



# Peritoneal Dialysis-Related Peritonitis; Tiptoeing Through the Better Approach

Fariba Samadian,<sup>1</sup> and Nooshin Dalili<sup>1,\*</sup>

<sup>1</sup>MD, Assistant Professor of Nephrology, Chronic Kidney Disease Research Center (CKDRC), Department of Internal Medicine Labbafinejad Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\*Corresponding author: Nooshin Dalili, MD, Assistant Professor of Nephrology, Chronic Kidney Disease Research Center (CKDRC), Department of Internal Medicine Labbafinejad Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Tel: +98-9122404331, E-mail: drn.dalili@sbmu.ac.ir

Received 2017 August 21; Accepted 2017 September 19.

## Abstract

Peritonitis is a common serious complication of peritoneal dialysis that results in significant morbidity, mortality, and health care costs. However peritonitis practices vary markedly among different centers and physicians. This article reviews the microbiology, clinical presentations diagnosis, and treatment of peritoneal dialysis related peritonitis focusing on different antibiotic regimens to reduce controversies and tiptoeing through the better approach.

*Keywords:* Peritonitis, Peritoneal Dialysis, Antibiotic

## 1. Introduction

Peritoneal dialysis (PD) is one of the known renal replacement therapy methods, used to treat end-stage kidney disease in more than 200,000 patients around the globe.

Each dialysis technique involve an evident risk of infectious complications because of the compromised immune system of these patients and also dialysis procedures that raise the possibility of microbial contamination. Peritoneal dialysis, especially continuous ambulatory peritoneal dialysis (CAPD), are known to have a higher risk of infection rate in comparison with automated peritoneal dialysis (APD) (1).

Even with new innovations in peritoneal dialysis procedures, for example using the Y-set tubing and double-bag systems, which provide flash before fill technique, peritonitis is still a serious complication for patients on PD (2). Recurrent peritonitis, with making changes in structural and functional integrity of the peritoneal membrane, will cause short and long-term complications and remain the foremost cause of mortality and hospitalization in these patients (3). According to different studies, nearly 18% of the infection-related mortality in PD patients is the result of peritonitis, which is possibly the most common reason of technique failure in peritoneal dialysis (4).

## 2. Microbiology

The most important cause of PD-related peritonitis is bacterial infection and fungal peritonitis seems to be the rare scenario whereas the exact role of viral infections remains to be understood. Gram-positive organisms are the most common cause of bacterial PD-related peritonitis and among those, coagulase-negative Staphylococci demonstrates considerable importance. Most of the times, Staphylococcus epidermidis-related infections would be accompanied by brief clinical signs and symptoms (5). On the other hand Staphylococcus aureus is known to be the first role in most of the severe peritonitis cases. One of the other causes for severe peritonitis is Pseudomonas, which may necessitate peritoneal catheter removal. Streptococcus counted to be the reason of peritoneal-related peritonitis in 10% of patients. It is noteworthy to mention that fungal infection is an infrequent but serious complication of PD, reported to be the cause of peritonitis in 2% - 13% of cases with mortality rate reaches up to 20% - 30% (6). Among risk factors of fungal peritonitis, most reports are from recent use of antibiotics and changes in normal intestinal flora (7). Dissemination of Candida from fallopian tubes in to peritoneal spaces has also been reported. Transmission of infectious cause, can also happen via catheter lumen following hands contamination during connecting the tubes and bag in which coagulase-negative Staphylococci play a noticeable role. Staphylococcus aureus, as the cause, can be transmitted in such situation

from the skin into the catheter's lumen. There are also rare reports of hematogenous transmission or via impaired integrity of gastrointestinal system following comorbidities like bowel ischemia, intra-abdominal infections, and ruptured diverticula. In regards to the important fact that most of the time 1 single organism is responsible in peritonitis, in case of any mixed species or anaerobic isolation, bowel perforation should be suspected.

### 3. Clinical Manifestations

The most common presentation of PD-related peritonitis is abdominal pain, which is seen in more than 90% of cases. Gastrointestinal manifestations like nausea, vomiting, and less commonly diarrhea or constipation can also be present, however, in nearly half of the peritonitis cases fever and chills are pioneer signs and symptoms. Differential diagnosis of cloudy peritoneal fluid will be discussed later.

