Considerations for Evidence-Based Evaluations of New and Evolving Proprietary Products for Infection Control

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Chlorhexidine-Impregnated (CGI) Dressings for Intravascular Catheter Exit Sites

- Background
- Recent Publications Combining Chlorhexidine Impregnated (CGI) Dressing types
- Current work
- Discussion
2011 CDC & HICPAC BSI Guideline Recommendations

- Use a chlorhexidine-impregnated sponge dressing for temporary short-term catheters in patients older than 2 months of age if the CLABSI rate is not decreasing despite adherence to basic prevention measures, including education and training, appropriate use of chlorhexidine for skin antisepsis, and MSB. **Category IB**

- No recommendation is made for other types of chlorhexidine dressings. **Unresolved issue**

II. Special approaches for preventing CLABSI

- 2. Use chlorhexidine-containing dressings for CVCs in patients over 2 months of age (quality of evidence: I) [1 SR, 5 RCT, 1 OBS].
  - a. It is unclear whether there is additional benefit to using a chlorhexidine-containing dressing if daily chlorhexidine bathing is already established and vice versa.
Recent Meta-analyses: Combining CGI Dressings

- Safdar, et. al. 2014:
  - Primary Analysis: Relative Risk of CRBSI with CGI Dressing vs. comparator (9 studies, 5,639 patients) \( RR: 0.57 \ (0.42-0.79); \ p=0.002; \ I^2 = 10\% \)

Combining CGI Dressings

- Cochrane Review, 2015: Dressings and securement devices for central venous catheters (CVC)

1.1.5 Frequency of CRBSI for CGI dressings compared with Standard Polyurethane (SPU) dressings (5 trials, 4876 participants):

  - Unclear evidence of reduction in CRBSI: \( RR \ 0.65 \ (0.40 - 1.05); \ p=0.08; \ I^2=26\% \) – Moderate quality evidence (downgraded for imprecision)

1.1.10 Frequency of CRBSI for CGI dressings compared with all other dressings (6 trials, 5687 participants):

- Significant reduction in CRBSI: **RR 0.60 (0.39 – 0.93); p=0.02; I²=19%** – High quality evidence

1.2.4 Frequency of CRBSI per 1000 patient days: CGI dressings compared with SPU dressings (4 studies, 42,689 days): significant evidence of benefit

- **RR 0.51 (0.33 – 0.78); p=0.002** – Moderate quality evidence (downgraded for imprecision)

Key Question

For patients older than two months with temporary, non-tunneled catheters how do CGI dressings, compared to standard dressings, impact the risk of catheter-related infections?

- Critical Outcomes: infection (e.g. catheter-related bloodstream infections (CRBSI), catheter-related infection (CRI), catheter-associated bloodstream infections (CABSI)),
- Outcome of interest: product related adverse events
51 potentially relevant studies identified in literature searches

11 Studies cited in 2011 CDC guideline
  • (4 RCT pulled from 1 SR)

2 studies suggested by content experts

65 title/abstracts screened

41 studies excluded
  28: not relevant to key question
  3: study design

24 full text review

18 studies excluded
  11: not relevant to key question
  4: study design
  3: to be cited in narrative summary

6 studies extracted into evidence and GRADE table
## Summary of RCTs

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<tbody>
<tr>
<td>Multicenter Adult ICU</td>
<td>Multicenter Adult ICU</td>
<td>Multicenter Adult ICU</td>
<td>Single Center Adult hem/onc patients</td>
<td>Single Center Cardiac PICU</td>
<td>Single Center Adult ICU</td>
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<thead>
<tr>
<th>Intervention</th>
<th>CHG gel</th>
<th>CHG sponge after first 24h</th>
<th>CHG sponge</th>
<th>CHG sponge (all had silver catheters)</th>
<th>CHG sponge</th>
<th>CHG sponge</th>
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<tbody>
<tr>
<td>Comparison</td>
<td>Standard or highly adhesive dressing</td>
<td>Semipermeable transparent dressing</td>
<td>Semipermeable transparent dressing</td>
<td>Standard sterile transparent dressing</td>
<td>Standard transparent dressing</td>
<td>Standard dressing</td>
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<thead>
<tr>
<th>N (patients)</th>
<th>1879</th>
<th>306</th>
<th>1525</th>
<th>601</th>
<th>145</th>
<th>32</th>
</tr>
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<tbody>
<tr>
<td>N Test/Ctrl Catheters</td>
<td>2108/2055</td>
<td>150/156</td>
<td>1847/1685</td>
<td>300/301</td>
<td>74/71</td>
<td>17/16</td>
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<tr>
<th>Infections</th>
<th>Decreased CRBSI and CRI</th>
<th>NS: CRBSI and CRI</th>
<th>Decreased CRBSI and CRI</th>
<th>Decreased CRBSI</th>
<th>NS: CA-BSI</th>
<th>NS: CRI</th>
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<tr>
<th>Product Related Adverse Events</th>
<th>Severe Contact Dermatitis, &amp; Abnormal ICDRG Score</th>
<th>No Severe Contact Dermatitis detected</th>
<th>Severe Contact Dermatitis &amp; Abnormal ICDRG scores</th>
<th>No patient had to be excluded due to allergic reaction to CHG</th>
<th>Local Redness – 4/74 vs. 1/74 p=NS</th>
<th>NR</th>
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Product Related Adverse Events

- **CHLORHEXIDINE RESISTANCE:**
  - One RCT suggested no suspicion of bacterial resistance to chlorhexidine dressings. (Ruschulte 2009)
  - One RCT: detected no changes microorganism profiles, an increase in MBCs of the most resistant strains could not be completely excluded. (Timsit 2009)
  - None of the other studies reported on chlorhexidine resistance.
Product Related Adverse Events: A deeper look

- Adverse Events Literature Search: September 2015
  - 2 Case Series: 7 patients each

- FDA adverse event data:
  - MAUDE
  - MedWatch
Next Steps

• Review Analysis
• Review Adverse Event Data
• Draft Recommendations
Discussion/ Feedback: CGI Dressings

- Combining products
  - Are there any reasons not to combine CGI dressings?

- Outcomes to consider:
  - Colonization data?
  - Other Product Related Adverse Events?

- Other considerations?
  - e.g. other sources of adverse event data?
Discussion/ Feedback: New and emerging proprietary products

• Considerations:
  – What products are similar enough to be in a product class?
  – Evaluating a new or emerging product/product class
    • Temporal thresholds?
    • Evidentiary thresholds?
    • Other factors?

• How do other organizations make recommendations for proprietary products?
Acknowledgements

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References