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Bulletin de la Dialyse à Domicile

Overview of ISPD 2022 guideline recommendations for peritonitis prevention and treatment

(Aperçu des recommandations des lignes directrices ISPD 2022 pour la prévention et le traitement de la péritonite.)

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Note : ce texte est disponible en Français à la même adresse url : https://doi.org/10.25796/bdd.v5i2.66753

Résumé

Cet article est un résumé des nouvelles recommandations ISPD pour la prévention et le traitement de la péritonite. Ces dernières recommandations apportent des clarifications de définition, de nouveaux objectifs vis-à-vis des taux de péritonite. Il apporte également de nouvelles recommandations sur la prévention et la prise en charge de la péritonite avec de nouvelles directives concernant l'utilisation empirique des antibiotiques, le dosage et le traitement de la péritonite due à des micro-organismes spécifiques. En cas de doute ou de besoin de précisions, l'article original (1) et la liste exhaustive des références qu'il contient doivent être consultés.

Mots clés :Recommandation, ISPD, péritonite, prévention, traitement, dialyse péritonéale

Summary

This article is a summary of the new ISPD recommendations for peritonitis prevention and treatment. The latter recommendations bring definition clarifications, new targets with respect to the rates of peritonitis. It also brings new recommendations on the prevention and the management of peritonitis with new guidelines regarding empirical use of antibiotics, dosage and treatment of peritonitis due to specific microorganisms. In case of doubt or need of precisions, the original article (1) and the exhaustive list of references that it contains should be consulted.

Keywords : Guideline, ISPD, peritonitis, prevention, treatment, peritoneal dialysis

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INTRODUCTION

Peritoneal dialysis (PD)-associated peritonitis is the most common PD-related infection and can be associated with PD discontinuation, transfer to hemodialysis and death. Recent guidelines from the International Society for Peritoneal Dialysis (ISPD) have been published in 2022, with respect to peritonitis prevention and treatment.
This article is an overview of the latter guidelines from ISPD (1).

DEFINITION AND MEASUREMENT OF PERITONITIS

Definition of peritonitis is heterogeneous in literature. Efforts for standardization are of certain importance. Similarly, definition of outcomes measures need standardization.

According to ISPD guidelines, peritonitis should be diagnosed when at least two of the following criteria are present: (1) Consistent clinical features (cloudy effluent, abdominal pain etc.), (2) Effluent white cells count: > 100/μl and > 50% of neutrophils and (3) Positive dialysis effluent culture. Figure1 summarizes definition and classification of cause-specific PD-associated peritonitis.

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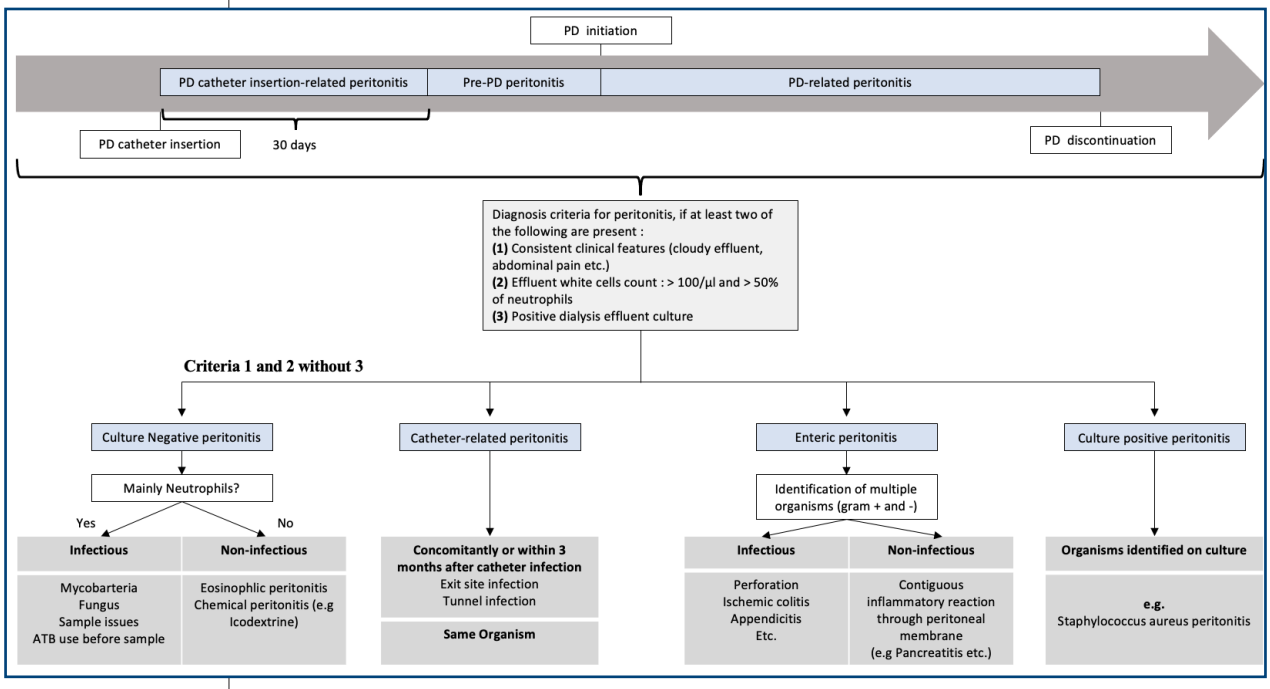
Peritonitis can be defined according to its etiology (cause-specific peritonitis, Fig. 1)

