

## Review of Peritonitis Associated with Peritoneal Dialysis Management

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### ABSTRACT

One frequent and serious side effect of peritoneal dialysis (PD) is peritonitis. Following the acquisition of the necessary microbiologic specimens, empirical antibiotic therapy covering both Gram-positive and Gram-negative organisms (including *Pseudomonas* species) should be initiated when a patient on PD exhibits clinical signs consistent with PD-associated peritonitis. The best administration route is intraperitoneal. To stop subsequent fungal peritonitis, antifungal prophylaxis should be administered, ideally in the form of oral nystatin. Antibiotic therapy can be modified in accordance with the results of the PD effluent Gram stain or culture and sensitivity tests. The most recent ISPD guidelines include a thorough explanation of how each antibiotic should be used. Antibiotics are often used for two to three weeks, depending on the particular organisms that are being treated. For refractory, relapsing, or fungal peritonitis, catheter removal and interim hemodialysis support are advised. Following full resolution of the peritonitis, a new PD catheter may be placed in certain individuals. Refractory exit site or tunnel infections should also be taken into consideration while removing PD catheters. The use of PD as a first-line dialysis modality is supported by a global trend of declining PD-associated peritonitis rates following improvements in clinical management.

**KEYWORDS:** end-stage renal disease, dialysis, Infection, Antibiotic, microbiology, peritoneal dialysis, Peritonitis

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### INTRODUCTION

One frequent and dangerous side effect of peritoneal dialysis (PD) is peritonitis. For more than 15% of PD patients, PD-associated peritonitis is the direct cause of mortality or a significant contributing factor. Furthermore, the most prevalent reason for conversion to long-term hemodialysis is a single incident of severe peritonitis or many bouts of peritonitis, which typically result in reduced peritoneal ultrafiltration capacity<sup>1,2</sup>.

Under the direction of the International Society for Peritoneal Dialysis (ISPD), guidelines for the management and avoidance of PD-associated peritonitis have been issued and updated often throughout the previous 30 years. Two sets of guidelines were released in the 2010 edition: one on the management of peritonitis linked to Parkinson's disease and

infections connected to catheter use, and the other on their avoidance. However, a distinct set of guidelines on catheter-related infections was released in 2017, and the treatment and prevention of PD-associated peritonitis were merged into one set in the most recent 2016 edition. Their precise recommendations varied somewhat because of this difference in focus. We concentrate on PD-associated peritonitis prevention and therapy in this study<sup>3</sup>.

### MANAGEMENT

The diagnosis. Any two of the following characteristics are necessary for the diagnosis of PD-associated peritonitis: (1) White cell count in the dialysis effluent >100/μl (after a dwell period of at least 2 hours), with >50% neutrophils; (2) positive dialysis effluent culture; and (3) clinical symptoms

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compatible with peritonitis, such as abdominal discomfort or hazy dialysis effluent. Nonetheless, the secret to a successful course of treatment is an early start to antibiotic medication and a rapid clinical diagnosis. Hence, until the diagnosis is verified or ruled out, individuals presenting with hazy effluent should be treated as though they have peritonitis. PD effluent should be examined for bacterial culture, Gram stain, cell count, and differential whenever peritonitis is suspected. For bacterial culture, blood culture bottle kits are the recommended method. The inoculation culture bottles should be incubated at 37°C if it is not possible to send them right away to the laboratory. Although they are laborious to utilize, other effluent concentration procedures may boost the output even more. Other innovative laboratory procedures (such as reagent strip or molecular-based assays) do not have enough data supporting them <sup>4</sup>.

**Antibiotic Empirical Therapy.** Empirical antibiotic treatment should begin as soon as the proper microbiologic specimens are acquired. It has not been demonstrated that any one antibiotic regimen is better than the others, hence the decision should be center-specific. The fundamental idea is to cover the necessary ground for both Gram-positive and Gram-negative organisms, including species of *Pseudomonas*. Vancomycin or first-generation cephalosporins are currently advised for covering Gram-positive organisms, whereas aminoglycosides or third-generation cephalosporins are advised for covering Gram-negative organisms. The frequency of methicillin-resistant organisms in each center should determine whether vancomycin or first-generation cephalosporin is the better option <sup>5</sup>.

Antibiotics should be administered intraperitoneally until systemic sepsis symptoms are present. To guarantee a timely course of therapy, however, the systemic route should be utilized as a stopgap when there is a predictable delay in the administration of intraperitoneal antibiotics. It is possible to combine cephalosporin, aminoglycosides, and vancomycin in one dialysis solution bag. Nevertheless, mixing ceftazidime and vancomycin in one injectable syringe will not work. The most recent ISPD guidelines provide a summary of suggested antibiotic doses; however, many of them are based more on clinical experience than pharmacokinetic research. It is necessary to modify the dose of several antibiotics for individuals who have significant residual renal function. The finding that treatment failure is linked to residual renal function might be explained by a single generic dose administered to all patients <sup>6</sup>.

Antibiotics administered intraperitoneally can be dosed intermittently or continuously (during each exchange). Because many antibiotics have significant systemic absorption during peritonitis, which allows reentry into the peritoneal cavity in following PD cycles, intermittent dosing is frequently feasible. To ensure proper absorption, the antibiotic-containing PD solution should be administered sporadically and left on the patient's body for at least six hours. Both intermittent and continuous intraperitoneal

dosing are acceptable options for  $\beta$ -lactams; however, continuous dosing should be preferred because it has a theoretical advantage because the bactericidal activity is time-dependent (that is, the reduction in bacterial density is proportionate to the time above minimal inhibitory concentration). On the other hand, intermittent dosing is frequently successful and could be the only practical regimen in cases when the patient needs caregivers or health care visits to provide the antibiotics, or in patients on automated PD who are unable to be temporarily switched to CAPD <sup>7</sup>.

