CHAPTER 185

Treatment of Peritonitis and Other Clinical Complications of Peritoneal Dialysis in the Critically Ill Patient

Paraish S. Misra and Joanne M. Bargman

OBJECTIVES

This chapter will:
1. Discuss the major complications of peritoneal dialysis pertinent to critical care.
2. Describe the principles underlying the management of these complications.
3. Review preventive measures to minimize complications in this population.

Peritoneal dialysis (PD) is a simple but effective treatment of renal failure that relies on the peritoneal membrane for solute clearance and ultrafiltration. The major complications of PD can be classified as infectious, consisting of peritonitis, tunnel infections, and exit site infections, and noninfectious, of which the major categories are pressure-related, metabolic, and related to the PD catheter. In this section, these complications and their management are discussed, with a special emphasis given to peritonitis. For management of electrolyte and volume imbalances in patients on PD, please refer to Section 12 of this book.

INFECTIOUS COMPLICATIONS OF PERITONEAL DIALYSIS

Peritonitis

Peritonitis is the major complication of PD and occurs when infectious agents enter the peritoneal cavity. The resultant inflammation can lead to a transient or permanent increase in the transport characteristics of the peritoneal membrane, in addition to the clinical sequelae of sepsis. The importance

of PD peritonitis is highlighted by its strong association with technique failure and mortality.[1,2]

Pathophysiology and Microbiology of Peritonitis

Microorganisms can access the peritoneal cavity through several routes. Contamination of PD fluid and the luminal tract is usually the result of touch contamination and breach of sterile technique during inflow. Migration along the catheter surface often is seen in conjunction with exit site and tunnel infections. Translocation through contaminated viscera such as bowel and bladder occurs during inflammation or infection of these organs, and this route may be germane in the critically ill patient. Hematogenous spread from distant sites of infection rarely occurs. Interestingly, secondary bacteremia from PD peritonitis appears to be essentially unheard of in the absence of underlying abdominal pathology.[3]

Most peritonitis episodes are caused by bacterial pathogens. Gram-positive organisms, particularly *Staphylococcus aureus* (SA) and coagulase-negative staphylococci (CNS), are seen most commonly and are usually the result of skin flora contamination during PD fluid instillation or catheter infection.[4] Gram negatives are less frequently cultured, although the *relative* rate of infections from organisms such as *Pseudomonas* may be increasing.[5] Polymicrobial or anaerobic peritonitis often is due to intraabdominal or gut pathology and should prompt an evaluation for underlying surgical pathology. Fungal peritonitis, most commonly from *Candida* species, is a serious complication, often preceded by antibiotic use, especially for a previous bacterial peritonitis.[6] Culture-negative peritonitis is not uncommon and was seen in 20% of cases in one observational study.[4]

Clinical Features, Evaluation of Suspected Peritonitis, and Diagnosis

The cardinal symptoms of PD peritonitis are abdominal pain and change in effluent color from clear to cloudy. Another important clue is a reduction in ultrafiltration consequent to peritoneal inflammation. Evolving signs of sepsis such as fever and hemodynamic instability may be seen. Exit site infection or tunnel abscess, with purulent discharge from the exit site or overlying cellulitis, also may be present and should be sought actively during any evaluation for PD peritonitis.

Patients with suspected peritoneal infection should undergo prompt drainage of all peritoneal fluid. A sample of the effluent should be sent for cell count and differential, gram stain, and culture. Samples ideally should have dwelled for 2 hours in the peritoneal cavity. Patients who are empty of PD fluid should have 1 L of PD fluid instilled for 2 hours, after which it should be drained and analyzed as outlined above. For optimal pathogen detection, the International Society for Peritoneal Dialysis (ISPD) recommends 5 to 10 mL of PD fluid be sent in aerobic and anaerobic blood culture bottles. Any catheter exit-site purulence also should be cultured. As mentioned, blood cultures are infrequently positive in PD-associated peritonitis but may more likely isolate pathogens when surgical pathology is present and can be sent in the proper clinical context.

