Evidence Fails to Support Routine use of Antibiotic Impregnated Catheters

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Objectives

1) Very brief overview of antibiotic/antiseptic impregnated catheters
2) CDC definition of a catheter related bloodstream infection
3) Present the equivocal data regarding these catheters
4) Expose the inadequacies of studies supporting their use
5) Explore how reinforcement of antiseptic techniques can alter line infection rates in the Intensive Care Unit
Current Antibiotic and Antiseptic Coated Central Venous Catheters

- Antibiotic: Minocycline and Rifampin coating applied to lumen and exterior of catheter
- Antiseptic: Chlorhexidine and Silver Sulfadiazine applied to both lumen and exterior of catheter

Initial studies with antiseptic catheters performed with 1st generation – only external coating.
A Catheter Related Bloodstream Infection

CDC\(^1\)

Clinical definition of a Catheter Related Bloodstream Infection
Clinical manifestation of infection & one pos. peripheral blood culture & no apparent source other than catheter w (1) of these:

a. (+) quant/semiquant culture of a catheter segment w identical organism as blood
b. Simultaneous quant blood culture w at least 5X the population from the catheter versus periphery
c. More than 2 hours elapsed from positive peripheral versus catheter blood cultures.
Evidence Against Use of Antibiotic Impregnated Catheters

Leon et al. 2003².

- Multicenter, randomized, double-blind, controlled Spanish trial
- 1999-2002, enlisted 465 pts, 228 minocycline-rifampin catheters & 237 control in 7 academic hospitals in Spain
- Baseline characteristics similar.
- 6.8% vs 27.8% colonization of catheters that was statistically significant
Leon et al. 2003\textsuperscript{2} 

- No statistically significant difference in catheter-related bloodstream infections
- Statistically significant increase in *C. albicans* colonizations in the experimental group

<table>
<thead>
<tr>
<th></th>
<th>All sections (tip and/or subcutaneous segment and/or hub)</th>
<th>Coagulase-negative staphylococci</th>
<th><em>Candida</em> spp.</th>
<th>Catheter-related bloodstream infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>7 (3.7)</td>
<td>10 (5.3)</td>
<td>6 (3.2)</td>
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<td></td>
<td></td>
<td>3.6</td>
<td>5.2</td>
<td>3.1</td>
</tr>
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<td></td>
<td></td>
<td>33 (18.3)</td>
<td>2 (1.1)</td>
<td>11 (6.1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17.6</td>
<td>1.1</td>
<td>5.9</td>
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<tr>
<td></td>
<td></td>
<td>0.21 (0.09–0.47)</td>
<td>4.87 (1.07–22.2)</td>
<td>0.53 (0.2–1.44)</td>
</tr>
</tbody>
</table>
Evidence Against Use of Antibiotic Impregnated Catheters

Chelliah et al. 2007³.

• Prospective observational trial in 13 months at CHOP
• Sept 2003 to Oct 2004, 263 catheters placed in 225 pediatric patients, 83% femoral
• Baseline characteristics similar.
• Incidence density 7.53 per 1000 catheter-days with coated catheters, 8.64 per 1000 with non-coated catheters – non-significant.
Chelliah et al. 2007

- No statistical significant difference in catheter-associated bloodstream infections

“...these observations suggest that the impact of antibiotic-coated catheters is likely during the first 14 days following line placement.”
Heard *et al.* 1998

- Randomized, controlled trial with antiseptic impregnated catheters
- \(n=365\) catheters in 251 pts.
- CRBSI in 3.3% in coated catheters and 3.8% in non-coated, \(p=0.81\)

![Graph showing cumulative percentage of cases without catheter-related bacteremia. There are no significant differences between the 2 curves.](image)
Heard et al. 1998

“Only when the expected duration of catheterization is beyond 7 to 10 days will the patient realize a benefit from a CSS catheter.”
Evidence Against Use of Antiseptic Impregnated Catheters

Rupp *et al.* 2005[^5].