- **Culture-negative peritonitis:** defined by the presence of criteria (1) and (2) in the absence of a positive effluent culture. All cases of culture-negative peritonitis should be counted in the peritonitis statistics. The latter can be either infectious or non-infectious.
- **Catheter-related peritonitis:** defined by the presence of peritonitis occurring concomitantly or up to 3 months after the onset of either exit-site infection and/or tunnel infection and with the same organism.
- **Enteric peritonitis:** defined as a peritonitis occurring from an intestinal source. It can be either infectious (in less than 20%, effluent culture may be positive to both gram positive and gram-negative bacteria) or non-infectious (secondary to contiguous inflammatory reaction through peritoneal membrane and therefore culture-negative). The latter should be counted as enteric peritonitis rather than culture-negative peritonitis.
- **Culture-positive peritonitis**

Peritonitis can be defined according to the timeline of occurrence (time-specific peritonitis, Fig.1)



⬆ *Figure 1. Definition and classification of cause-specific and time-specific peritonitis, according to ISPD guideline recommendations*

- **Pre-PD peritonitis**: Under recognized. Defined as a peritonitis occurring after PD catheter insertion but before initiation of the technique. Weekly flushing of the catheter should not be considered as PD initiation.
- **PD catheter insertion-related peritonitis:** defined as a peritonitis occurring within 30 days of PD catheter insertion.
- **PD-related peritonitis:** starting from PD initiation. According to the ISPD Guidelines on Creating and Maintaining Optimal PD Access in the Adult Patient.

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Peritonitis can be defined according to its outcomes (outcome-specific definitions of peritonitis)

The ISPD recommends frequent monitoring (as a part of a continuous quality improvement (CQI) program) of peritonitis rate and outcomes, using the following definitions to describe outcomes following peritonitis.

At least on a yearly basis:
- *Rate of peritonitis:* number of episodes per patient-year.
  - o Overall peritonitis rate: should not exceed 0.4 episodes per patient-year (year at risk).
  - o Culture-negative peritonitis: should be reported as a percentage of all peritonitis episodes per unit time and should be less than 15% of all peritonitis episodes.

On a monthly basis, or at least quarterly, for local reports to inform local practices:

- *PD catheter insertion-related peritonitis:* should be <5% of catheter insertion.
- *Mean time to first peritonitis episode:* where time counts from the first day of PD initiation.
- *Percentage of patients free of peritonitis per unit time:* target >80% per year.
- *Pre-PD peritonitis:* reported as episodes per year
- *Other:* medical cure, recurrent peritonitis, relapsing peritonitis, peritonitis-associated catheter removal, peritonitis-associated transfer to hemodialysis and peritonitis - associated hospitalization or death (occurring within 30 days of peritonitis onset).