The diagnosis, as established by the ISPD guidelines,[7] relies on the presence of any two of the following features: (1) abdominal pain or cloudy effluent, (2) PD cell count of >100 cells/μL or PMNs >50% after a 2-hour dwell, and (3) positive dialysate culture. Patients on automated peritoneal dialysis (APD) with rapid cycles, such as acutely ill patients being managed for volume overload, may not have sufficient dwell times to reach an absolute PD fluid leukocyte count of more than 100 cells/μL, in which case a differential of more than 50% consisting of neutrophils is indicative of infection. A predominance of eosinophils usually indicates noninfectious inflammation such as allergic reactions to icodextrin-based PD fluids or after catheter insertion, although infection must be ruled out. Patients occasionally may have nondiagnostic cell counts or negative cultures, and repeat testing after 12 to 24 hours may be indicated if clinical suspicion remains high. If signs of peritonitis persist despite negative cultures after 3 to 5 days, cultures in special media for mycobacteria, fungi, and fastidious organisms can be considered. Last, because critically ill patients are at high risk of developing peritonitis and may not be able to complain of abdominal symptoms, careful monitoring of effluent is critical. In such cases, daily PD cell counts for screening may be useful for the rapid detection of peritonitis. This is particularly important in acute PD and may be accomplished in resource-poor settings by daily effluent testing for leukocytes with urinalysis Chemstrips.

Certain findings may raise suspicion for underlying abdominal or surgical pathology. These include localized abdominal pain or tenderness, the isolation of multiple enteric organisms, greater severity of presentation, and persistent signs of infection despite appropriate initial treatment. Peritoneal fluid analysis may aid in the diagnosis of secondary peritonitis, with amylase levels above 50 IU/L or lipase levels greater than 15 being suggestive.[8–10] Peritoneal free air often is seen in PD patients and is not necessarily indicative of bowel perforation. Abdominal computed tomography is rarely useful and does not definitely eliminate an underlying process. Surgical evaluation should not be delayed when secondary peritonitis is suspected, irrespective of imaging findings.

Antibiotic Therapy

The cornerstone of effective PD peritonitis management is the prompt administration of empiric antibiotic therapy once a presumptive diagnosis has been made. Given the frequency of gram-positive skin flora and gram-negative enteric organisms, empiric therapy should be simultaneously directed toward both. For gram-positive coverage, recommended agents include first-generation cephalosporins or vancomycin. The latter is preferred in centers where methicillin resistance is common. Gram-negative coverage usually is obtained with third- or fourth-generation cephalosporins or aminoglycosides. A typical empiric regimen may consist of cefazolin and ceftazidime administered intraperitoneally (IP).

Concern over accelerated loss residual renal function (RRF) may lead to avoidance of aminoglycosides, although there is some evidence that short-term aminoglycoside therapy does not significantly affect RRF.[11,12] It is nonetheless our practice to avoid aminoglycosides when patients produce more than 100 mL of urine daily, given the association of RRF with long-term outcomes.[13]

Aminoglycosides are associated further with significant ototoxicity, and if selected as initial therapy, switching antibiotics as soon as susceptibility results are available may be ideal. Other appropriate agents for gram-negative coverage include aztreonam in penicillin-allergic patients and, local resistance patterns permitting, fluoroquinolones. Therapy eventually should be narrowed based on results of cultures and sensitivities. Re-culture and serial PD cell

counts can be monitored to follow the response to therapy. Duration of antibiotic therapy depends on clinical context and the organism isolated. The reader is referred to the 2016 ISPD guidelines on management of PD peritonitis for further details[7] (www.ispd.org).

In atypical cases, initial antibiotic choice may be individualized. A recent Cochrane review was unable to demonstrate any consistent benefit of one antibiotic regimen over another because of the general poor quality and heterogeneity of available studies.[14] In cases of suspected surgical peritonitis, the ISPD recommends initial therapy with metronidazole, IP vancomycin, and gram-negative coverage with either ceftazidime or an aminoglycoside. Suspected fungal peritonitis should be treated with azole or echinocandin therapy. Most antibiotics appear to be compatible with coadministration in a single dwell, with the possible exception of penicillins and aminoglycosides. Vancomycin and ceftazidime should be mixed in a solution with a volume of at least 1L. Icodextrin has been shown to be compatible with vancomycin, aminoglycosides, cefazolin, and ceftazidime. In the case of multi-drug–resistant organisms, consultation with an infectious diseases specialist is advised.

