Major Infectious Complications

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Learning Objectives

- At the end of this session the listener will be able to:
  - Describe the major infectious complications occurring in children on peritoneal dialysis and hemodialysis, and primary approaches to prevention
  - Describe the approach to the management of an acute infectious complication in a child undergoing chronic dialysis

Modalities

- Peritoneal Dialysis
  - Peritonitis
  - Exit site, tunnel infections
- Hemodialysis
  - HD catheter-associated bloodstream infections (BSI)
  - Exit site, tunnel infections
Peritoneal Dialysis

- Infectious complications are the most significant cause of morbidity in children on chronic PD
- Peritonitis occurs more frequently in children on PD than in adults on PD
- Peritonitis is the most common reason for hospitalization and dialysis modality change

Peritonitis Rates

- NAPRTCS 2011:
  - Annualized peritonitis rate of 0.64 = 1 episode every 18.8 pt months
- IPDN:
  - 1 episode every 38 pt months
- SCOPE:
  - 1 episode every 42 pt months
Prevention of PD Catheter Associated Infections

Catheter Insertion
- Double-cuff (vs single)
- Downward exit-site orientation
- Peri-operative antibiotic prophylaxis
- No sutures at exit site

Prevention of PD Catheter Associated Infections

- Insertion/Post-op Care
  - Catheter immobilization until exit-site healed
  - Sterile dressing changes no more than once weekly

Prevention of PD Catheter Associated Infections

ISPD GUIDELINES/RECOMMENDATIONS

A SYLLABUS FOR TEACHING PERITONEAL DIALYSIS TO PATIENTS AND CAREGIVERS

Day by day descriptions of topics with suggested teaching methods based on Adult Learning Principles.
• Assessment of learning style (VARK or Kolb)
• Schedule- suggest 5 consecutive days
• Training ~10 days after catheter placement
• Breaks every 2 hours - sessions ~3 hours/day
• Home visit for first home treatment
• Skill must be demonstrated at least 3 times without error.

Compliance with Key Components of ISPD Guidelines among SCOPE Centers

<table>
<thead>
<tr>
<th>ISPD Recommendation</th>
<th>SCOPE Compliance, N(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;= 10 Days between Insertion/Training</td>
<td>293 (62%)</td>
</tr>
<tr>
<td>Home Visit</td>
<td>375 (80%)</td>
</tr>
<tr>
<td>1:1 Trainer-to-family Ratio</td>
<td>446 (95%)</td>
</tr>
<tr>
<td>&lt;=3 Hours Per Session</td>
<td>239 (51%)</td>
</tr>
<tr>
<td>All or None</td>
<td>104 (22%)</td>
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Prevention of PD Catheter Associated Infections

- Exit Site Care
  - Regular exit site cleansing
  - Antibiotic cream based on center-specific patterns
- Antibiotics with contaminations
- Re-evaluation and re-training
SCOPE PD Catheter/Exit Site Follow-Up Care Bundle

- Monthly visit
  - Exit-site scored by RN (IPPN scoring)
  - Key aspects of hand hygiene, exit site care and aseptic technique reviewed
- Every 6 month demo test and concept test
- Re-training after peritonitis episode
- Prophylactic antibiotics with touch contamination or other break in aseptic technique according to ISPD guidelines

SCOPE: Care Bundle Compliance

<table>
<thead>
<tr>
<th>Care Bundle Compliance</th>
<th>OR</th>
<th>95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insertion</td>
<td>1.02</td>
<td>(0.99,1.04)</td>
<td>0.064</td>
</tr>
<tr>
<td>Training</td>
<td>1.02</td>
<td>(0.99,1.05)</td>
<td>0.105</td>
</tr>
<tr>
<td>Follow up</td>
<td>1.10</td>
<td>(1.10,1.11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Follow up (w/ random Hosp Effect)</td>
<td>1.15</td>
<td>(1.11,1.19)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
SCOPE: Peritonitis Rates

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Launch</td>
<td>0.63</td>
<td>(0.43, 0.92)</td>
<td>0.026</td>
</tr>
<tr>
<td>Post-Launch</td>
<td>0.42</td>
<td>(0.31, 0.57)</td>
<td></td>
</tr>
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</table>

Generalized Linear Mixed Model assuming a negative binomial distribution with a natural log link function. A random center effect was included to account for center specific variability in peritonitis rates.


SCOPE: Peritonitis Rates

0.44 infections per patient year vs 0.31 infections per patient year; p=0.031

Neu A, et al. PAS 2018, ISPD 2018

Diagnosis of Peritonitis

- Cloudy peritoneal effluent
- Clinical signs: abdominal pain/tenderness, chills, emesis
- Cell count, differential and culture
  - WBC > 100/mm³, at least 50% PMNs
Overview of Treatment of Acute Peritonitis

- Empiric treatment with IP antibiotics
- IV if systemically ill or if can’t perform PD
- Initial loading dose followed by maintenance dosing
- Fungal ppx
- Adjunctive therapies – heparin, decreased fill volumes
- Focus on preservation of peritoneum rather than preservation of catheter

Empiric Treatment of Peritonitis

Start intraperitoneal antibiotic as soon as possible.
Allow to dwell for 3 - 6 hours.
Ensure gram-positive and gram-negative coverage.
Base selection on historical patient and center susceptibility patterns, as available.

