In the name of GOD

The 19th International Congress of Nephrology, Dialysis and Transplantation (ICNDT)

12-15 December 2023
Homa Hotel, Tehran

Peritonitis in Peritoneal Dialysis(PD)

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TEHRAN 2023

Peritonitis in PD

- ✓Peritonitis is a major complication of peritoneal dialysis and a primary reason for patients to switch from peritoneal dialysis to hemodialysis.

- ✓Peritonitis is associated with significant morbidity, catheter loss, transfer to hemodialysis, transient loss of ultrafiltration, possible permanent membrane damage, and occasionally death.

Peritonitis in PD

- ✓Risk factor & prevention of peritonitis in PD
- ✓Clinical manifestation & diagnosis of peritonitis in PD
- ✓Microbiology & therapy of peritonitis in PD

Peritonitis in PD
PATHOPHYSIOLOGY

✓Among patients on peritoneal dialysis, peritonitis is caused by introduction of microbes to the usually sterile peritoneum in the setting of compromised host defenses.

Source of infection — Sources of peritonitis include:

1)intraluminal contamination

2)periluminal contamination

3)transvisceral migration from a bowel or, rarely, vaginal leak

4)hematogenous dissemination from a remote source, as may occur during dental procedures.

Peritonitis in PD
PATHOPHYSIOLOGY : Biofilms

- ✓ A biofilm is a slimy film of bacteria or fungi that adheres to a surface
- ✓ Biofilms on the catheter may contribute to relapsing or recurrent infection and to antibiotic resistance
- ✓ Biofilms may contribute to relapsing or recurrent peritonitis with the same organism
- ✓ Intraperitoneal **urokinase** has been suggested as a treatment of biofilm as a potential cause of relapsing infection

Peritonitis in PD
PATHOPHYSIOLOGY:Host defence

✓ An intact peritoneum and the defense mechanisms of the mesothelium are important barriers to the development of peritonitis in patients on PD. These host defenses are compromised by the peritoneal dialysis procedure:

1. The continuous presence of a large amount of fluid in the peritoneal cavity can impair host defenses
2. The composition of the peritoneal dialysis fluid may promote microbial growth and inhibit host defense
3. Resident macrophages and cytokines that potentially prevent infection are constantly removed during each exchange of dialysis fluids.

Peritonitis in PD
EPIDEMIOLOGY

- ✓**Incidence** — The reported incidence of peritonitis ranges widely . A study of 1677 patients on incident PD revealed a first-year peritonitis rate of 42 per 100 patient-years.
- ✓**Risk factors** — Important modifiable risk factors include :

1. Recent invasive intervention (colonoscopy, sigmoidoscopy, cystoscopy, hysteroscopy) or dental procedures
2. Nasal *S. aureus* carriage
3. Exit-site and/or tunnel infections .
4. Other factors include :**constipation**, **smoking** and **COPD**, **domestic pets**, **obesity**, **depression**, **hypokalemia**, **hypoalbuminemia**, **prior hemodialysis**, use of **bioincompatible solutions**, and **living far away from the PD clinic**

Peritonitis in PD
PREVENTION

✓It is important to prevent peritonitis. Peritonitis often results in morbidity, transfer to hemodialysis, and, occasionally, death.

1. **Proper training and home visits**
2. **Transfer set**
3. **Modality and choice of dialysate**
4. **Approach after breaks in technique**
5. **Prophylactic treatment with procedures**
6. **Prophylactic antibiotics for catheter exit-site leaks**
7. **Prevention and treatment of catheter infections**
8. **Antifungal prophylaxis during antibiotic therapy**

Peritonitis in PD
Causes of peritonitis

- ✓ Patients on (PD), peritonitis may be:

1) **Directly** related to peritoneal dialysis (ie, due to contamination with pathogenic skin bacteria during exchanges or to an exit-site or tunnel infection), or
2) **Secondary** to a nondialysis-related intra-abdominal or systemic process. Secondary peritonitis is caused by underlying pathology of the GI tract and occasionally (albeit rarely) due to hematogenous spread (ie, following dental procedures).

