HEMODIALYSIS CATHETER COATINGS AND LOCKING SOLUTIONS - EFFECT ON INFECTION AND PATENCY – IS THERE ANY EVIDENCE?

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DISCLOSURES

- None
- Surface coated catheters and catheter lock solutions are off-label use

OBJECTIVES

- Dysfunctional catheters
- Infection - Role of biofilm
- Thrombosis - Virchow’s triad
- Catheter lock solutions
- Surface treated catheters

BIOFILMS AND INFECTION

- Initial contact of a planktonic bacteria with a foreign surface (e.g. catheter)
- Bacteria adhere irreversibly to the surface and proliferate to transform into bacterial micro-colonies
- Also generate a coating of exopolysaccharide (Biofilm) – a sticky glycocalyx matrix that further enhances adherence

PATHOPHYSIOLOGY - THROMBOSIS

- Virchow’s Triad:
  - Disruption in vessel walls (Initial insertion of catheter leading to endothelial damage of the vessel wall)
  - Coagulability (Initiation of the coagulation and inflammatory cascade)
  - Blood flow (Intra-luminal stasis of blood in the inter-dialytic period)
- Lead to a continuum of thrombus and fibrin sheath formation – as early as 24 hours within insertion
INFECTION AND THROMBOSIS – IS THERE A LINK?
- Once a pericatheter thrombus or fibrin sheath occurs, the patient is predisposed to infection and infectious complications increase the risk of catheter-related thrombosis.

CATHETER LOCK SOLUTIONS
- Anti-thrombotic
- Anti-microbial
  - Antiseptic - inhibits the growth of microorganisms without necessarily killing them
  - Antibiotic - inhibits the growth of or kills other microorganisms
  - Distinction important as sub-therapeutic levels of antibiotic solutions may induce resistant strains, though this is not the case with antiseptic solutions.

LOCK SOLUTIONS - THROMBOSIS

<table>
<thead>
<tr>
<th>YEAR</th>
<th>DRUGS USED</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>tPA vs Heparin</td>
<td>Flow significantly better in the tPA group; Small n=12, limited 4 month crossover</td>
</tr>
<tr>
<td>2005</td>
<td>30% trisodium citrate vs heparin</td>
<td>Comparable patency, Citrate with lower costs and decreased CRB</td>
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<tr>
<td>2006</td>
<td>4% trisodium citrate vs heparin</td>
<td>Comparable patency</td>
</tr>
<tr>
<td>2007</td>
<td>4% trisodium citrate vs heparin</td>
<td>Comparable patency</td>
</tr>
<tr>
<td>2008</td>
<td>4.5% trisodium citrate vs heparin</td>
<td>Comparable patency</td>
</tr>
</tbody>
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CATHETER LOCK SOLUTIONS – EFFECT ON BIOFILM
- Heparin induces biofilm formation in the presence of Staphylococcus aureus.

LOCK SOLUTIONS - THROMBOSIS
- Concern for inadvertent systemic anticoagulation
- Risk for major bleeding complications increases with increasing concentration of heparin.

CATHETER LOCK SOLUTIONS – EFFECT ON BIOFILM
**Lock Solutions - Thrombosis**

- Randomized controlled trial
- 225 patients randomized to catheter locking regimen of heparin (5000 U/ml) thrice weekly or rtPA substituted for heparin at the midweek session
- Primary outcome catheter malfunction
- Secondary outcome catheter related bacteremia


**Lock Solutions - Infection**

![Graph showing risk of catheter-related bacteremia](graph1.png)


**Conclusions**

- The use of rt-PA instead of heparin once weekly, as compared with the use of heparin three times a week, as a locking solution for central venous catheters significantly reduced the incidence of catheter malfunction and bacteremia.
- However, incremental costs of caring for patients with rtPA - $13,956 - per episode of CRB prevented

**Lock Solutions - Antimicrobials**

- Antimicrobial catheter lock solutions may potentially
  - Reduce colonization
  - Reduce biofilm formation
  - Minimize the risk of catheter related bacteremia
  - Antibiotic lock solutions concerning for
    - Systemic side effects
    - Potential for drug resistance

LOCK SOLUTIONS - ANTIMICROBIALS

- Short duration of follow-up of the original studies
- Potential for systemic toxicity
- Potential for resistance
- Economic ramifications
- Regulatory issues – None are FDA approved