The ideal route for antibiotic administration appears to be IP, because inflammation is likely limited to few cell layers beyond the peritoneum and bacteremia is rare. IP administration results in high levels at the site of infection, and enough antibiotic is thought to be absorbed systemically during peritoneal inflammation to provide continuous peritoneal drug delivery. Fluoroquinolones, if deemed appropriate, are administered orally.

Antibiotics may be given in one prolonged dwell daily (intermittent administration) or in each exchange (continuous administration). Vancomycin in particular is best dosed intermittently. One recommended regimen would be to monitor vancomycin blood levels daily and redose when levels fall below 15 μg/mL, or alternatively readminister doses every 4 to 5 days. The higher the RRF, the more frequently the drug will have to be given. Aminoglycosides appear to be equally effective with both methods of dosing, but intermittent administration may be preferable to avoid toxicity. For all other antibiotics, we prefer intermittent over continuous dosing because of ease of administration and efficacy. Antibiotics should be allowed to dwell for at least 6 hours. As mentioned earlier, continuous peritoneal antibiotic delivery with intermittent dosing is obtained through diffusion of the antibiotic back into the cavity from the blood. In patients on automated PD, enhanced antibiotic clearance may be seen, which can be circumvented either through continuous administration where possible or switching to manual exchanges for the duration of antibiotic therapy.

Other Considerations

All patients should get fungal prophylaxis while on antibiotic therapy for any indication to prevent secondary fungal peritonitis. One regimen consists of 100,000 units of Nystatin orally, four times daily (although azole therapy also can be used), for 1 week beyond the duration of antibacterial therapy. Icodextrin may be helpful when there is diminished ultrafiltration, in which case special glucometers insensitive to maltose should be employed. Diabetic control also may worsen with peritoneal inflammation because of the increased absorption of glucose. Last, fibrin formation may impair catheter function, and IP heparin 500 to 1000 units/L can be added preemptively during initiation of therapy for peritonitis, or only upon detection of cloudy dialysate or fibrin. Heparin is not absorbed systemically and does not pose a risk of systemic bleeding (see later in this chapter).

Temporary cessation of PD is not necessary in most cases of peritonitis but may be considered in select severe cases. Because PD patients generally have some degree of RRF, a short period of peritoneal rest generally is well tolerated. In an effort to prevent secondary peritonitis with enteric organisms, we routinely stop PD for a few days when the patient has colitis or enteritis (e.g., ischemic bowel or *Clostridium difficile* infection) and in the face of other surgical complications, such as cholecystitis or diverticulitis.

If patients fail to respond to appropriate antibiotic therapy, PD effluent should be sent for repeat culture. A thorough evaluation for underlying abdominal disease or a surgical process should be undertaken. Intensification of antibiotic therapy can be considered by increasing antibiotic dwell times or switching to continuous administration if not initially used. Broadening of coverage may be helpful until control of the underlying process is obtained. Consultation with the infectious disease professionals would be beneficial. Ultimately, catheter removal with peritoneal rest may be necessary in refractory cases and in the case of fungal peritonitis.

Prevention

In critical care settings, a number of risk factors for the development of peritonitis arise, making preventive measures an important element of the care of these patients. Antibiotic prophylaxis is recommended in a number of commonly observed scenarios in hospitalized PD patients; antibiotic regimens provided in the following discussion are suggestions only, and ultimate choice of prophylactic agent should be dictated by local patterns of resistance. Before catheter insertion for acute PD, antibiotics reduce infectious complication, and vancomycin and cephalosporins are used commonly for this purpose. Prophylactic antibiotics also should be used before invasive procedures of the gastrointestinal and gynecologic tracts, including the oral cavity. We use a single dose of amoxicillin 2 hours before oral procedures, and IV ampicillin and aminoglycoside immediately before colonoscopies in which biopsies or other mucosal breach is anticipated. Breach of sterile technique during inflow with possible infusion of contaminated PD fluid should prompt further the administration of a single dose of IV antibiotics covering skin flora, such as first-generation cephalosporins or vancomycin. Antifungals should be prescribed any time antibacterials are administered to prevent the secondary development of fungal peritonitis (see Other Considerations earlier in this chapter for suggested antifungal regimens).

