<td>P=0.016</td>
</tr>
<tr>
<td>Ho, 2006</td>
<td>Meta-analysis</td>
<td>6 RCTs (2 pediatric)</td>
<td>2446 catheters</td>
<td>chlorhexidine-impregnated sponge (BiopatchØ)</td>
<td>CC CRBSI</td>
<td>OR: 0.47 (0.34-0.65) OR: 0.61 (0.30-1.26)</td>
<td>P&lt;0.00001 P=0.19</td>
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<tr>
<td>Chambers, 2005</td>
<td>RCT</td>
<td>Adult, tunneled CVC</td>
<td>112 catheters</td>
<td>Exit-site/tunnel/tip infections</td>
<td>CC CRBSI</td>
<td>OR: 0.13 (0.04-0.37)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Levy, 2005</td>
<td>RCT</td>
<td>Age 0-18</td>
<td>145 patients</td>
<td></td>
<td>CC CRBSI</td>
<td>RR: 0.61 (0.37-1.0) Infection Rate: CH 54%, control 4.2%</td>
<td>P=0.04 P=1.0</td>
</tr>
<tr>
<td>Garland, 2001</td>
<td>RCT</td>
<td>NICU, PICC and tunneled CVC</td>
<td>705 neonates</td>
<td></td>
<td>CC CRBSI</td>
<td>RR: 0.6 (0.5-0.9) RR: 1.2 (0.5-2.7)</td>
<td>P=0.004 P=0.65</td>
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Are antibiotic or ethanol lock therapies effective in decreasing CC and/or CRBSI?

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| Cober, 2011 | Retrospective review    | Patients <25 years old, ≥5 kg, silicone CVC     | 15 | 70% ethanol | Bloodstream infection         | Pre-EtOH lock: 8.0 ± 5.4  
Post-EtOH lock: 1.3 ± 3.0                  | P<0.001 |
| Jones, 2010 | Retrospective review    | 3 mo<18 years, ≥5 kg, silicone CVC & PICC       | 23 | 70% ethanol | Median CVC infection rate     | Pre-EtOH lock: 9.9 (IQR 4.4-16.0)  
Post-EtOH lock: 2.1 (IQR 0.0-7.6)      | P=0.03  |
| Kayton, 2010 | Prospective Phase I     | Pediatric, neuroblastoma, mediport              | 12 | 70% ethanol | (+) cultures                  | 1/12 patients (8%)- Strep pneumoniae       |          |
|             | single-armed            |                                                 |    |            |                                | 3 cases of catheter thrombosis              |          |
| Sanders, 2008 | RCT                    | Adult, cancer, tunneled CVC                     | 64 | 70% ethanol | CABS i                        | OR: 0.18  
(95% CI: 0.05-0.65)                    | P=0.008 |
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<tr>
<td>Garland, 2005</td>
<td>RCT</td>
<td>NICU, PICC</td>
<td>85</td>
<td>Vancomycin-heparinized saline</td>
<td>Combined definite and probable CRBSI</td>
<td>RR 0.16 (95% CI 0.04-0.66)</td>
<td>P=0.002</td>
</tr>
</tbody>
</table>
Recommendations

- Based on adult data, use of chlorhexidine with alcohol as cutaneous antisepsis decreases the risk of CC and CRBSI when compared to 10% povidone-iodine. (*Care should be taken in neonates and premature infants.*)

- Use of a chlorhexidine-impregnated sponge (Biopatch®) at the CVC insertion site decreases the risk of catheter related infections. (*Sponge should not be used in premature infants.*)

- Ethanol lock therapy for silicone CVCs can be administered safely and may reduce the incidence of catheter related infections.

- Vancomycin lock solution can reduce the incidence of CABSII.
Process improvement

- “Bundle” – a collection of evidence-based care processes
- Allows for implementation of a collective set of quality improvement processes in a consistent, organized manner
- Examples:
  - CVC insertion bundle: hand washing, prep description, standard catheters, prepackaged instruments, checklist, training video
  - CVC maintenance bundle: daily assessment, site care instructions, hub care instructions, prepackaged kit, training video
- Shown to decrease frequency of CVC infections
Case discussion

24 month old with short bowel syndrome, on long-term TPN. Infant admitted for 3rd line infection over past 8 months...

Plan:

• Obtain peripheral and catheter blood culture
• Start empiric therapy, i.e., Vancomycin & Meropenem
• Sequential blood cultures until negative, change to target therapy
• Complete appropriate length of target therapy with concurrent antibiotic lock therapy
• Start ethanol lock therapy to prevent recurrent infection