- ✓ Most cases are peritoneal dialysis-related.

Peritonitis in PD
Clinical presentation

✓The **most common** symptoms are:

abdominal pain and cloudy peritoneal effluent.

✓ **Exceptions** are patients undergoing (APD) who often do not state that they have had cloudy fluid.

✓Among all patients, physical exam reveals:

abdominal tenderness, rebound tenderness, and occasionally systemic signs, including hypotension.

Peritonitis in PD
Clinical presentation

✓ Frequency of symptoms and signs:

1. Abdominal pain – 79 to 88 percent
2. Fever (greater than 37.5ºC) – 29 to 53 percent
3. Nausea or vomiting – 31 to 51 percent
4. Cloudy effluent – 84 percent
5. Hypotension – 18 percent

Peritonitis in PD
Evaluation

- ✓ All patients on PD who are suspected of having peritonitis, the peritoneal fluid should be sent for cell count and differential, gram stain and culture.

- ✓ Culture of any purulent drainage from the exit site should be performed.

- ✓ If the patient is febrile or appears **septic**, we also check a complete blood count (CBC) and blood cultures

Peritonitis in PD
Clinical presentation

- ✓An **optimal technique** for culturing peritoneal fluid in (CAPD) and (APD) patients is the combination of sediment culturing of 50 mL effluent and bedside inoculation of 3 to 5 mL of effluent dialysate in each of two blood culture bottles
- ✓To perform sediment culturing, 50 mL of dialysate fluid is centrifuged at 3000 g (ie, relative centrifugal force) for 15 min& the supernatant decanted off.
- ✓The sediment is resuspended in 3 to 5 mL of sterile saline, and the suspension is inoculated on solid culture medium and into standard blood culture bottles.

Peritonitis in PD
Diagnosis

- ✓Patients with cloudy effluent should be presumed to have peritonitis, even in the absence of other findings on history and physical. Such patients should be empirically treated until the diagnosis is confirmed or excluded.
- ✓ Peritonitis should be diagnosed if two or more of following are present:

1. Consistent clinical features (abdominal pain or cloudy effluent).
2. Peritoneal fluid white count is greater than 100 cells/mm^3 (or 0.1 x 10^9/L after dwell time of at least two hours) and the percentage of neutrophils is greater than 50 percent.
3. Positive effluent culture.
4. The diagnosis of peritonitis is confirmed by a positive dialysate culture.

Peritonitis in PD
Differential diagnosis

- ✓The differential diagnosis of peritonitis in peritoneal dialysis patients includes all the causes of abdominal pain without peritonitis in the general population

And

- ✓all the causes of cloudy peritoneal fluid in the absence of or with variable amounts of abdominal pain

Peritonitis in PD
MICROBIOLOGY

- ✓The vast majority of peritonitis cases are caused by **bacteria**. Approximately 3 to 5 percent are caused by **fungi**, mostly *Candida* species .
- ✓ A **viral** etiology of peritonitis has not been proven conclusively
- ✓Approximately 45 to 65 percent of cases are caused by gram-positive organisms and 15 to 35 percent by gram-negative organisms.
- ✓More than one organism has been reported in 1 to 4 percent of cases

Peritonitis in PD
MICROBIOLOGY

- ✓**Gram positive** — Gram-positive pathogens include coagulase-negative *Staphylococcus* spp, *Streptococcus* spp, *Staphylococcus aureus, Enterococcus* spp, and *Corynebacterium* spp

- ✓**Gram negative** — Gram-negative organisms can be from the bowel, skin, urinary tract, contaminated water, or animal contact.Common causes of gram-negative peritonitis include *Escherichia coli, Klebsiella* spp, and *Pseudomonas aeruginosa*

Peritonitis in PD
Treatment

Tx for peritoneal dialysis-associated peritonitis consists of :

1. **Antimicrobial** therapy
2. In some cases, **catheter removal** is also warranted.
3. Additional therapies may include the addition of **heparin** to dialysate and **rapid exchanges** to reduce symptoms.

