Infectious Complications in PD – Peritonitis and Exit Site Infections

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It is the responsibility of the health care practitioner to determine diagnosis and appropriate treatment for their patients.
-Covered in talk-

- Exit site infections
- Peritonitis
- Structure and monitoring outcomes related to PD infections.

Most catheter infections are due to S aureus and P aeruginosa

From Gupta B, Bernardini J, Piraino B. Peritonitis associated with exit site and tunnel infections  AJKD 1996; 28: 415-419
**Trend of S. aureus PD related infections over the years of the Pittsburgh PD Registry**

*S. aureus episodes / patient - year*

- **Catheter Infections**
- **Peritonitis**

**Mupirocin Prophylaxis** given throughout 1990’s

*Piraino B, Bernardini J, Fried L. S aureus prophylaxis and Trends in GN infections in PD Patients*  
*PDI* 2003; 23: 456-459

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**But….Mupirocin has no impact on P. aeruginosa episodes / patient - year**

*Clearly no change over time!*

*Piraino B, Bernardini J, Fried L. S aureus prophylaxis and Trends in GN infections in PD Patients*  
*PDI* 2003; 23: 456-459
So we did a randomized trial comparing gentamicin cream to mupirocin at the exit site, beginning in 2001

Our hypothesis
- Gentamicin cream at the exit site would be as effective as mupirocin in preventing *S. aureus* infections
- Gentamicin cream at the exit site would reduce *P. aeruginosa* exit site infections by 50%

Since baseline *P. aeruginosa* exit site infection rate was 0.11/year, the study was powered for 140 dialysis years f/up


Methods
- Randomized, double-blinded at 3 centers
- Prevalent and incident patients
- Central drug preparation and blinding by the Investigational Drug Service at Pittsburgh.
- Prospective data collection of all catheter infections and peritonitis.
  - Rates expressed as episodes per year at risk

Patient characteristics of the randomized groups were similar—

<table>
<thead>
<tr>
<th></th>
<th>Mupirocin</th>
<th>Gentamicin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number patients</td>
<td>66</td>
<td>67</td>
</tr>
<tr>
<td>Patient years follow-up</td>
<td>54</td>
<td>64</td>
</tr>
<tr>
<td>Age</td>
<td>51</td>
<td>54</td>
</tr>
<tr>
<td>Diabetic, insulin dependent</td>
<td>41%</td>
<td>40%</td>
</tr>
<tr>
<td>Male</td>
<td>58%</td>
<td>51%</td>
</tr>
<tr>
<td>White</td>
<td>88%</td>
<td>93%</td>
</tr>
<tr>
<td>Incident to PD</td>
<td>59%</td>
<td>46%</td>
</tr>
</tbody>
</table>

No difference in the two groups for any of these variables.

Results: the group on gentamicin cream had a longer time to first exit site infection

![Graph showing survivorship](Bernardini....Piraino JASN 2005)
**Results:** catheter infection rate was much lower with gentamicin

<table>
<thead>
<tr>
<th></th>
<th>Mupirocin</th>
<th>Gentamicin</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>episodes per year at risk</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. aureus</td>
<td>0.06</td>
<td>0.08</td>
<td>NS</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>0.11</td>
<td>0</td>
<td>0.003</td>
</tr>
<tr>
<td>Fungal</td>
<td>0</td>
<td>0.05*</td>
<td>0.05</td>
</tr>
</tbody>
</table>

**ESI overall** 0.54 0.23 0.003

*All fungal catheter infections resolved with course of fluconazole and none led to fungal peritonitis

Bernardini....Piraino  JASN 2005

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**Catheter infections per patient-year in incident and prevalent patients**

![Chart showing catheter infections per patient-year in incident and prevalent patients](chart.png)

- *P<0.01*
- *P<0.01*
To our surprise, peritonitis rates were also lower in the gentamicin group