The figure 2 summarizes the outcome-specific definitions following peritonitis.

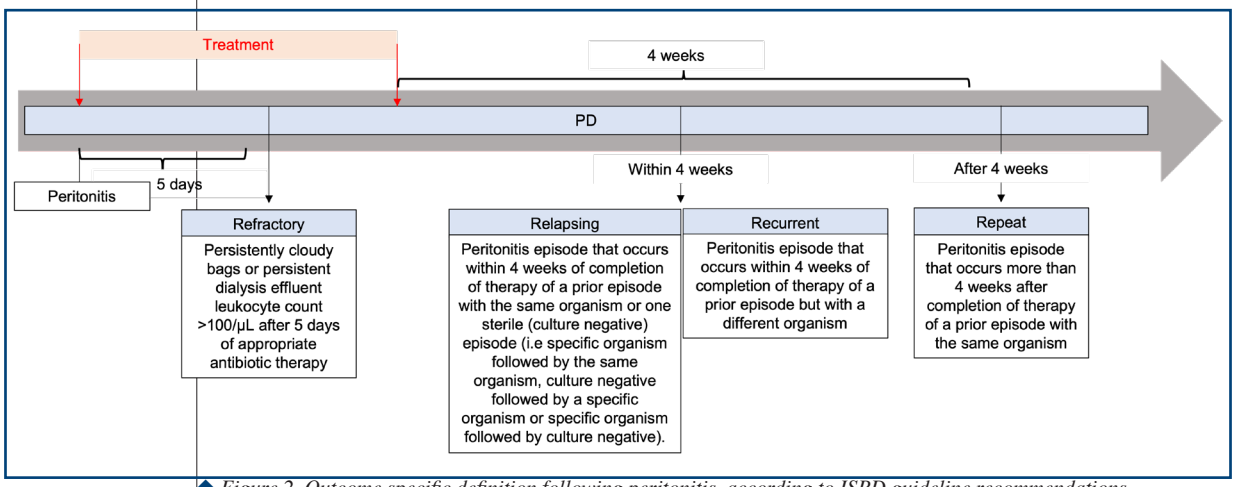

Figure 2. Outcome specific definition following peritonitis, according to ISPD guideline recommendations

PREVENTION OF PERITONITIS

The table 1 summarizes ISPD recommendations with respect to the prevention of peritonitis.

Catheter placement: systemic prophylactic antibiotics should be administered immediately prior to catheter placement. The choice of antibiotic should be determined after considering the local spectrum of antibiotic resistance. There is no data regarding the effectiveness of routine screening and eradication of *S. aureus* nasal carriage before catheter insertion.

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www.bdd.rdplf.org Volume 5, n° 2, June 2022
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Prevention of peritonitis
Catheter placement: Prophylactic antibiotics prior to catheter placement No data regarding the effectiveness of screening and eradication of S. aureus nasal carriage before catheter insertion.
Exit site care: Topical application of antibiotic Proper PD catheter immobilization Prompt treatment of exit-site or catheter tunnel infection
Contamination of PD system: Prophylactic antibiotic Change of a sterile transfer set PD effluent culture Close monitoring
Invasive gastrointestinal and gynecological procedures: Prophylactic antibiotics prior to colonoscopy and invasive gynecological procedure. The abdomen should preferably be empty before the procedure.
Training program: reassessment of PD exchange technique and knowledge, and direct inspection of practice of PD technique. Consider : Home visit by PD nurses, retraining (e.g. following prolonged hospitalization, peritonitis and/or catheter infection, change in dexterity, vision or mental acuity, etc.)
Domestic pet and zoonotic infection: Avoid pet in the same room where PD exchanges are taking place and equipment are stored.
Other modifiable risk factors: Treatment of hypokalemia (higher risk of enteric peritonitis) Avoiding or limiting the use of histamine-2 receptors inhibitors. Constipation prevention (regular lactulose use is associated with a lower rate of peritonitis).
Secondary prevention: Anti-fungal prophylaxis (either oral nystatin or fluconazole) is recommended after an antibiotic course (regardless of the indication), in order to prevent fungal peritonitis. Oral Nystatin (500,000 U qid during ATB course)

Table I. Prevention of peritonitis according to the ISPD peritonitis guideline recommendations

Exit-site care: topical antibiotic cream on the PD catheter exit site is recommended. Also, proper PD catheter immobilization may be useful, and rapid treatment of exit-site or catheter tunnel infection is mandatory to prevent peritonitis.

