An Evaluation of the Empiric Antibiotic Regimen for the Treatment of Peritoneal Dialysis-Associated Peritonitis at Vancouver General Hospital

Amanda Driver, B.Sc., B.Sc.(Pharm); Elaine Cheng, B.Sc.(Pharm), PharmD, ACPR; Suneet Singh M.D., FRCPC.
Departments of Pharmaceutical Sciences and Nephrology, Vancouver General Hospital and University of British Columbia

Background

- Peritonitis is a serious complication of peritoneal dialysis (PD) that can result in unfavorable outcomes including hospitalization, peritoneal membrane failure, conversion to hemodialysis or death
- The International Society of Peritoneal Dialysis (ISPD) 2016 guidelines provide the following recommendations for PD-associated peritonitis:
  - **Diagnostic criteria:** ≥ 2 of the following criteria must be present:
    - Clinical features (abdominal pain and/or cloudy dialysate)
    - Dialysis effluent WBC > 100/μL with > 50% polymorphonuclear cells
    - Positive dialysis effluent culture
  - **Empiric intraperitoneal (IP) antibiotic regimen:**
    - Gram positive: First generation cephalosporin or vancomycin, and
    - Gram negative: Third generation cephalosporin or aminoglycoside
- The 2016 ISPD guidelines recommend antifungal prophylaxis for all PD patients receiving antibiotics to prevent fungal peritonitis
- **Current practice at Vancouver General Hospital (VGH):**
  - Empiric antibiotic regimen: IP cefazolin together with IP ceftazidime, unless allergic to cephalosporins or history of resistant infection
  - Antifungal prophylaxis with fluconazole is not routinely prescribed

Objectives

- Characterize pathogens and resistance patterns of PD-associated peritonitis episodes at VGH over the past 5 years
- Evaluate the effectiveness of the empiric antibiotic regimen used at VGH for the treatment of PD-associated peritonitis based on clinical outcomes
- Assess fungal peritonitis rates at VGH over the past 5 years and determine the need for routine fluconazole prophylaxis

Methods

- **Design:** Retrospective chart review of PD-associated peritonitis episodes (identified from the PROMIS database) at VGH over a 5 year period
- **Inclusion Criteria:**
  - Peritonitis episodes from January 1, 2013 – December 31, 2017 in patients aged ≥ 18 yrs who meet the criteria for PD-associated peritonitis
  - Peritonitis episodes with PD effluent analyzed for cell count, differential, gram stain and culture and sensitivity
  - Peritonitis episodes treated with empiric intraperitoneal (IP) antibiotics
- **Exclusion Criteria:**
  - Episodes with exit site infection only or eosinophilic peritonitis
- **Analysis:** Descriptive statistics

Results

Table 1: Peritonitis Rate (# episodes per patient-year on PD)

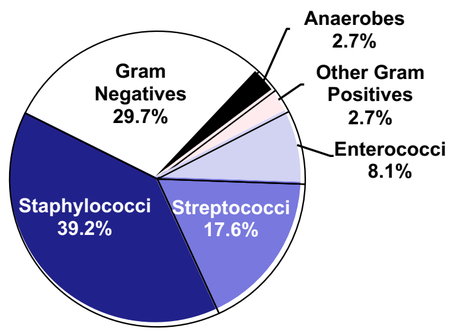
Year	2013	2014	2015	2016	2017
BC	0.38	0.27	0.25	0.26	0.33
VGH	0.33	0.17	0.12	0.13	0.09

Results

Table 2: Patient Characteristics

Characteristic	n (%)
Number of patients	42
Male	18 (42.9)
Mean Age (years)	65 ± 13.3
Ethnicity	
Caucasian	12 (28.6)
Filipino	12 (28.6)
East Asian	10 (23.8)
Number of peritonitis episodes	62
Exit Site Antibiotics	
Mupirocin	30 (48.4)
Gentamicin	32 (51.6)
Dialysis Modality	
Continuous Cycling PD	47 (75.8)
Continuous Ambulatory PD	14 (22.6)
Hemodialysis	1 (1.6)
Mean Duration of Dialysis (days)	938.6 ± 898.6
Resistant Organisms	
MRSA	1 (1.6)
Immunosuppression	8 (12.9)
Antibiotics in past 3 months	15 (24.2)
Extraperitoneal fungal infection	3 (4.8)
Empiric gram positive	
Cefazolin IP	48 (77.4)
Vancomycin IP	10 (16.1)
Empiric gram negative	
Ceftazidime IP	51 (82.3)
Tobramycin IP	4 (6.5)
Fluconazole Prophylaxis	15 (24.2)