Microbiologically confirmed peritonitis

Empiric antibiotic regimen

- Gram-positive coverage
- Empiric regimens for enterococci or coagulase-negative staphylococci

- Gram-negative coverage
- Empiric regimens for enterobacteriaceae or enterococci

Modification of Therapy: Gram Positive Peritonitis

- Gram positive peritonitis on culture.
- Stop gram negative coverage.

- Treatment guidelines:
  - Discontinue recent antibiotics.
  - Initial antibiotics:
    - Broad-spectrum.
    - Ceftazidime.
    - Linezolid.
  - Consider adding an aminoglycoside.

- Treatment options:
  - Treat with changes.
  - Add second agent.

Treatment Course: Gram Positive Peritonitis

- Gram positive peritonitis generally responds well to treatment.
- Delayed response in 1-5%.
- Delayed response = no improvement after 3 days of empiric abx.
- Rifampin.

Modification of Therapy: Gram Negative Peritonitis

- Gram-negative bacteria on culture.
- Stop vancomycin or teicoplanin.

- Treatment guidelines:
  - Pseudomonas op.
  - Enterobacter spp., Proteus spp., or Klebsiella spp.
  - E. coli, Proteus spp., or Klebsiella spp.: resistant to first-generation cephalosporin.
  - Other gram-positive bacteria:
    - Discontinue carbapenem.
    - Treat with colistin, imipenem, or tigecycline.
Treatment Course:  
Gram Negative Peritonitis

Modification of Therapy:  
Culture-Negative Peritonitis

- If initial culture remain sterile at 72 hours and signs and symptoms of peritonitis are improved on empiric therapy:
  - Continue therapy with cefepime, ceftazidime, cefazolin, or glycopeptide x 2 weeks
  - Discontinue aminoglycoside at 72 hours

- If no improvement at 72 hours:
  - Repeat cell count and culture; if cell count elevated with – culture, culture for unusual organisms
  - Catheter removal if no improvement after 5 days

Outcome of Peritonitis by Organism
Relapsing Peritonitis

- Seen following 10-20% of primary episodes
- Increased risk of peritoneal membrane failure
- Recurrent peritonitis with same organism within 4 weeks of completing antibiotic therapy
- Reinitiate therapy based on initial culture
- Intraluminal instillation of fibrinolytic agent
- Catheter removal if:
  - Relapsing peritonitis is accompanied by persistent tunnel infection
  - Second relapsing episode

Modification of Therapy: Fungal Peritonitis

- Prompt catheter removal
- Fluconazole
  - Systemic amphotericin with poor peritoneal penetration
- At least 2 weeks of antifungal treatment after catheter removal
- Timing of catheter replacement?

Other Catheter-Related Infections

- Catheter Exit Site Infection – peri-catheter swelling, redness, tenderness
  - 2x risk for peritonitis
- Tunnel Infection:
  - Redness, tenderness
  - and edema along subcutaneous portion of catheter, +/- drainage

Treatment of ES/Tunnel Infection

PD Catheter Removal and Replacement

- Refractory bacterial peritonitis
  - Bacterial peritonitis that fails to resolve after 5 days of appropriate antibiotic therapy
- Fungal peritonitis
- Persistent/recurrent exit site or tunnel infxn
  - Simultaneous catheter removal and replacement
- ESI or TI with peritonitis with same organism
- Second relapsing peritonitis, or relapse associated with ESI or tunnel infection
  - Simultaneous removal and replacement after clearing of the effluent (WBC < 100) in relapsing peritonitis
- Timing of replacement?

Hemodialysis-Access Associated Infections

- HD access infections in children
  - 1.5-8.6 episodes/1000 pt days*
  - 21.1 episodes/100 pt months**
  - 7.3 episodes/1000 catheter days***
  - 3.45 episodes/1000 pt days****

Data Source: Special analyses, USRDS ESRD Database. Includes incident pediatric ESRD patients in the years 2003-2012, surviving the first 90 days after ESRD initiation and followed from day 90. Adjusted for sex, race, primary cause of ESRD, and Hispanic ethnicity. Retained ESRD patients aged 0-21, 2003-2013. Abbreviations: HD, hemodialysis; PD, peritoneal dialysis; Tx, transplant.