Peritonitis in PD. Treatment : Antimicrobial therapy

- ✓ Initial empiric antibiotic coverage for peritoneal dialysis-associated peritonitis consists of coverage for **gram-positive organisms** (by vancomycin or a first-generation cephalosporin) **and gram-negative organisms** (by a third-generation cephalosporin, an aminoglycoside, or aztreonam).

- ✓ IP administration of antibiotics is preferred to IV administration, unless the patient appears septic.

Peritonitis in PD. Treatment : Antimicrobial therapy

Empiric antibiotics — Empiric antibiotics should be initiated as soon as possible after specimens obtained for cell count, Gram stain, and culture.

- ✓Gram-positive organisms may be covered by vancomycin or a first-generation cephalosporin (such as cefazolin). In centers with a high rate of methicillin-resistant organisms, vancomycin should be used.
- ✓Gram-negative organisms may be covered by a third- or fourth-generation cephalosporin (such as cefepime or ceftazidime), an aminoglycoside, or aztreonam

Peritonitis in PD. Treatment : Antimicrobial therapy

- ✓**Polymicrobial peritonitis** – Peritonitis due to multiple enteric organisms or mixed gram-negative/gram-positive organisms should raise concern for a concurrent intra-abdominal condition such as ischemic bowel or diverticular disease

- ✓**Culture-negative peritonitis** – Culture-negative peritonitis should be treated with empiric antibiotic therapy that covers both gram-positive and negative organisms. A repeat cell count and culture should be obtained after three to five days of empiric therapy and determines further therapy

Peritonitis in PDTreatment
Monitoring clinical response

- ✓ Clinical improvement should be observed within 48 hours of initiating therapy
- ✓ By 48 hours, the fluid should be less cloudy. Repeat cell counts to assess response to therapy
- ✓The absence of improvement in the cell count suggests lack of response to treatment
- ✓ If the patient does not appear to be improving clinically by 48 hours and cultures demonstrate a susceptible organism, switch from intermittent to continuous dosing

Peritonitis in PD.Treatment
Monitoring clinical response

- ✓ **Second antibiotic:** Some organisms may require the addition of a second antibiotic:

1)For *S. aureus* infections, add rifampin if there is no or little clinical response by 48 hours.

2)For gram-negative infections, add a second antibiotic based on sensitivities if there is no response at 48 .

- ✓ **Antifungal prophylaxis** — Treatment with systemic antibiotics is a major risk factor for the development of fungal peritonitis among peritoneal dialysis patients

Peritonitis in PD:Treatment
Indications for catheter removal

✓ Indications for catheter removal include:

1. Relapsing or refractory peritonitis,
2. Fungal or mycobacterial peritonitis,
3. Peritonitis associated with intra-abdominal pathology,
4. Culture-negative peritonitis with persistent symptoms.

Peritonitis in PD
Prognosis

- ✓Most episodes of peritoneal dialysis-associated peritonitis resolve with **outpatient antibiotic** treatment.
- ✓Approximately 20 percent require **catheter removal** to eradicate infection.
- ✓Reported associated **mortality** of 2 to 6 percent
- ✓**Transfer to hemodialysis** — Peritonitis results in a 5 to 20 percent risk of patients needing to switch to hemodialysis

Title:

Intraperitoneal antibiotic dosing recommendations for continuous administration in adult patients on peritoneal dialysis

Intraperitoneal antibiotic dosing recommendations for continuous administration in adult patients on peritoneal dialysis