LOCK SOLUTIONS - THROMBOSIS

- Catheter lock solutions
  - Heparin – Currently accepted as standard of practice, but varying concentrations in use, concern for inadvertent systemic anticoagulation – 1000 units/ml (ASDIN)
  - Alteplase – High fibrin specificity, no antigenicity, expensive for prophylaxis
  - Trisodium Citrate – Varying concentrations being evaluated as an alternative to heparin. Chelates free ionized calcium, making it unavailable to the coagulation cascade

CATHETER LOCK SOLUTIONS

- An ideal catheter locking solution:
  - Anticoagulant properties comparable to heparin
  - Safe for prophylactic use
  - Ability to kill bacteria in biofilm
  - No known bacterial resistance to components
  - Not an antibiotic
  - Relative density of 1.040
  - Preferably has a color, so that it is apparent when catheters are locked

SURFACE COATED CATHETERS

- Extensively studied in the critical-care literature
- CDC: Antimicrobial coated catheters may be used in populations where the rate of infection exceeds 3.3 per 1000 catheter days
- Acute setting
- Short-term use

CDC Guidelines for the prevention of intravascular catheter-related infections. Morbidity and Mortality Report 2002
SURFACE COATED CATHETERS

- Antithrombotic coatings
  - Heparin
- Antimicrobial coatings
  - Silver sulfadiazene
  - Chlorhexidine / Silver sulfadiazene
  - Minocycline / rifampin
  - Ciprofloxacin

HEPARIN COATED CATHETERS

- Basic principle: Heparin covalently bonded to the surface of catheter
  - Anticoagulant
  - May reduce thrombin activated factors
  - May reduce proliferation of SM cells
  - May thus potentially reduce biofilm, fibrin sheath and thrombus formation.

HEPARIN COATED CATHETERS

Maya et al. Does heparin coating improve patency or reduce infection in HD patients? CJASN 2009

COATED CATHETERS

- Silver impregnated catheters
  - Patients randomized to 2 groups
  - No differences in
    - Bacteremia
    - Exit site infections
    - Colonizations
  - Concerns for hyperpigmentation from the silver coating.


COATED CATHETERS

Kakkos et al. Effectiveness of a new tunneled catheter in preventing malfunction. JVIR 2008

(Kakkos et al. Effectiveness of a new tunneled catheter in preventing malfunction. JVIR 2008)
SURFACE COATED CATHETERS

- An ideal catheter coating or surface treatment
  - Biocompatible
  - Prevents both thrombus and fibrin sheath formation
  - Has broad-spectrum antimicrobial activity without inducing resistance
  - Is effective long-term

Amy Dwyer. Surface-Treated Catheters – A review. Seminars in Dialysis 2008

SUMMARY

- Surface coated catheters:
  - May have a place in the critical care setting
  - Lack convincing data in patients on chronic hemodialysis
  - Need to show longevity of the coating protection
  - Cost comparison – the cost of the catheter itself vs the overall costs of treating infections and/or thrombosis

SUMMARY

- Catheter lock solutions
  - Antithrombotic locks
    - May improve patency
    - Concern for systemic anticoagulation
  - Antimicrobial locks
    - May decrease incidence of catheter related bacteremia
    - Concern for antibiotic resistance

SUMMARY

- No surface treated catheter / catheter lock solution is “just right”
- Well-designed long-term randomized controlled trials are needed to establish safety and efficacy
- Best prophylaxis
  - Minimize catheter use
  - Have a plan in place to get rid of catheters

THANK YOU!

LOCK SOLUTIONS - ANTIMICROBIALS

- Another meta-analysis evaluated 8 RCTs
  - 3 times less risk of catheter-related bacteremia as compared to heparin
- BUT
  - Achieved incidence of CRB in the groups with antimicrobial catheter locks was similar to published reports from HD units
    - With low CRB incidence
    - And presumably stricter hygienic measures

Bleyer AJ. Use of antimicrobial catheter lock solutions to prevent CR. CJASN 2007
LOCK SOLUTIONS - ANTIMICROBIALS

- Recommended
  - Intensifying the education of all dialysis staff on adequate catheter care
  - Reserving antibiotic lock solutions for patients
    - At high-risk of infection
    - Or those in whom a catheter-related bacteremia would have devastating consequences

Bleyer AJ. Use of antimicrobial catheter lock solutions to prevent CB. CJASN 2007

HEPARIN COATED CATHETERS

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Tal et al. Initial clinical experience with heparin coated catheters. HI 2009

SURFACE COATED CATHETERS

Amy Dwyer. Surface-Treated Catheters – A review. Seminars in Dialysis 2008