Contamination of PD system: Dry contamination should be distinguished from wet contamination (contamination occurring before dialysis fluid infusion or if the catheter administration set has been left open for an extended period). Prophylactic antibiotic is recommended for wet contamination (Fig. 3). Also, advice from the treatment team is recommended if contamination during PD exchange is noted.

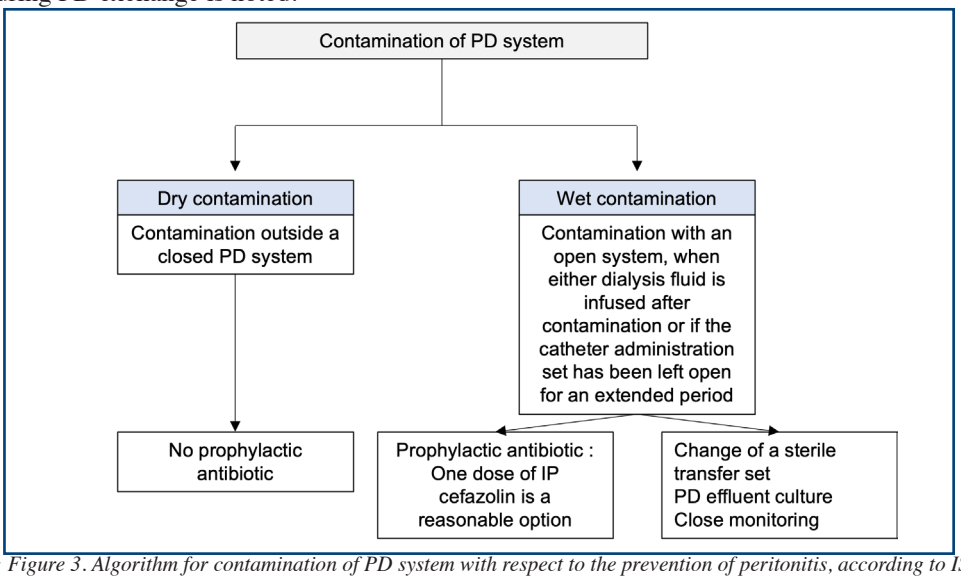

Figure 3. Algorithm for contamination of PD system with respect to the prevention of peritonitis, according to ISPD guideline recommendations

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Invasive gastrointestinal and gynecological procedures: antibiotic prophylaxis prior to colonoscopy and invasive gynecological procedure is recommended, however there is no recommendation of antibiotic choice and administration route, but the latter should cover gram-positive and gram-negative bacteria. The abdomen should preferably be empty before the procedure. There is insufficient evidence to recommend antibiotic prophylaxis prior to gastroscopy, however some data showed a lower rate of peritonitis when antibiotics were used within 7 days of gastroscopy.

Training program: PD exchange technique should be regularly reassessed and updated. Direct inspection of the practice technique is of particular interest. There are no recommendations regarding the optimal PD training program. Flexibility should be allowed to deliver training according to local resources (distance learning, remote monitoring, video materials can be used). Home visit by PD nurses can be useful to detect risk factors for peritonitis. Retraining can therefore be proposed, however optimal timing is uncertain. Indications of retraining are listed in the updated 2022 ISPD guidelines on prevention and treatment of peritonitis.

Domestic pet and zoonotic infection: Avoid pets in the same room where PD exchanges are taking place and equipment is stored. Diagnosis of unusual organisms suspicious of zoonoses should raise suspicion for no-observance of the latter recommendation.

Other modifiable risk factors: treatment of hypokalemia and avoiding or limiting the use of histamine-2 receptors inhibitors are recommended. The regular use of lactulose is associated with a lower rate of peritonitis.