### 4. Lab Findings

The cloudiness of the dialysate throughout occurrence of peritonitis is because of peritoneal fluid leukocytosis from peritoneal inflammation or infection. Normally peritoneal fluid has very few ( $< 10 \text{ cell/m}^3$ ) white blood cell (WBC) count, which are dominantly macrophages and monocytes. WBC count of  $> 100/\text{m}^3$  with more than 50% of the cells polymorphonuclear neutrophils (PMN) is used for diagnosis of PD-related peritonitis. WBC count in the fluid can differ significantly based on dialysate fluid dwell time and this should be taken into consideration when interpreting the cell count results. Dilution or suboptimal timing of peritoneal fluid sampling (after a short dwell) may affect total cell counts and in these cases peritonitis may be present with  $< 100 \text{ cell/m}^3$ . Dialysate effluent should be sent for testing after a minimum dwell time of 2 hours. Other differential diagnosis of cloudy peritoneal fluid are: eosinophilia of the effluent, hemoperitoneum (menstrual periods) or chylous effluent (rare), malignancies, fibrin clots, taking calcium-channel blockers, and sample taken after a long dwell or from a dry abdomen.

During PD-related peritonitis, 80% - 90% of cases will have a positive peritoneal fluid culture result within 24 hours and 75% will have a result at 72 hours, however, blood cultures are negative most of the time. In contrast with secondary peritonitis, amylase and lipase levels are frequently within normal ranges during PD-related peritonitis.

### 5. Treatment

At the beginning, treatment should be started empirically. Regarding localization of infective process in the peritoneal cavity, the cornerstone of treatment is focused on using intra-peritoneal antibiotics. For choosing the initial treatment of PD-related peritonitis, which still remains a challenge to nephrologists, [Table 1](#) can be used.

The optimal empirical treatment includes 1 drug from the 1st group added to a drug from the 2nd group. Some studies were able to identify the superiority of using a glycopeptide (vancomycin or teicoplanin) plus ceftazidime (8). Interestingly, in other studies using cefazolin with appropriate doses, no obvious difference was made in the cure rate when compared with a glycopeptide, however in centers with high rate of methicillin-resistant microorganisms it seems much better to wisely choose vancomycin. The uptake of vancomycin from normal peritoneal cavity is about 50%, which is enhanced up to 90% during episodes of peritonitis (9). Accepting the importance of saving residual renal function in peritoneal dialysis patients for longer times, the potential nephrotoxicity with aminoglycosides should taking in to accounts, although some studies did not demonstrate such results (10). In case of any allergy to cephalosporines, aztreonam is a good alternative. Intraperitoneal administration of mixed antibiotics like vancomycin, cephalosporine, and aminoglycoside via 1 container of PD solution is practical and safe (11). It is also possible to administrate antibiotics continuously in a long dwell during a day (or throughout the night dwell). [Tables 2 and 3](#) demonstrate the recommended antibiotic doses in peritoneal dialysis when using the continuous method versus intermittent.

Some studies do not approve of using aminoglycosides intra-peritoneally. Choosing co-trimoxazole as an anti-infective intra-peritoneal drug is not also recommended. For linezolid, limited activity was found in peritoneal dialysis fluid, regardless of the concentration, however daptomycin demonstrated trusted dose-dependent activity in peritoneal cavity (12).

Selection of antimicrobials should start empirically and be revised later in light of both patient's clinical signs and culture results/micro-organisms susceptibilities. Following obtaining the results of the culture and sensitivities, it is recommended that the empiric antibiotic therapy be changed to a narrow spectrum antibiotic to cover the specific organism. Generally, clinical improvement should occur within the first 3 days after antibiotic initiation. Peritoneal fluid should be tested after 48 - 72 hours, which is expected to be more clear with decreased cell count. In case of no clinical improvement after 5 days of appropriate antibiotic therapy, catheter removal should take into con-

**Table 1.** Choice of Initial Treatment in PD-Related Peritonitis

	Treatment
For best coverage of gram-positive bacteria	Vancomycin or Cefazolin
For best coverage of gram-negative bacteria	Ceftazidim or Cefepime or Aminoglycosides or Aztreonam