Figure 1: Organisms Isolated from Dialysate (N=74)



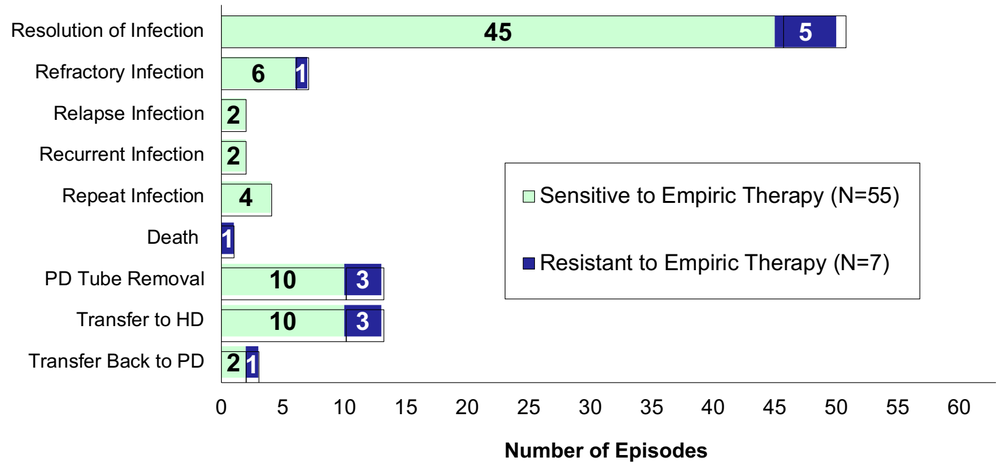
Fungal Peritonitis: 0%
Culture Negative Peritonitis: 9.7%

Table 3: Antibiotic Sensitivity of Organisms Isolated from Dialysate

Organism	Antibiotic	% Sensitive (n_s/n_t*)	Organism	Antibiotic	% Sensitive (n_s/n_t*)
Streptococci (N=13)	Penicillin G	76.9 (10/13)	**Staphylococci (N=29)**	Cefazolin	92.3 (24/26)
	Vancomycin	100 (13/13)		Vancomycin	100 (5/5)
Enterococci (N=6)	Vancomycin	83.3 (5/6)	**Gram Negatives (N=22)**	Ceftazidime	100 (12/12)
	Gentamicin	66.7 (4/6)		Tobramycin	93.8 (15/16)

*(n_s/n_t) = number of sensitive isolates/total number of isolates analyzed

Figure 2: Peritonitis Episode Outcomes (N=62 episodes)



Outcome Definitions
Resolution of Infection – no signs/symptoms after 5 days of antibiotics with no relapse for 4 weeks
Refractory Infection – failure to clear PD effluent after 5 days of antibiotics
Relapse Infection – episode with same organism ≤ 4 weeks after antibiotics completed
Recurrent Infection – episode with different organism ≤ 4 weeks after antibiotics completed
Repeat Infection – episode with same organism > 4 weeks after antibiotics completed

Limitations/Confounders

- Number of peritonitis episodes may be under-reported due to missed or inappropriate PROMIS entry
- Small sample size precluded ability to associate patient characteristics with clinical outcomes
- Patients with multiple peritonitis episodes may impact resistance patterns
- Additional antibiotics (eg. piperacillin/tazobactam) administered in 32.3% of episodes

Discussion/Conclusions

- Isolated organism(s) was sensitive to empiric antibiotic therapy in 88.7% of episodes
- Current empiric antibiotic regimen adequate for the treatment of PD-associated peritonitis at VGH
  - Resolution of infection achieved in 80.6% of episodes
- No episodes of fungal peritonitis at VGH over past 5 years, therefore routine fluconazole prophylaxis not required unless risk factors (eg. immunosuppression, recent antibiotics, extraperitoneal fungal infection) for fungal peritonitis are present