Taurolidine versus Heparin Lock to prevent Catheter-related Bloodstream Infections in Patients on Home Parenteral Nutrition

Geert Wanten, Cindy van Eldijk, Renate Vissers
Intestinal Failure Unit
Department of Gastroenterology & Hepatology
Radboud University Nijmegen Medical Centre
The Netherlands

ASPEN New Orleans, 4 February 2009
Home parenteral nutrition

- Main therapy for chronic intestinal failure
- Venous access: central tunneled catheter / subcutaneous port
- Main problem: catheter-related bloodstream infections (CRBSI)

- Effect on quality of life and healthcare costs
- Determine outcomes of HPN programs
- Mainly in subset of patients
- Growth of microbes in biofilm on inner catheter surface
- Resistance to antibiotics: no penetration into biofilm
- Repeated catheter removal compromises access
Catheter-related bloodstream infections

- in HPN: 0.34 episodes / catheter year

- Measures to decrease CRBSI
  - training to perform aseptic techniques
  - antimicrobial filters
  - topical antimicrobial agents
  - fibrinolytic agents (alteplase)
  - systemic antibiotics:

No measure sufficiently effective to prevent CRBSI

¹ Howard L, Gastroenterology 2003;124:1651
Taurolidine

- potent antiseptic agent
- broad spectrum activity against all bacteria and yeasts \(^1;^2\)
  - non-toxic: end-products taurine, \(CO_2\) and water
- mechanism: reaction with microbial cell wall
  - prevents bacterial adhesion to biological surfaces \(^3;^4\)
- no reported side effects or bacterial resistance to taurolidine \(^5\)
- efficacy against CRBSI in hemodialysis, chemotherapy \(^1;^6\)

\(^1\) Allon M, Clin Infect Dis 2003;36:1539
\(^2\) Koldehoff M, Int J Antimicrob Agents 2004;24:491
\(^3\) Gorman SP, J Appl Bacteriol 1987;62:315
\(^4\) Erb F, Eur J Drug Metab Pharmacokinet 1983;8:163
\(^5\) Torres-Viera C, Antimicrob Agents Chemother 2000;44:1720
\(^6\) Yahav D, Clin Infect Dis 2008;47:83
Aim

- first prospective trial in setting of HPN
- compare catheter lock therapy with taurolidine versus standard (heparin) for efficacy to prevent CRBSI
- in patients with recent episode of CRBSI (i.e. proven susceptibility to infection)
Methods

✓ study population: largest Dutch HPN centre
  60 with Hickman or Porth-a-cath (20 arteriovenous fistula)

✓ patients developing CRBSI: clinical signs AND positive blood cultures
  no other focus

✓ infection treatment, with new or old new access device
  randomize: continue HPN using as catheter lock
  heparin (5 mL, 150 U/mL) or taurolidine (5 mL, 2% solution)

✓ primary end-point: new episode of CRBSI

✓ therapy failure: cross-over to other arm
Kaplan Meier analysis: infection-free survival

percent survival

infection free days until event

taurolidine

p < 0.0001

heparin
Results: trial profile

30 HPN pts with treated CRBSI
12 new; 18 old device

14 heparin arm
10 re-infections
76%
cross-over to taurolidine
1 re-infection on taurolidine

16 taurolidine arm
1 re-infection
6%
cross-over refused
Main Results

- 30 patients included with CRBSI between 2006 and 2008

<table>
<thead>
<tr>
<th></th>
<th>Heparin</th>
<th>Taurolidine</th>
</tr>
</thead>
<tbody>
<tr>
<td>catheter days</td>
<td>4939</td>
<td>5370</td>
</tr>
<tr>
<td>infection-free survival (d)</td>
<td>176 ± 46</td>
<td>641 ± 44</td>
</tr>
</tbody>
</table>

- no side effects in either group
- no catheter occlusions in either group
## Results: demographics

<table>
<thead>
<tr>
<th></th>
<th>Heparin</th>
<th>Taurolidin P</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female (n)</strong></td>
<td>10 (71%)</td>
<td>12 (75%)</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Age (yrs ±SD)</strong></td>
<td>49 ± 16</td>
<td>55 ± 13</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Cause of IF</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motility disorder</td>
<td>5 (36%)</td>
<td>5 (31%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>High output stoma</td>
<td>1 (7%)</td>
<td>1 (6%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Short bowel syndrome</td>
<td>5 (36%)</td>
<td>6 (38%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Other</td>
<td>3 (21%)</td>
<td>4 (25%)</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Type of access</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hickman</td>
<td>8 (57%)</td>
<td>11 (69%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Port-a-cath</td>
<td>6 (43%)</td>
<td>5 (31%)</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>New device pre-study</strong></td>
<td>6 (43%)</td>
<td>6 (38%)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>
## Results: culture at inclusion

<table>
<thead>
<tr>
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<th>Taurolidine</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Staphylococcus sp.</strong></td>
<td>7 (50%)</td>
<td>9 (56%)</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>epidermidis</strong></td>
<td>5 (36%)</td>
<td>7 (44%)</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>lugdunensis</strong></td>
<td>1 (7%)</td>
<td>1 (6%)</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>aureus</strong></td>
<td>1 (7%)</td>
<td>1 (6%)</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Other Gram +</strong></td>
<td>4 (29%)</td>
<td>2 (13%)</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Gram -</strong></td>
<td>3 (21%)</td>
<td>4 (25%)</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>0</td>
<td>1 (6%)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>


## Results

<table>
<thead>
<tr>
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<th>Heparin</th>
<th>Taurolidine</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infections/1000 catheter days before inclusion (n)</strong></td>
<td>2.33</td>
<td>2.36</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Infections/1000 catheter days after inclusion (n)</strong></td>
<td>2.02</td>
<td>0.19</td>
<td>0.008</td>
</tr>
<tr>
<td><strong>Culture at end-point</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staph</td>
<td>5</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Other Gram +</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Gram -</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>fungi</td>
<td>0</td>
<td>1</td>
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Conclusions

- Strong evidence for protective effect of taurolidine in prevention of CRBSI in the first RCT in HPN vs heparin in patients with proven susceptibility to these infections.

- No evidence for side effects or catheter occlusions.

- Taurolidine has changed our perspective on line sepsis.
Discussion

✓ based on small non-controlled study by Jurewitsch & Jeejeebhoy (Clin Nutr 2005;24:462)

✓ strength: single centre: same protocol
   individuals with proven susceptibility to infections
   similar effect after crossing over

✓ weakness: single centre / study size due to restrictions: open-label

✓ will resistance develop?

Confirmation in large multicenter / multinational trial

g.wanten@mdl.umcn.nl