Intraperitoneal vancomycin is more frequently given sporadically every 4-5 days, in contrast to  $\beta$ -lactams. To sustain effectiveness, the serum vancomycin level needs to be kept above 15  $\mu\text{g/ml}$ . It is also preferable to provide intraperitoneal aminoglycoside in daily, sporadic doses. The loss of remaining kidney function is not accelerated by short-term aminoglycoside treatment; nonetheless, recurrent or protracted exposure is linked to vestibular toxicity and should be avoided <sup>8</sup>.

In order to ease intraperitoneal antibiotic treatment, patients on automated PD who develop peritonitis may temporarily transition to CAPD; however, conversion is not always practical. The intermittent intraperitoneal dose for patients on automatic PD should be administered during the day. Regrettably, there is a significant lack of information about the appropriate dosage of antibiotics for treating peritonitis in automated Parkinson's disease. A larger daily dosage is frequently necessary because patients on automated PD may experience severe underdosing as a result of extrapolating pharmacokinetic data from CAPD to automated PD <sup>9</sup>.

**Adjacent Actions.** The majority of PD-related peritonitis patients may be treated as outpatients. The clinical severity, hemodynamic state, and frequently treatment-related practical concerns all play a role in the decision to admit a patient to the hospital. In addition to antibiotic therapy, antifungal prophylaxis—ideally in the form of oral nystatin—should be used. When the PD effluent is hazy, intraperitoneal heparin is typically administered to avoid fibrin-induced catheter blockage. Furthermore, those with diabetes should have close blood glucose monitoring since peritonitis may enhance glucose absorption from the PD solution. Malnutrition may emerge rapidly during peritonitis and is accompanied by an increase in peritoneal protein loss <sup>9</sup>.

**Management That Follows.** Antibiotic therapy should be modified when the findings of the PD effluent Gram stain or culture are known. Generally speaking, antibiotic coverage for Gram-negative bacteria (such as aminoglycoside or third-generation cephalosporin) might be discontinued if Gram-positive organisms are found, and vice versa if sensitivities are known. Particularly in cases where there is no clinical improvement, PD effluent leukocyte counts and bacterial culture should be carried out once more two to three days following antibiotic medication. On day 3, a PD effluent leukocyte count more than 1090/ $\mu\text{l}$  may indicate treatment failure <sup>10</sup>.

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A comprehensive discussion of how to manage bouts of peritonitis brought on by certain organisms may be found in the current ISPD guidelines. Basically, peritonitis brought on by streptococci, coagulase-negative staphylococci, or culture-negative events should be treated for two weeks if the clinical response is adequate. It's still up for debate whether or not to stop using the antibiotic for Gram-negative coverage in cases of culture-negative episodes. Although a small research has demonstrated that N-acetylcysteine may reduce aminoglycoside-related ototoxicity, the current recommendations specify that if aminoglycoside is used as the empirical Gram-negative coverage, it should be halted to decrease the risk of ototoxicity from recurrent exposure <sup>11</sup>.

Effective antibiotics should be used for three weeks in order to treat episodes of peritonitis brought on by *S. aureus*, enterococci, *Corynebacterium* species, Gram-negative bacilli (*Pseudomonas* or non-*Pseudomonas* species), and polymicrobial peritonitis. Enterococcal peritonitis should be treated with intraperitoneal vancomycin until vancomycin resistance is present, as enterococci have inherent resistance to cephalosporin and ampicillin soon becomes inactive when administered intraperitoneally. *Pseudomonas* peritonitis, in contrast to other bacterial causes, should be treated with two potent antibiotics that have distinct modes of action (e.g., oral ciprofloxacin with ceftazidime or cefepime) or gentamicin. A surgical examination should be sought right once if several enteric organisms are found in the PD effluent and if empirical antibiotics do not produce a quick clinical response. Metronidazole should be given in conjunction with vancomycin and either an aminoglycoside or ceftazidime. However, antibiotic therapy alone is typically beneficial if several Gram-positive organisms are found from the PD effluent. When *Mycobacterium tuberculosis* causes peritonitis, standard antituberculous chemotherapy is a very successful treatment. Catheter removal is typically required for nontuberculous mycobacterial peritonitis, while the exact treatment plan is unknown <sup>12</sup>.

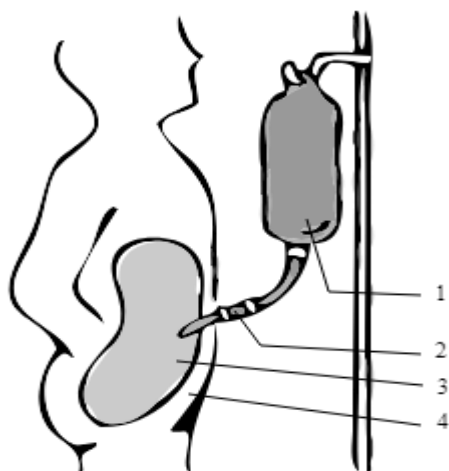


Figure 1. Intraperitoneal administration

### CONCLUSIONS

Even though there are thorough guidelines on PD-related peritonitis, there are still significant knowledge gaps that need

for more research. Notably, adjusting for a number of modifiable risk factors for PD-associated peritonitis does not seem to lower the risk; the best course of treatment for patients undergoing machine-assisted automated Parkinson's disease (PD) is inadequately defined; significant pharmacokinetic data for numerous novel antibiotics are unavailable; the chemical stability of a large number of antibiotics in current PD solutions is uncertain; and there are insufficient effective measures to prevent relapses or recurrent episodes of peritonitis.

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