Secondary prevention: Anti-fungal prophylaxis (either oral nystatin or fluconazole) is recommended after an antibiotic course (regardless of the indication), in order to prevent fungal peritonitis.

INITIAL PRESENTATION AND MANAGEMENT OF PERITONITIS

Peritonitis should be diagnosed when at least two of the following criteria are present: (1) Consistent clinical features (cloudy effluent, abdominal pain etc.), (2) Effluent white cells count: > 100/μl and > 50% of neutrophils in a dwell of at least 2 hours and (3) Positive dialysis effluent culture.

White blood cells count depends on the length of the dwell.

The presence of a cloudy effluent should be considered as a peritonitis until the diagnosis is confirmed or excluded. However differential diagnosis of cloudy effluent should be assessed.

Initial workup should include cell count, differential count, gram stain and effluent culture, culture of any discharge of the exit site and blood culture if the patient is septic or on immuno-suppression. Tunnel infection / collection should also be assessed.

IDENTIFICATION OF CAUSATIVE ORGANISMS

Identification of the causative organism is of importance in order to guide adequately the

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choice of antibiotics. Culture-negative peritonitis rate should be less than 15%. Sampling and culture methods should be reviewed if the latter rate is superior to 15%. Gram staining is recommended even if often negative. Blood culture bottles should be preferred for PD effluent culture. Centrifugation of the PD fluid and culturing of the pellet and lysis centrifugation can also be considered. If PD effluent culture is negative after 3-5 days, cell count, differential count, fungal and mycobacterial cultures should be performed. Other diagnostic techniques are under evaluation but are not routinely used and have not been shown to be superior to conventional techniques.

EMPIRIC ANTIBIOTIC SELECTION

Antibiotics should be started as soon as possible since the contact-to-treatment time is associated with treatment failure. If IP route is not possible (for example in the emergency department), IV route should be used initially in order to avoid adverse outcome. A switch to IP route is recommended as soon as possible. Treatment should cover gram-positive and gram-negative germs. First-generation cephalosporin (or vancomycin in centers with high prevalence of methicillin-resistant organisms, with uncertain threshold) is usually associated with a third-generation cephalosporin or aminoglycoside. Monotherapy with fourth generation cephalosporin (i.e. cefepime) can be an option. Adjuvant treatments such as IP heparin, antalgics should be considered.

DOSAGE OF ANTIBIOTICS

IP route should be preferred. Detailed IP and systemic antibiotics dosing recommendations for treatment of peritonitis are presented in the ISPD guidelines. When an aminoglycoside is chosen, it should be administered on a daily intermittent basis and prolonged course should be avoided. Oral N-acetylcysteine may be administered to prevent ototoxicity. For vancomycin treatment, whether to prefer fixed dosing or target-guided dosing according to serum trough level is not clear.

ANTIBIOTIC DELIVERY AND STABILITY

Detailed stability and compatibility of antibiotics in PD solutions are summarized in the ISPD guidelines. Stability of an antibiotic can vary according to the PD solution injected (dextrose-based or icodextrin-based), but also, the temperature of preservation (room temperature or refrigerated temperature), or other medication such as heparin are added to the mixture. For example, gentamicin's stability is reduced by admixture with heparin, vancomycin's stability is reduced when preserved at ambient temperature, and its stability is higher in dextrose-based compared to icodextrin-based solution.

SPECIAL CONSIDERATION FOR APD

APD is characterized by a greater peritoneal antibiotic clearance and therefore a potential underdosing. In order to achieve adequate bioavailability a minimal dwell time of 4 hour should be respected, however dwelling for 6 hours may be a better option.

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www.bdd.rdplf.org Volume 5, n° 2, June 2022
https://doi.org/10.25796/bdd.v5i2.66753
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ADJUNCTIVE TREATMENTS

In order to prevent fibrin occlusion of the PD catheter, patients with cloudy effluent could benefit from IP heparin. Analgesics should also be considered depending on symptoms.

Before IP antibiotics, peritoneal lavage (one or two rapid PD exchanges) can be proposed for pain control, however it should not be performed for improving peritoneal cure or prevent relapses.