	Initial IP loading dose	Maintenance IP dose administered with all exchanges following a loading dose, if indicated **NOTE:** Intermittent regimens, which are listed in a separate table, are preferred for initial treatment in most patients with peritoneal dialysis-associated peritonitis. For additional information refer to legend below and UpToDate topic on microbiology and therapy of peritonitis in peritoneal dialysis.
Aminoglycosides		
We do not administer IP aminoglycosides continuously		
Carbapenem		
Imipenem-cilastatin *	250 mg/L dialysate	50 mg/L dialysate
Meropenem	None	125 mg/L dialysate
Cephalosporins		
Cefazolin	500 mg/L dialysate	125 mg/L dialysate
Cefepime	500 mg/L dialysate	125 mg/L dialysate
Cefoperazone ¶	500 mg/L dialysate	62.5 to 125 mg/L dialysate
Ceftazidime	500 mg/L dialysate	125 mg/L dialysate
Penicillins		
Amoxicillin Δ	None	150 mg/L dialysate
Ampicillin ◇	None	125 mg/L dialysate
Ampicillin-sulbactam §	750 to 1000 mg/L dialysate	100 mg/L dialysate
Penicillin G	50,000 units/L dialysate	25,000 units/L dialysate
Glycopeptides		
Teicoplanin ¶	400 mg in one bag	20 mg/L dialysate
Vancomycin	2 grams in one bag	25 mg/L dialysate ¥
Others		
Aztreonam	500 mg/L dialysate	250 mg/L dialysate
Ciprofloxacin ‡	None	50 mg/L dialysate
Clindamycin	None	600 mg per bag
Daptomycin	100 mg/L dialysate	20 mg/L dialysate
Ofloxacin Δ‡	200 mg in one bag	25 mg/L dialysate
Polymyxin B	None	300,000 units (30 mg) per bag
Oral options that provide adequate levels within the peritoneum: Refer to separately available table of intermittently administered antibiotics in peritoneal dialysis-associated peritonitis.		

Intraperitoneal antibiotic dosing recommendations for intermittent administration in adult patients on peritoneal dialysis

Intraperitoneal antibiotic dosing recommendations for intermittent administration in adult patients on peritoneal dialysis

	IP dose instilled in the longest dwell of the day of at least 6 hours
Aminoglycosides *	
Amikacin	2 mg/kg in one exchange per day ¶
Gentamicin	0.6 mg/kg in one exchange per day ¶
Netilmicin Δ	0.6 mg/kg in one exchange per day ¶
Tobramycin	0.6 mg/kg in one exchange per day ¶
Carbapenems	
Imipenem-cilastatin	500 mg in alternate exchanges ◇
Meropenem	1 gram in one exchange per day
Cephalosporins ¶	
Cefazolin	15 to 20 mg/kg in one exchange per day
Cefepime	1 gram in one exchange per day
Cefotaxime	500 to 1000 mg in one exchange per day
Ceftazidime	1 to 1.5 grams in one exchange per day
Ceftriaxone	1 gram in one exchange per day
Glycopeptides	
Vancomycin	25 mg/kg ideal body weight; re-dose once serum level is ≤15 mcg/mL §
Teicoplanin Δ	15 mg/kg in one exchange every 5 days
Penicillins	
NOTE: For dosing of most penicillins for IP administration, refer to separately available UpToDate table for continuous administration of IP antibiotics.	
Amoxicillin	**Oral:** 500 mg every 8 hours
Ampicillin ¥	4 grams in one exchange per day
Other	
Aztreonam	2 grams in one exchange per day
Ciprofloxacin ‡	**Oral:** 250 mg twice per day
Daptomycin	300 mg in one exchange per day
Fosfomycin †	4 grams in one exchange per day
Linezolid	**Oral:** 600 mg twice per day
Moxifloxacin ‡	**Oral:** 400 mg once per day
Trimethoprim-sulfamethoxazole (co-trimoxazole)	**Oral:** One double-strength tablet (trimethoprim 160 mg and sulfamethoxazole 800 mg) two times per day
Antifungal	
Fluconazole	200 mg in one exchange every 24 to 48 hours