In addition to antibiotic prophylaxis, several simple practices may lower peritonitis rates further. Before any procedure involving the abdomen or pelvis, PD fluid should be drained completely to prevent seeding. Ensuring that patients are having regular bowel movements with administration of laxatives as necessary also may reduce peritonitis rates, in addition to enhancing catheter function and PD efficiency. Standard practices aimed to reduce peritonitis rates in non–critically ill patients also should be applied, such as adherence to hand hygiene and the observance of sterile technique during manual exchanges. Meticulous attention should be paid to exit site care and prevention of exit site infections (ESIs) with antibacterial ointments because ESIs run the risk of spreading into the peritoneal cavity.[15] At the current time, there is no evidence supporting the use of neutral pH low-glucose degradation products for the express purpose of peritonitis prevention.

Likewise, there is no clear evidence that automated PD is superior to manual exchanges in the prevention of infectious complications; thus the selection of PD modality should be individualized to each patient and the ICU practice.

Exit Site and Tunnel Infections

The clinical signs of ESI may be missed easily, and daily examination of the catheter is imperative for early detection and treatment. Cuff extrusion from the tunnel can lead to skin inflammation and predisposes to infection; these can be managed easily with shaving of the exposed cuff by a trained operator. Early infection may manifest as erythema or crust formation, although this simply may represent irritation at the exit site. Serous or purulent discharge from the catheter tract is diagnostic. Topical antimicrobials such as chlorhexidine with hydrogen peroxide twice daily may be sufficient for mild infections, but the presence of drainage should prompt the administration of systemic antibiotics. Two weeks of gram-positive coverage should treat ESIs adequately. Refractory ESIs or those accompanied by tenderness or erythema of the subcutaneous tunnel should be investigated further by computed tomography (CT) or ultrasonography for the presence of tunnel abscess. Bedside ultrasonography, widely available in critical care settings, has been shown to be useful in ESIs to monitor the response to treatment.[16]

Indications for Catheter Removal or Exchange

Some peritonitis episodes are associated with extensive colonization of the catheter by pathogens and may not resolve or may be prone to relapse unless the catheter is removed. Absolute indications for catheter removal include tunnel abscess and peritonitis caused by virulent organisms, particularly SA and *Pseudomonas*. Refractory (not responding to 5 days of appropriate antibiotics) and relapsing (recurrence with same organism within 4 weeks) peritonitis should suggest further the need for catheter removal, as would refractory ESI. In the case of relapsing CNS peritonitis, the catheter can be replaced immediately if infection is not active and therapeutic antibiotics are administered. Otherwise, particularly with SA and *Pseudomonas* species, a period of peritoneal rest is necessary to prevent relapse or contamination of the new catheter. In the presence of underlying abdominal pathology, peritonitis may not resolve unless the catheter is removed. In contrast, it is not necessary to remove the catheter in the patient needing abdominal surgery unrelated to PD unless there is surgical peritonitis. In most cases, return to PD may be feasible after at least 2 weeks of peritoneal rest and complete resolution of symptoms. Temporary switch to hemodialysis may be necessary if the patient needs dialysis in the interim.