IP urokinase with oral rifampicin may be useful for PD catheter salvage in case of coagulase-negative *staphylococcus* peritonitis, however urokinase has shown no benefit in terms of relapse or refractory peritonitis.

Peritonitis is also associated with increased glucose reabsorption and protein loss that could cause reduced ultrafiltration and lead to volume overload; this should be managed actively with such measures as temporary use of icodextrin.

SUBSEQUENT MANAGEMENT OF PERITONITIS

Antibiotics should be adjusted to the sensitivity when the latter is identified. *Staphylococcus aureus* peritonitis should be treated for 21days. *Streptococcus*, as well as other gram-positive organisms peritonitis should be treated for 14 days.

Refractory peritonitis: Catheter removal is indicated, however longer antibiotic treatment without catheter removal can be an option if the effluent white cell count is decreasing. This approach should be guided by the virulence of the cultured organism. In case of catheter removal, antibiotics should be continued for 14 days after the procedure.

Relapsing, recurrent and repeat peritonitis: catheter removal is indicated, with concomitant catheter reinsertion. This should be performed after culture has become negative and the white cell count is below 100/mL, in the absence of concomitant exit site or tunnel infection. In case of catheter removal, antibiotics should be continued for 14 days after the procedure. A prolonged course of antibiotic is not recommended to prevent the risk of relapsing, recurrent or repeat peritonitis. Prolonged antibiotic is associated with repeat and fungal peritonitis.

COAGULASE-NEGATIVE *STAPHYLOCOCCUS* PERITONITIS

Coagulase-negative staphylococcus (e.g. staphylococcus epidermidis) peritonitis should be treated for 14 days, with IP cephalosporin or vancomycin, according to susceptibility. The prevalence of methicillin resistance is increasing over the past years; therefore, vancomycin is a valid empirical option in *coagulase-negative staphylococcus peritonitis*.

Patient's technique should be reassessed, and retraining proposed to patients.

Since the latter peritonitis is associated with a higher risk of refractory and repeat peritonitis, due to the colonization of the PD catheter with biofilm, removal of the PD catheter with simultaneous reinsertion should be considered in these cases. However, effluent must be clear, and culture must be negative, and the procedure must be performed under antibiotic coverage.

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Intraluminal use of urokinase 100,000 IU for 2 h and oral rifampicin 600 mg daily for 3 weeks can be an option.

STAPHYLOCOCCUS AUREUS PERITONITIS

Staphylococcus aureus peritonitis should be treated for 21 days with a first-generation cephalosporin or vancomycin in cases of methicillin resistance. Rifampicin treatment for 5 to 7 days may be an option in order to reduce relapse or repeat peritonitis and in case of unfavorable evolution, IP daptomycin with or without oral rifampicin can be used as salvage therapy. Also, catheter removal should be considered in case of associated tunnel or exit-site infection.

STREPTOCOCCAL PERITONITIS

The latter peritonitis should be treated for 14 days, with usually a good response to treatment, however *viridans* streptococcal peritonitis is associated with a higher risk of relapse.

CORYNEBACTERIUM PERITONITIS

Corynebacterium peritonitis should be treated for 14 days. In case of beta-lactam resistance, vancomycin should be used. In case of repeat peritonitis, a 21-day course of vancomycin can be an option. Vancomycin should be used for peritonitis associated with *Corynebacterium jeikeium* and *Corynebacterium striatum* because of their resistance to beta-lactams. Also, catheter removal should be considered in case of associated tunnel or exit-site infection.

ENTEROCOCCUS PERITONITIS

Enterococcus peritonitis should be treated for 21 days with oral amoxicillin or IP vancomycin, depending on the local prevalence of ampicillin resistance. Vancomycin use is a risk factor for vancomycin-resistant *Enterococcus* (VRE) colonization. VRE peritonitis should be treated with oral or intravenous linezolid or IP daptomycin, or teicoplanin if susceptibility is confirmed.