- Multicenter, randomized, double-blind, controlled US trial.
- Chlorhexidine and Silver sulfadiazene impregnated catheter versus uncoated
- CDC definition of clinical catheter related bloodstream infection was used
Rupp et al. 2005

Patients randomly assigned
(n = 780)
(3 randomly assigned patients
did not receive a study catheter)

Control catheters
(n = 393)

De novo insertion
(n = 267)
Catheters not cultured
(n = 24)
Catheters cultured
(n = 243)

Guidewire exchange
(n = 126)
Catheters not cultured
(n = 7)
Catheters cultured
(n = 119)

Antiseptic catheters
(n = 384)

De novo insertion
(n = 258)
Catheters not cultured
(n = 27)
Catheters cultured
(n = 231)

Guidewire exchange
(n = 126)
Catheters not cultured
(n = 12)
Catheters cultured
(n = 114)
There was no statistically significant rate of catheter-related bloodstream infections between two different catheter types
- 1.24 versus 0.42 per 1000 catheter days with a p=0.6

Again, a statistically significant rate of decreased colonized catheters with the use of antiseptic-coated catheters

Authors conclusion: study design overestimated infections in pts with central catheters, now underpowered to detect a statistically significant difference.
Systematic Review

Twenty-one trials reviewed:
(A) 5 antibiotic-coated
(B) 13 antiseptic-coated
(C) 1 heparin-coated
(D) 3 antibiotic versus antiseptic coating
(E) 1 trial of heparin versus antiseptic treated catheter
“4/5 found that CRBSI…more common in standard CVC group; in none of these was the result statistically significant at 5% level.”

translation: 0/5 studies had significantly lower rates of catheter related infections
(B) “12/13 found that CRBSI…more common in standard CVC group; just one of these results was statistically significant at the 5% level.”

translation: 1/13 studies had significantly lower rates of catheter related infections
### Niel-Weise et al. 2007

#### Outcome: Cases with catheter-related bloodstream infection

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment nN</th>
<th>Control nN</th>
<th>RR (random) 95% CI</th>
<th>Weight %</th>
<th>RR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>01 Anti-Infective (overall) versus standard</strong></td>
<td></td>
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<tr>
<td>Bach 1996</td>
<td>0/116</td>
<td>3/117</td>
<td>2.65 [0.14, 2.76]</td>
<td><strong>2.65</strong></td>
<td>0.14 [0.01, 2.76]</td>
</tr>
<tr>
<td>Brun-Buisson 2004</td>
<td>3/188</td>
<td>5/175</td>
<td>10.06 [0.56, 2.30]</td>
<td><strong>10.06</strong></td>
<td>0.56 [0.14, 2.30]</td>
</tr>
<tr>
<td>Chatzinikolau 2003</td>
<td>0/66</td>
<td>7/64</td>
<td>2.85 [0.06, 1.11]</td>
<td><strong>2.85</strong></td>
<td>0.06 [0.00, 1.11]</td>
</tr>
<tr>
<td>Collin 1993</td>
<td>1/98</td>
<td>4/139</td>
<td>4.71 [0.35, 3.12]</td>
<td><strong>4.71</strong></td>
<td>0.35 [0.04, 3.12]</td>
</tr>
<tr>
<td>Corral 2003</td>
<td>0/70</td>
<td>1/58</td>
<td>2.30 [0.28, 0.42]</td>
<td><strong>2.30</strong></td>
<td>0.28 [0.01, 0.42]</td>
</tr>
<tr>
<td>George 1997</td>
<td>1/44</td>
<td>3/35</td>
<td>4.54 [0.27, 2.44]</td>
<td><strong>4.54</strong></td>
<td>0.27 [0.01, 2.44]</td>
</tr>
<tr>
<td>Hannan 1999</td>
<td>1/174</td>
<td>3/177</td>
<td>4.42 [0.36, 3.23]</td>
<td><strong>4.42</strong></td>
<td>0.36 [0.04, 3.23]</td>
</tr>
<tr>
<td>Haard 1998</td>
<td>5/151</td>
<td>6/157</td>
<td>13.76 [0.87, 2.78]</td>
<td><strong>13.76</strong></td>
<td>0.87 [0.00, 2.78]</td>
</tr>
<tr>
<td>Leon 2004</td>
<td>6/187</td>
<td>11/180</td>
<td>17.97 [0.53, 1.29]</td>
<td><strong>17.97</strong></td>
<td>0.53 [0.00, 1.29]</td>
</tr>
<tr>
<td><strong>Maki 1997</strong></td>
<td>2/208</td>
<td>9/195</td>
<td>8.93 [0.26, 0.95]</td>
<td><strong>8.93</strong></td>
<td>0.26 [0.00, 0.95]</td>
</tr>
<tr>
<td>Manik 1990</td>
<td>1/76</td>
<td>2/39</td>
<td>4.02 [0.26, 2.82]</td>
<td><strong>4.02</strong></td>
<td>0.26 [0.00, 2.82]</td>
</tr>
<tr>
<td>Moretti 2005</td>
<td>0/282</td>
<td>1/262</td>
<td>2.28 [0.28, 8.47]</td>
<td><strong>2.28</strong></td>
<td>0.28 [0.00, 8.47]</td>
</tr>
<tr>
<td>Orsme 2006</td>
<td>4/64</td>
<td>1/69</td>
<td>4.76 [0.44, 37.87]</td>
<td><strong>4.76</strong></td>
<td>0.44 [0.00, 37.87]</td>
</tr>
<tr>
<td>Pine 2000</td>
<td>1/87</td>
<td>19/103</td>
<td>5.54 [0.35, 0.41]</td>
<td><strong>5.54</strong></td>
<td>0.35 [0.00, 0.41]</td>
</tr>
<tr>
<td>Raad 1997</td>
<td>0/130</td>
<td>7/136</td>
<td>2.83 [0.08, 1.21]</td>
<td><strong>2.83</strong></td>
<td>0.08 [0.00, 1.21]</td>
</tr>
<tr>
<td>Piceps 2005</td>
<td>1/345</td>
<td>3/362</td>
<td>4.40 [0.36, 3.38]</td>
<td><strong>4.40</strong></td>
<td>0.36 [0.04, 3.38]</td>
</tr>
<tr>
<td>Sheng 2000</td>
<td>1/113</td>
<td>2/122</td>
<td>3.97 [0.54, 5.87]</td>
<td><strong>3.97</strong></td>
<td>0.54 [0.00, 5.87]</td>
</tr>
<tr>
<td>Yücel 2004</td>
<td>0/118</td>
<td>0/105</td>
<td></td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>2439</td>
<td>2435</td>
<td>100.00 [0.50, 0.62]</td>
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</tr>
</tbody>
</table>

