

Treatment of Relapsing, Repeat & Recurrent Peritonitis

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Objectives

- Definitions
- Clinical Vignettes
- Epidemiology
- Microbiology
- Outcomes
- Treatment Considerations

“Many of the studies evaluating treatment of PD-related peritonitis are small, out-dated, of poor quality, and had inconsistent definitions and dosing regimens.

Definitions

- Relapsing Peritonitis:
 - Peritonitis episode that occurs within 4 weeks of completion of therapy of a prior episode with the same organism or one sterile (culture negative) episode (i.e. specific organism followed by the same organism, culture negative followed by a specific organism or specific organism followed by culture negative).

Definitions

- Repeat Peritonitis:
 - Peritonitis episode that occurs more than 4 weeks after completion of therapy of a prior episode with the same organism

Definitions

- Recurrent Peritonitis:
 - Peritonitis episode that occurs within 4 weeks of completion of therapy of a prior episode but with a different organism

Clinical Vignette #1

- 54 yo WF on APD x 13 months with an extended PD cath in place presented with abdominal pain, cloudy PD effluent

- PD fluid analysis: TLC = 61600, pH = 7.60, protein = 1.1

- **RELAPSING PERITONITIS** 2 weeks ago (IP Vanc+Gent total therapy x 2 weeks)

- For the 2nd episode of peritonitis, restarted IP Vanc+Gent
- Culture- Coag Negative Staph

Clinical Vignette #2

- 65 yo WM on APD x 3 years was treated for CNS peritonitis with IP vancomycin
- 8 days later he presents with 2nd episode of IP
- **RECURRENT PERITONITIS**
- 20 days after completion of the IP Vancomycin he presents with a 3rd episode of peritonitis and PD fluid culture shows Staph aureus

Epidemiology

- ¹ANZDATA Registry 2003-2007 Observational Cohort study
 - 14% rate of relapsing peritonitis
 - 6% rate of recurrent peritonitis
- Repeat peritonitis rate ~ 10% (ANZDATA²) & 11% (Canadian registry³), 9.4% (Hongkong)⁴

1. Burke M et al., Am J Kidney Dis. 2011 Sep;58(3):429-36.

2. Thirugnanasambathan et al., 2012. Am J Kidney Dis 59:84-91

3. Nessim et al., 2012. Perit Dial Int 32:316-321

4. Szeto CC, et al. *Clinical Journal of the American Society of Nephrology* [6\(4\):p 827-833, April 2011](#)

Microbiology

- Retrospective study from Hongkong (1994-2007):
 - Relapsing vs Control:
 - Pseudomonas species (16.6% versus 9.4%)
 - Culture negative (29.9% versus 16.4%)
 - Recurrent vs control
 - Enterococcus species (3.2% versus 1.2%)
 - Other Gram-negative organisms (27.2% versus 11.1%)
 - Mixed bacterial growth (17.6% versus 12.7%)

Microbiology

- Retrospective study from Hongkong (1995-2009):
 - Relapsing peritonitis episodes were primarily due to Gram negative (62%), vs Gram positive (56%) in the Repeat group
 - Repeat Group, 24% were due to Staphylococcus aureus, as compared with 5.5% in Relapsing Group

Microbiology

- *ANZDATA Registry 2003-2007 Observational Cohort study:
 - Coag Negative Staph and Staph aureus accounted for 48% of relapsing peritonitis
 - Recurrent peritonitis was associated more frequently with fungi

Microbiology

- Single center retrospective study from Portugal (1998-2019)
 - Gram-positive peritonitis more common in the repeat/relapsing group (91 vs 61%) especially Streptococci viridans (43.5% vs 21.3%) and Gram-negatives in the control group (26.6% vs 9.0%)

TABLE 2: Causative microorganisms of the repeat/relapsing and control group.

	Repeat/relapsing peritonitis N= 46	Control peritonitis N= 94	p value
<i>Streptococci viridans</i>	20, 43.5%	20, 21.3%	0.01
Coagulase-negative <i>Staphylococcus</i>	14, 30.4%	21, 22.3%	0.38
<i>Staphylococcus aureus</i>	8, 17.4%	17, 18.1%	0.78
<i>Enterococcus</i> spp.	0, 0%	3, 3.2%	0.55
<i>Corynebacterium</i> spp.	0, 0%	3, 3.2%	0.55
Gram negative	4, 9.0%	25, 26.6%	0.02
<i>Pseudomonas</i> spp.	0	7, 7.4%	0.96
Fungi	0, 0%	5, 5.3%	0.32

Microbiology-Summary

- Relapsing, Recurrent and Repeat peritonitis episodes are caused by different species of bacteria
- Causative organisms can differ based on the center practices relating to antibiotic use patterns and other factors
- Likely represent distinct clinical entities with different pathogenic mechanisms

Outcomes

Outcomes

- ANZDATA Registry:
- Compared with uncomplicated peritonitis, relapsed and recurrent peritonitis were associated with
 - Higher rates of catheter removal (22% vs 30% vs 37%)
 - Higher rates of permanent HD transfer (20% vs 25% vs 32%)
 - Similar rates of hospitalization (73% vs 70% vs 70%)
 - Similar rates of death (2.8% vs 2.0% vs 1.2%).