<table>
<thead>
<tr>
<th></th>
<th>Mupirocin</th>
<th>Gentamicin</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>P aeruginosa</td>
<td>0.04</td>
<td>0</td>
<td>0.14</td>
</tr>
<tr>
<td>Other Gram negative</td>
<td>0.11</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>S aureus</td>
<td>0</td>
<td>0.03</td>
<td>NS</td>
</tr>
<tr>
<td>Fungal</td>
<td>0.04</td>
<td>0.03</td>
<td>NS</td>
</tr>
</tbody>
</table>

Peritonitis overall   0.52  0.34  0.03

Summary of the randomized trial findings

Gentamicin cream applied daily to the exit site compared to mupirocin significantly reduced:

exit site infections (57%)
and peritonitis (35%)

Funded by Paul Teschan and NKF
Bernardini....Piraino JASN 2005; 16: 539-545
How to determine if an exit site infection is present?
Exit site scoring system

- Swelling
- Crust
- Redness
- Pain
- Drainage

Each scored 0-3
If score >3 than an ESI present.


Replacing the catheter for refractory ESI

- S aureus and P aeruginosa exit site infections may prove refractory or relapsing.
- Catheter change highly effective in resolving.

**GUIDELINE:** For refractory exit site infections, catheter replacement should be done and can be done as same day procedure

Finkelstein AJKD 2002;39:278-1286
Summary: exit site infections

1. Catheter placement to prevent trauma
2. Protocol to reduce risk of ESI
3. If infection occurs, culture exit site drainage and treat until completely resolved
4. Replace catheter as simultaneous procedure if refractory

Peritonitis

PD patients presenting with abdominal pain OR cloudy effluent should be presumed to have peritonitis.

Diagnosis is confirmed with cell count and culture.
1. ≥100 WBC per mcL with more than 50% polys
2. Positive culture (approximately 80%) will depend on culture technique
Structured approach to training improves outcomes on PD

- Tells the learner what they will learn
- What the teacher will do
- What the learner needs to do
- How teacher and learner will recognize when learning has occurred.

Hall et al. Nephr Nursing J 2004; 31: 149-163

Memory: The learner will gather supplies for exchange

Concept: The learner will differentiate between sterile and not sterile.

Principle: The learner will recognize and state the principles: if something sterile touches something not sterile, it is contaminated; if contamination occurs, peritonitis may result

Judgment: The learner will recognize situations that may lead to peritonitis and appropriate action to prevent

Problem solving: The learner will recognize contamination and demonstrate action to take.
**Preventing peritonitis**

2005 ISPD PD Related Infections Recommendations are in the most recent issue of *Peritoneal Dialysis International* and emphasize these points


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**What organisms do we expect to see in PD related peritonitis?**
**ORGANISMS causing peritonitis:**

149 patient years, 110 incident PD patients

<table>
<thead>
<tr>
<th>Organism</th>
<th>episodes per year</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>S aureus</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>CN Staph</td>
<td>0.03</td>
<td>37%</td>
</tr>
<tr>
<td>Other GP</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>0.05</td>
<td>33%</td>
</tr>
<tr>
<td>Other GNR</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Polymicrobial</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Culture negative</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>AFB</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>0.30</strong></td>
<td></td>
</tr>
</tbody>
</table>

or 41 months per episode

Li et al AJKD 2002;40:373-380

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**What should we use as empiric therapy of peritonitis?**

2000 ISPD Guidelines:

- Cefazolin
- And
- Ceftazidime
**However,**

Methicillin resistance in coagulase negative Staphylococcal infections is very high in many programs.

In addition, MRSA peritonitis is an extremely serious infection, even life threatening and certainly a risk to the peritoneal membrane.