**Total events:** 27 (Treatment), 87 (Control)

**Test for heterogeneity:** Chi² = 15.88, df = 16 (P = 0.46), P = 0%

**Test for overall effect:** Z = 4.02 (P < 0.0001)

**RD:** -0.02 [-0.03, -0.01]

**NNT:** 1 / 0.02 = 50
Maki et al. 1997

- Study was double-blinded, failed to control for \textit{de novo} central line placements versus line replacements over wire.
- Statistically significant difference (increase) in use of antiseptic-coated catheters for replacing existing lines.
- 7.6 CRBSI per 1000 catheter days in control group versus 1.6 in the antiseptic. \(p=0.03\)
Maki et al. 1997

• Controlling for *de novo* insertions, failed to show significant benefit in reducing catheter-related bacteremias with experimental catheters

• Total of 12 bloodstream infections: 9 by control catheter.

“…but seven bloodstream infections occurred in patients *exposed* to an antiseptic study catheter, 2 of which were caused by the antiseptic study catheter.”
Antiseptic techniques

- Pronovost et al. 2006\textsuperscript{8} NEJM
- Michigan ICUs, 108 agreed to participate in a collaborative cohort study.
- Focused on 5 evidence-based procedures: hand-washing, full-barrier precautions, chlorhexidine prep, no femoral lines, remove unnecessary catheters
Pronovost et al. 2006\textsuperscript{8}

- Strategies for compliance included:
  - Education
  - Central line cart
  - Checklist used to ensure adherence; RN can stop procedure with noncompliance
  - Daily discussions about removal of catheters

- Overall median rate of catheter-related bloodstream infections decreased from 2.7 per 1000 catheter-days to 0 per 1000 catheter-days
Pronovost et al. 2006

- Median was zero at 0-3 months, during implementation. Remained with a median of zero to 18 months

- At a cost savings of 35 dollars per central catheter.
Conclusions

- There is insufficient data to support use of antibiotic or antiseptic impregnated central venous catheters
- There is sufficient data to support team education as a means to reduce catheter-associated bloodstream infections
- Other concerns: encouraging resistant organisms with antibiotic-impregnated catheters, allergic reactions to coatings.
References


References