**Table 2.** Recommended Continuous Antibiotic Dosing for Treatment of PD-Related Peritonitis

Drug	Loading Dose	Maintenance Intra-peritoneal Dose
Cefazolin	500 mg /1L of dialysate	125 mg /1L of dialysate
Amikacin	25 mg /1L of dialysate	12 mg /1L of dialysate
Ceftazidim	500 mg /1L of dialysate	125 mg /1L of dialysate
Vancomycin	1000 mg /1L of dialysate	25 mg /1L of dialysate
Imipenem-Cilastatin	250 mg /1L of dialysate	50 mg /1L of dialysate

**Table 3.** Recommended Intermittent Antibiotic Dosing for Treatment of PD-Related Peritonitis

Drug	Dose
Cefazolin	15 mg/Kg in one exchange/day
Ceftazidim	1 - 1.5 g in one exchange/day
Amikacin	2 mg/Kg in one exchange/day
Vancomycin	15 - 30 mg/Kg every 3 - 7 days based on drug level in blood
Imipenem	1 g in one exchange every 12 hours

sideration with suspicious of refractory peritonitis, however, atypical or fungal peritonitis can't be excluded. [Table 4](#) summarized the duration of treatment based on specific microorganisms.

**Table 4.** Duration of Treatment

Microorganism	Duration of Treatment
Coagulase-negative staphylococci	2 weeks
Staphylococcus aureus	At least 3 weeks
Streptococcus	2 weeks
Enterococcus	3 weeks
Pseudomonas aeruginosa	At least 3 weeks

Rifampin 600 mg/day for 1 week is a valuable adjunct in preventing relapse and repeat Staph. aureus peritonitis, however, its' single administration is not recommended (13).

For treatment of severe Pseudomonas peritonitis, some references recommend 2 effective drugs on these

microorganisms simultaneously (Ceftazidim, Cefepime, Aminoglycosides, Piperacillin-tazobactam). Pseudomonas peritonitis accompanied by tunnel infection needs prompt catheter removal (14). Fungal and micobacterial peritonitis also need catheter removal and prompt appropriate antibiotic therapy.

Indications for catheter removal in PD-related peritonitis are as following:

- 1- Relapsing peritonitis, defined as recurrent peritonitis in less than 4 weeks after completion of treatment with the same microorganism
- 2- Refractory peritonitis, defined as failure of the peritonitis to improve after 5 days of appropriate antibiotics.
- 3- Refractory catheter infection (tunnel or exit-site infection)
- 4- Fungal infection
- 5- Mycobacterial infection
- 6- Anytime peritonitis is accompanied by intra-abdominal pathologies

Taking into account the possibilities of fibrin clot construction in peritoneal effluent during a peritonitis episode, which can induce catheter obstruction, Heparin administration, 1000 - 5000 IU/L is recommended until peritoneal fluid totally clears-up. As heparin has been shown to have anti-inflammatory properties, the fibrin inhibitory effect of heparin may have profits for long-term PD patients, apart from the usual use in maintenance of catheter patency (15).

Regarding ongoing inflammatory process and increased peritoneal vasculature, which result in high transportation peritoneum, a number of exchanges may need to be reduced or shorter dwell times should be prescribed in order to save appropriate ultrafiltration.

## 6. Summary

Peritonitis has been the most common complication of continues ambulatory peritoneal dialysis (CAPD) and it remains the foremost cause of treatment failure and move to other renal replacement therapies. This mini-review presents a systematic approach towards diagnosis and treatment of PD-related peritonitis.