Outcomes

- Szeto et al., 2009
 - Compared to control and relapsing groups, recurrent group had
 - Significantly lower primary response rate (86.4%, 88.5%, and 71.2%)
 - Lower complete cure rate (72.3%, 62.4%, and 42.4%)
 - Higher mortality rate (7.7%, 7.0%, and 20.8%)
- Szeto et al., 2011
 - Repeat group with lower complete-cure rate (70.7% *vs* 54.9%) than relapsing
 - Primary response, catheter removal, and mortality rates similar

Treatment

General Treatment Considerations

- Empiric antibiotic coverage for the first organism identified
- Empiric use of Vancomycin for Gram positive coverage in centers with high prevalence of methicillin resistance + Gram negative coverage until C&S results available
- Timely treatment of any exit site issues
- Consideration of intraluminal instillation of a fibrinolytic agent due to the potential role of biofilm in complicated peritonitis with organisms like CNS
- *No effect of fibrinolytic on the clinical course, relapse risk, preventing PD catheter loss when given to patients with first peritonitis episode

Relapsing Peritonitis

- The cure rate of relapsing peritonitis following antibiotic therapy alone ~ 71% (Szeto et al., 2011)
- ISPD guidelines advise against extending duration of antibiotic therapy beyond the recommended time frame (may increase repeat peritonitis risk)

Fibrinolytic Therapy in Relapsing Peritonitis

- More success with Fibrinolytic therapy in relapsing/resistant cases
- ¹Double-blind, placebo-controlled study:
 - Resolution of peritonitis within 4 days of intraluminal urokinase instillation (1,000 IU/ml)
 - No recurrence with the same organism for 6 months in 8/12 patients vs 1/12 in placebo group
- ²Intraluminal urokinase (5,000 IU/ml) in 9 children with relapsing peritonitis w/o second relapse vs 75% of untreated historical cohort
- ³Anecdotal reports of success with intraluminal administration of high-dose recombinant tissue plasminogen activator – 3/5 patients with CNS relapsing peritonitis with resolution

1. Innes A et al., *Nephrology Dialysis Transplantation*, Volume 9, Issue 7, 1994, Pages 797–799

2. Klaus et al., 1992. *Adv Perit Dial* 8:302–305

3. Zorzanello et al., 2004 *Nephrol Nurs J* 31:534–537

Catheter Replacement vs Fibrinolytic Therapy

- ¹Tenckhoff catheter replacement as a one-stage procedure vs IP urokinase, for recurrent peritonitis in CAPD
 - 17 patients with IP urokinase (5000 i.u.) on the 2nd, 4th days of antibiotics vs 14 patients with catheter replacement
 - 6 patients also underwent catheter replacement following the recurrence of peritonitis after urokinase treatment
 - Subsequent recurrence rate of peritonitis following catheter replacement (5%) was significantly less than after urokinase (41%) ($p < 0.001$)

Treatment of Repeat Peritonitis

- Lower complete cure rate with antibiotic therapy compared to relapsing episodes as well as a greater rate of further relapsing or repeat peritonitis episodes
- Prudently treat any exit/tunnel infections
- Higher likelihood of Gram-positive organisms causing repeat peritonitis due to the possibility of biofilm formation on PD catheters playing an important etiologic role
- Fibrinolytic therapy could be a consideration
- Catheter removal should be considered due to their high likelihood of subsequent relapsing, recurrent or repeat peritonitis

Treatment of Recurrent Peritonitis

- More frequently due to Fungal organisms (ANZDATA), Gram negatives/mixed bacteria (Szeto et al.,)
- High likelihood of catheter removal

Catheter Removal

- ¹A Cochrane database review assessing different treatment options for peritonitis suggested that PD catheter removal may be the best option for relapsing or persistent peritonitis
- ²Simultaneous removal and reinsertion of PD catheters is an option to manage or reduce the risk of relapsing, recurrent or repeat peritonitis
 - Allows continuation of PD without transfer to HD
 - Should be considered only after culture of PD effluent is negative
 - PD effluent white cell count lower than 100/mL
 - Only in the absence of concomitant exit-site or tunnel infection
 - Done under perioperative antibiotic coverage

1. Ballinger et al., Cochrane Database Syst Rev. 2014 Apr 26;(4):CD005284

2. Li et al., Peritoneal Dialysis International 2022, Vol. 42(2) 110–153

Clinical Vignette #1 Follow-up

- 54 yo WF on APD x 13 months with an extended PD cath had 1st episode of culture negative peritonitis treated with IP vanc+gent
- 2nd episode of peritonitis with CNS @ 3 weeks- Relapsing peritonitis
- 3rd episode of CNS peritonitis 5 weeks after completion of abx – Repeat Peritonitis
- Titanium connector was switched out after appropriate antibiotic therapy
- Had 4th episode of peritonitis again with CNS 6 weeks after titanium connector was switched out – Repeat Peritonitis
- Catheter removed and replaced 8 weeks later without any further issues

Clinical Vignette #2

- 65 yo WM on APD x 3 years was treated for CNS peritonitis with IP vancomycin
- 2nd episode of CNS peritonitis 8 weeks after Rx – Repeat Peritonitis
- 3rd episode of peritonitis with Staph aureus 20 days after Rx – Recurrent Peritonitis
- Pt was noted to have tunnel infection at the same time
- Catheter was removed and IV vancomycin therapy completed
- Catheter replaced 8 weeks later without further issues

Summary

- Relapsing, repeat and recurrent peritonitis are thought to be distinct clinical entities with different causative organisms and therapeutic response
- Complicated peritonitis episodes are associated with higher rates of adverse outcomes
- Prompt initiation of empiric antibiotics based on resistance patterns
- Duly treat exit site problems
- Consideration of fibrinolytic therapy for organisms with biofilm production
- Catheter removal with/without simultaneous replacement (depending on effluent counts/culture results)
- Save the Peritoneum, Not the Catheter

Questions?