Pressure Considerations

The instillation of PD fluid into the peritoneal cavity increases intraabdominal pressure, which may lead to several complications, particularly in patients newly initiated on PD. With catheters that have been implanted recently, this pressure may cause fluid to leak along the catheter tract, or in some cases, subcutaneously through the incision site or laparoscopic hole. Clinical manifestations include visualization of leakage from the exit site, edema of the abdomen, penis, or mons pubis in the case of subcutaneous leak, and decreased PD fluid outflow and ultrafiltration failure. Instillation of contrast-containing PD fluid through the catheter followed by CT scan can be used to make the diagnosis. In contrast, abdominal wall hernias, typically umbilical or incisional, appear more frequently in patients with longer PD vintage. In acute care settings, this complication is uncommon because patients remain supine for longer periods of the day, resulting in decreased transmission of intraabdominal pressure to the abdominal wall. Nonetheless, the presence of a significant hernia may be a relative contraindication to the initiation of PD. In some patients, compression of gastric contents may predispose to gastroesophageal reflux and a higher risk of aspiration, and thus limit enteral nutrition.

More serious complications of PD-induced increased abdominal pressure involve the respiratory apparatus. Patients may develop hydrothorax from PD resulting from leakage of fluid through a diaphragmatic defect. Although rare, this may occur rapidly and lead to significant respiratory compromise, requiring urgent therapeutic thoracentesis. The fear over the development of hydrothorax should not lead to the routine discontinuation of PD after cardiothoracic surgery (see Other Considerations later in this chapter). In our experience this complication is very unlikely, even in patients undergoing thoracic surgery. Although there is a paucity of literature on the subject, we avoid PD if a patient has a pericardial window or pericardiectomy, because this structure normally functions as a barrier between the peritoneal cavity and the heart. Other causes of PD-related respiratory impairment include pressure-induced atelectasis and reduction of lung volumes and functional reserve capacity, more evident in patients with underlying respiratory compromise.

All pressure-related PD complications are managed similarly. PD often can be continued with reduction in fill volumes as tolerated. In life-threatening or refractory cases, complete cessation of PD may be required with a temporary switch to hemodialysis if necessary. Upon resolution, PD could be reinstated gently using lower fill volumes or an intermittent modality.

Metabolic Complications of Peritoneal Dialysis

The use of dextrose-containing PD fluids is a useful source of calories and could provide 20% to 30% of daily caloric requirements in patients in whom nutritional therapy otherwise has been stopped.[17] This glucose load also may have deleterious consequences, such as exacerbating hyperglycemia and increasing carbon dioxide production, which may make ventilation more challenging. Effective management of these complications involves aggressive glucose monitoring and insulin therapy. Glucose delivery can be reduced if necessary by decreasing fill volumes (to 750–1000 mL) and solution tonicity if feasible, or through the use of non-dextrose–based solutions such as icodextrin. Use of the latter requires a special glucometer for glycemic management because the generation of maltose from icodextrin metabolism may lead to spurious hyperglycemia if conventional glucometers are used. Equally important is the possibility of hypoglycemia in patients on stable insulin therapy when PD tonicity is reduced; vigilance must be maintained in such circumstances.

Catheter-Related Complications

Catheter malfunction is a common problem in PD patients and manifests as inability to completely drain instilled PD fluid. The major causes of catheter malfunction are

constipation, catheter malposition, intraluminal blockage (which causes absent inflow and outflow), extraluminal blockage, catheter kinking, and pericatheter leak (see earlier). In all patients, the first step should be optimizing the patient's bowel regimen and treating constipation, regardless of the cause. Should difficulty with outflow persist, a plain film x-ray of the abdomen should be obtained to confirm proper catheter positioning, with the tip within the pelvic rim. If this is not improved after regular bowel movements have been established, catheter manipulation or replacement may be required. Clues to the presence of intraluminal obstruction by fibrin include cloudy dialysate, visualization of fibrinous strands in the effluent, or difficulty with inflow as well as outflow. Instillation of heparin, 500 to 1000 units/L of PD fluid, may be used for treatment of established obstruction by fibrin and prevention of clotting in the case of the bloody or cloudy effluent. Severe or refractory cases may require thrombolytic therapy. Our preferred regimen consists of 4.6 mL of tPA IP.