(b) Modality

Figure 8.5 One-year adjusted hospitalization rates for infection in incident pediatric patients (aged 0-21 years), by (a) age and (b) modality, 2003-2007 and 2008-2012

Vol 2, ESRD, Ch 8 34


- Permanent access in the form of a fistula or graft is preferred for most
- Circumstances in which a catheter may be acceptable for pediatric long-term access include:
  - Lack of local surgical expertise
  - Patient size too small to support
  - Bridging HD for PD training or PD catheter removal for peritonitis
  - Expectation of expeditious kidney transplantation

Data Source: Special analyses, USRDS ESRD Database. Incident dialysis and transplant patients defined at the onset of dialysis or the day of transplant without the 60-day rule; followed to December 31, 2013. Adjusted for age, sex, race, Hispanic ethnicity, and primary cause of ESRD. Retained ESRD patients aged 0-21, 2003-2013. Abbreviations: HD, hemodialysis; PD, peritoneal dialysis; Tx, transplant.

Figure 8.8 One-year adjusted rates of mortality due to infection in incident pediatric patients with ESRD (aged 0-21 years), by (a) age and (b) modality, 2003-2007 and 2008-2012

Vol 2, ESRD, Ch 8 35
Distribution of vascular access type in prevalent pediatric hemodialysis patients (aged 0-21 years* as of December 31, 2015), 2015

Data Source: Special analyses, USRDS ESRD Database. Hemodialysis patients initiating treatment for ESRD at least 90 days prior to December 1, 2015, were under 12 years old as December 1, 2015, were under 17 years old as December 1, 2015, were under 18 years old as December 1, 2015, were under 21 years old as of December 31, 2015; those younger than 21 year old were not the use of a catheter. Abbreviations: AV, arteriovenous; ESRD, end-stage renal disease.

CDC Priority Areas:
- Adherence to recommended infection prevention practice
- Screening and detection of infections
- Implementation of clinical protocols to ensure accurate detection & treatment
- Collaboration between nephrologists and state/federal healthcare-associated infection programs

Mission: Engaging nephrologists as team leaders to "target zero infections" by actively pursuing the elimination of preventable infections in dialysis facilities.

Project Convener
Dr. Kliger, MD
Co-Chairs
Anitha Vijayan, MD
Eugene Livar, MD
Co-Chairs
SCOPE HD Project

- Standardized Practices for Accessing:
  - Tunneled Hemodialysis catheter
  - AV Graft
  - AV Fistula

SCOPE: Access Related BSI

Access Related BSI Rate by Month: Pre- vs 36 Months Post

- 30% decrease in infection rate from 4.0 BSI per 100 patient-months to 2.8 BSI per 100 patient-months.

HD Catheter Associated Infections: Definition

- Primary bloodstream infections (BSI): Laboratory-confirmed bloodstream infections (LCBI) that are not secondary to an infection at another body site
- Central line-associated BSI (CLABSI): A laboratory-confirmed bloodstream infection (LCBI) where central line (CL) or umbilical catheter (UC) was in place for >2 calendar days on the date of event
HD Catheter Associated Infections: Definitions

- Exit site infection
  - Inflammation confined to/within 2 cm of catheter exit site, not extending beyond cuff, positive exudate culture
- Tunnel infection
  - Catheter tunnel inflamed beyond cuff, painful, +/- culture positive exudate

IDSA Guidelines for Intravascular Catheter-Related Infection • CID 2009; 49: 1-45

Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infections 2009 Update by the Infectious Diseases Society of America

IDSA Guidelines for Intravascular Catheter-Related Infection • CID 2009; 49: 1-45

HD Catheter Infection-Treatment

IDSA Guidelines for Intravascular Catheter-Related Infection • CID 2009; 49: 1-45
35. In uncomplicated CRBSI involving long-term catheters due to pathogens other than *S. aureus*, *P. aeruginosa*, *Bacillus* species, *Micrococcus* species, *Propionibacteria*, fungi, or mycobacteria, because of the limited access sites in many patients who require long-term intravascular access for survival (e.g., patients undergoing hemodialysis or with short-gut syndrome), treatment should be attempted without catheter removal, with use of both systemic and antimicrobial lock therapy (B-II).

IDSA Guidelines for Intravascular Catheter-Related Infection • CID 2009;49: 1-45

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49. Indications for catheter removal for children are similar to those for adults, unless there are unusual extenuating circumstances (e.g., no alternative catheter insertion site). However, the benefits of catheter removal must be weighed against the difficulty of obtaining alternate venous access for an individual patient (A-II).

50. Children treated without catheter removal should be closely monitored with clinical evaluation and additional blood cultures; the device should be removed if there is clinical deterioration or persistent or recurrent CRBSI (B-III).

51. In general, empirical antibacterial therapy for children with CRBSI should be similar to that for adults (A-II).

52. Antibiotic lock therapy should be used for catheter salvage (B-II). However, if antibiotic lock therapy cannot be used in this situation, systemic antibiotics should be administered through the colonized catheter (C-III).

IDSA Guidelines for Intravascular Catheter-Related Infection • CID 2009;49: 1-45
Conclusions

- Dialysis access-related infections are a significant cause of morbidity in our dialysis patients
- Emphasize prevention
- Treat early and effectively
- Continue to monitor practices and outcomes through collaborative studies and registries so we can collectively improve

Thank you!