## References

- Bianchi P, Buoncristiani E, Buoncristiani U. Antisepsis. *Contrib Nephrol*. 2007;**154**:1-6. doi: [10.1159/000096809](https://doi.org/10.1159/000096809). [PubMed: [17099297](https://pubmed.ncbi.nlm.nih.gov/17099297/)].
- Daly CD, Campbell MK, MacLeod AM, Cody DJ, Vale LD, Grant AM, et al. Do the Y-set and double-bag systems reduce the incidence of CAPD peritonitis? A systematic review of randomized controlled trials. *Nephrol Dial Transplant*. 2001;**16**(2):341-7. [PubMed: [11158410](https://pubmed.ncbi.nlm.nih.gov/11158410/)].
- Susan Y, Tak MC. Pathophysiological changes to the peritoneal membrane during PD-related peritonitis: The role of mesothelial cells. *Mediators Inflamm*. 2012:21.
- Li PK, Szeto CC, Piraino B, Bernardini J, Figueiredo AE, Gupta A, et al. Peritoneal dialysis-related infections recommendations: 2010 update. *Perit Dial Int*. 2010;**30**(4):393-423. doi: [10.3747/pdi.2010.00049](https://doi.org/10.3747/pdi.2010.00049). [PubMed: [20628102](https://pubmed.ncbi.nlm.nih.gov/20628102/)].
- Fahim M, Hawley CM, McDonald SP, Brown FG, Rosman JB, Wiggins KJ, et al. Coagulase-negative staphylococcal peritonitis in Australian peritoneal dialysis patients: predictors, treatment and outcomes in 936 cases. *Nephrol Dial Transplant*. 2010;**25**(10):3386-92. doi: [10.1093/ndt/gfq222](https://doi.org/10.1093/ndt/gfq222). [PubMed: [20466663](https://pubmed.ncbi.nlm.nih.gov/20466663/)].
- Matuszkiewicz J, Rowinska Update on fungal peritonitis and its treatment. *Perit Dial Int*. 2009;**29**(2):S161-5.
- Prasad KN, Prasad N, Gupta A, Sharma RK, Verma AK, Ayyagari A. Fungal peritonitis in patients on continuous ambulatory peritoneal dialysis: a single centre Indian experience. *J Infect*. 2004;**48**(1):96-101. [PubMed: [14667798](https://pubmed.ncbi.nlm.nih.gov/14667798/)].
- Barretti P, Doles JV, Pinotti DG, El Dib R. Efficacy of antibiotic therapy for peritoneal dialysis-associated peritonitis: a proportional meta-analysis. *BMC Infect Dis*. 2014;**14**:445. doi: [10.1186/1471-2334-14-445](https://doi.org/10.1186/1471-2334-14-445). [PubMed: [25135487](https://pubmed.ncbi.nlm.nih.gov/25135487/)].
- Badve SV, Hawley CM, McDonald SP, Brown FG, Boudville NC, Wiggins KJ, et al. Use of aminoglycosides for peritoneal dialysis-associated peritonitis does not affect residual renal function. *Nephrol Dial Transplant*. 2012;**27**(1):381-7. doi: [10.1093/ndt/gfr274](https://doi.org/10.1093/ndt/gfr274). [PubMed: [21633101](https://pubmed.ncbi.nlm.nih.gov/21633101/)].
- Blunden M, Zeitlin D, Ashman N, Fan SL. Single UK centre experience on the treatment of PD peritonitis-antibiotic levels and outcomes. *Nephrol Dial Transplant*. 2007;**22**(6):1714-9. doi: [10.1093/ndt/gfm079](https://doi.org/10.1093/ndt/gfm079). [PubMed: [17369615](https://pubmed.ncbi.nlm.nih.gov/17369615/)].
- de Vin F, Rutherford P, Faict D. Intraperitoneal administration of drugs in peritoneal dialysis patients: a review of compatibility and guidance for clinical use. *Perit Dial Int*. 2009;**29**(1):5-15. [PubMed: [19164246](https://pubmed.ncbi.nlm.nih.gov/19164246/)].
- Kussmann M, Schuster L, Zeitlinger M, Pichler P, Reznicek G, Wiesholzer M, et al. The influence of different peritoneal dialysis fluids on the in vitro activity of ampicillin, daptomycin, and linezolid against *Enterococcus faecalis*. *Eur J Clin Microbiol Infect Dis*. 2015;**34**(11):2257-63. doi: [10.1007/s10096-015-2477-8](https://doi.org/10.1007/s10096-015-2477-8). [PubMed: [26337433](https://pubmed.ncbi.nlm.nih.gov/26337433/)].
- Szeto CC, Chow KM, Kwan BC, Law MC, Chung KY, Yu S, et al. Staphylococcus aureus peritonitis complicates peritoneal dialysis: review of 245 consecutive cases. *Clin J Am Soc Nephrol*. 2007;**2**(2):245-51. doi: [10.2215/CJN.03180906](https://doi.org/10.2215/CJN.03180906). [PubMed: [17699420](https://pubmed.ncbi.nlm.nih.gov/17699420/)].
- Kam TLP, Chun SC, Piraino B. ISPD Peritonitis recommendation: 2016 update on prevention and treatment. *Perit Dial Int*. 2016;**36**(5).
- Margetts P. Heparin and the peritoneal membrane. *Perit Dial Int*. 2009;**29**(1):16-9. [PubMed: [19164247](https://pubmed.ncbi.nlm.nih.gov/19164247/)].