Because neither heparin nor tPA are absorbed systemically from the peritoneal cavity, increased bleeding risk is not a contraindication to their use. Catheter malfunction in the absence of constipation, malposition, or intraluminal obstruction may result from extraluminal obstruction because of adhesions, fallopian tube or omentum, kinking, or pericatheter leak. Suspicion of extraluminal obstruction warrants surgical consultation for omentopexy or lysis of adhesions if feasible. Other catheter-related complications usually arise acutely postinsertion and include intraperitoneal hemorrhage and intestinal perforation. Intraperitoneal bleeding, if associated with a tolerable drop in hemoglobin and hemodynamic stability, may be observed closely and treated with IP heparin to prevent clotting of the catheter, as detailed above. Intestinal perforation may manifest as hemorrhage, peritonitis with enteric organisms, or diarrhea upon instillation of PD fluid. The treatment generally includes prompt catheter removal, surgical repair, and systemic antibiotics.

OTHER CONSIDERATIONS

Peritoneal Dialysis in the Surgical Patient

Before major surgery, all peritoneal fluid should be drained and antibiotic prophylaxis administered as detailed above and in the 2016 ISPD guidelines. Cardiothoracic surgery does not preclude postoperative resumption of PD over concerns for PD hydrothorax, unless a gross diaphragmatic defect was induced or observed intraoperatively. In our opinion intraoperative assessment of the diaphragm is sufficient to rule out a significant defect, and PD usually can resume successfully postoperatively, which permits ongoing metabolic and volume optimization. Intraabdominal surgery requires temporary peritoneal rest until the peritoneum has been deemed to have had enough time to recover. Patients may require a temporary switch to hemodialysis during this period, particularly with little or no RRF.

Preserving Residual Renal Function

PD provides significant benefits over other RRT modalities with regard to the quality of life of patients with end-stage renal disease, but its success is related strongly to RRF.[13] Thus nephrotoxic substances such as aminoglycosides, intravenous radiographic contrast material, and nonsteroidal antiinflammatory agents should be avoided as much as possible.

Peritoneal Rest

Although PD can be continued generally in most acutely ill patients, several situations deserve mention. Presence of any acute intraabdominal inflammation, such as colitis, diverticulitis, or cholecystitis, particularly if associated with PD peritonitis, should be treated with peritoneal rest. In addition, it is our practice to hold PD during peritonitis associated with anaerobes or multiple gram-negative agents in the absence of intraabdominal pathology, because these may be due to occult intestinal microperforations. PD can be resumed in most cases upon resolution of the acute abdominal process and when the peritoneum has been deemed to have had enough time to recover. As previously mentioned, a temporary transition to hemodialysis may be required. However, most PD patients can tolerate several days of peritoneal rest.

Key Points

1. Critically ill patients have multiple risk factors for the development of peritonitis, and every effort to prevent its development should be employed to optimize outcomes. These include routine administration of topical antibiotics to the exit site, draining of the fluid and prophylactic use of antibiotics before invasive procedures, addition of antifungal prophylaxis during antibiotic therapy, and resting the peritoneum during intercurrent intraabdominal events such as colitis.
2. The management of suspected PD peritonitis includes effluent cell count and differential, effluent culture, and the prompt administration of empiric antibiotics.
3. Secondary peritonitis should be suspected in the event of focal abdominal pain or tenderness, isolation of anaerobes or multiple organisms from peritoneal fluid, or failure to respond to appropriate antibiotic therapy.
4. Pressure-related complications include pericatheter leakage of PD fluid, hernias, and rarely, hydrothorax and worsening of ventilatory status. These generally can be managed by reduction in fill volumes and switching to hemodialysis if feasible.
5. Catheter malfunction manifests as failure of outflow and possibly inflow and usually is due to constipation, catheter malposition, pericatheter leak, catheter kinking, or intraluminal obstruction with fibrin. Initial management includes administration of laxatives, verification of catheter position, and administration of intraluminal thrombolytics when appropriate.
6. Preservation of residual renal function is essential to ensuring good long-term outcomes in PD patients. The use of nephrotoxins such as aminoglycosides and radiocontrast material should be avoided wherever possible.

Key References

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