Enterococcus can be associated with other microorganisms in the setting of polymicrobial peritonitis which worsens the prognosis. In case of polymicrobial peritonitis or *enterococcus faecium*, oral amoxicillin is not recommended.

PSEUDOMONAS PERITONITIS

Pseudomonas peritonitis should be treated for 21 days with two antibiotics but is often associated with the need of catheter removal. Catheter removal is recommended in case of associated tunnel or exit-site infection, but also in case of insufficient clinical response after 5 days of adequate treatment. Early removal of the PD catheter improves the chance of returning to PD.

ACINETOBACTER PERITONITIS

Acinetobacter peritonitis should be treated for 21 days. Treatment options are broad spectrum cephalosporin, a combination beta-lactam/beta-lactamase inhibitor or a carbapenem (except ertapenem). Treatment should be adapted according to local susceptibility. In case of carbapenem

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www.bdd.rdplf.org Volume 5, n° 2, June 2022
https://doi.org/10.25796/bdd.v5i2.66753
ISSN 2607-9917

resistance, the use of an aminoglycoside and a sulbactam-containing agent is recommended.

STENOTROPHOMONAS MALTOPHILIA PERITONITIS

Stenotrophomonas peritonitis should be treated for 21 days with two antibiotics including trimethoprim–sulfamethoxazole.

ENTERIC GRAM-NEGATIVE BACTERIA PERITONITIS

Enteric gram-negative bacteria peritonitis should be treated for 21 days.

POLYMICROBIAL PERITONITIS

Polymicrobial peritonitis should be treated for 21 days, based on sensitivities.

In case of multiple gram-negative or mixed gram-positive and negative peritonitis, gastrointestinal pathology should be suspected. In case of hemodynamic instability, computed tomographic (CT) scan may help to identify a surgical cause of peritonitis. Assessment by a surgeon is needed. If the latter cause of peritonitis is suspected, the antibiotics of choice are metronidazole plus vancomycin, in combination with ceftazidime or an aminoglycoside.

In case of multiple gram-positive peritonitis, contamination of the PD system or PD catheter infection should be considered. Catheter removal should be considered in case of associated tunnel or exit-site infection. Conservative management without catheter removal, with antibiotic therapy may be an option.

FUNGAL PERITONITIS

Immediate catheter removal is recommended followed by appropriate antifungal agent for at least 14 days.

Treatment options are oral or IP fluconazole (oral route is preferred), IV echinocandins or oral voriconazole, depending on the pathogen. Amphotericin B should be considered for *Aspergillus* peritonitis.

CULTURE-NEGATIVE PERITONITIS

Culture-negative peritonitis should be treated for 14 days.

If PD effluent culture is still negative after 3 days, cell count and differential count should be repeated, and special culture (i.e. *mycobacteria, nocardia, fungus* etc.) can be performed, especially in the absence of clinical improvement. Antibiotic should not be adapted according to recent exit-site culture.

In case of clinical improvement, peritonitis is probably caused by gram-positive organisms, therefore antibiotic covering gram-negative organisms can be discontinued.

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https://doi.org/10.25796/bdd.v5i2.66753
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After 5 days, in the absence of clinical improvement and persistence of negative culture despite special cultures, catheter removal should be considered, and antibiotic should be continued for at least 14 days after the procedure.

If PD effluent cultures are positive after repeated or special cultures, antibiotic should be adapted to sensitivity.

TUBERCULOUS PERITONITIS

Early diagnosis is crucial for tuberculous peritonitis. Oral anti-tuberculous therapy is recommended, without PD catheter removal. Drug dosing recommendations for treatment of tuberculous peritonitis are presented in the ISPD guidelines.

NON-TUBERCULOUS MYCOBACTERIAL PERITONITIS

Non-tuberculous mycobacterial peritonitis should be treated for at least 6 weeks, with two agents and based on sensitivities. In cases of suspected non-tuberculous mycobacterial peritonitis (e.g.persistent culture-negative peritonitis), Ziehl–Neelsen staining for acid-fast bacilli should be performed. Effective antibiotics and catheter removal is recommended for the treatment of the latter peritonitis.

CONFLICT OF INTEREST

The authors declare no conflict of interest for this article.

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