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**Empiric therapy---2005 Guidelines**

- Cefazolin or Vancomycin
- Ceftazidime or Gentamicin

AND
Considerations for making the decision

- Each center must know its own history regarding organisms and resistance patterns

- Practicality must also be considered—
  - In particular in patient vs out patient treatment
  - Insurance coverage for meds
  - CAPD versus CCPD

Dosing of antibiotics

- IP dosing is preferred; absorption enhanced with peritonitis (“high transporter”)

- Drug may be given in each exchange or intermittently. Dwell time must be 6 hours minimum

- Little data on drug dosing in APD
  - Can switch to around the clock cycles with dwell of 3-4 hours
  - Alternatively, switch patients to CAPD
Why switch to CAPD when an APD patient gets peritonitis?

- IP cephalosporin levels will not be adequate in APD unless the antibiotic is given in all exchanges.
- Guidelines and most of the data are for CAPD with continuous administration.

However, it is not always possible to switch the patient to CAPD.

Alternative

If vancomycin being used, an alternative is to place the antibiotics in the long dwell.

However, it still may be difficulty to achieve adequate levels in all exchanges if rapid exchanges on the cycler are being done. MORE DATA NEEDED!!
Subsequent therapy

- Tailor choice of drug to sensitivities
- Use least toxic antibiotic (that is, avoid long courses of aminoglycosides)
- Treat for 2-3 weeks.

Case of the 28 year old man on CAPD 13 years

- Previously one mild episode of peritonitis [CNS] that resolved readily and one severe episode due to E coli [also resolved].
- Several episodes of *S aureus* ESI successfully treated with oral antibiotics
- Presents with *severe* abdominal pain, clear fluid, hypotension, no fever.
Continued

- Exit site looks fine
- Fluid quickly becomes cloudy
- Given vancomycin and gentamicin
- Fluid by day 3 begins to clear
- 4th day, increase in cloudiness, increase in pain, and increase in cell count

_What would you do now?_

Management of peritonitis---
refractory peritonitis

- About 5% patients with peritonitis die
- 18% of episodes of peritonitis resulted in transfer to HD.
- If the fluid was still cloudy after 5 days, failure rate was 46%.

_ISPD guideline: remove catheter if effluent fails to clear by 5 days._

Results of waiting 10 days to remove catheter in refractory peritonitis

- Subsequent PD failure: 32%
- Died during treatment: 28%
- Died <4 wks catheter removal: 7%
- Replacement successful

Note indications for catheter removal

- Refractory peritonitis
- Fungal peritonitis
- Relapsing peritonitis
- Refractory exit site infection
- Should be considered for mycobacterial peritonitis and multiple enteric
Summary: Treatment of peritonitis

- Choose empiric therapy for program based on sensitivities
- *Always* examine exit site/tunnel—preferably replace catheter for refractory exit site infection *before* peritonitis.
- If no response in 5 days, remove catheter
- If relapse, treat and replace catheter
- *Avoid* extended use of aminogylcosides

Monitoring peritonitis in a PD program

*Should always be expressed as rates [episodes per year at risk]*

- 7 episodes in 6 patients in a program with 70 patients
- One episode per 75 months
- NO national data on peritonitis rates
What happened in our program in 2004?

- 7 episodes in January alone!!
- Most were avoidable episodes due to contamination
- Our approach
  - Root cause analysis for each episode
  - Individual re-training
  - Everyone in program given a sheet with pointers on preventing peritonitis

OUTCOMES DCI of Oakland PD Program
Peritonitis rates, episodes per year at risk

YEAR
PD Registry Data–DCI Oakland

11 more episodes in rest of the year
OUTCOMES DCI of Oakland PD Program
Peritonitis rates, episodes per year at risk

This year (3 months data) our rates are back down to one episode per 50 months

Final point

Dialysis Patient Mortality
Adjusted cause-specific mortality, by modality: *prevalent* patients

Period prevalent dialysis patients; rates adjusted for age, gender, race, & primary diagnosis. Dialysis patients, 2001, used as reference cohort. Slide courtesy Dr Alan Collins (modified)