Intraperitoneal Antibiotic Administration Guidelines
Sharp Healthcare
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Purpose

- To establish a standardized approach for empiric antibiotic treatment in peritoneal dialysis patients.

Background

- Peritoneal dialysis (PD)-associated peritonitis is the most common type of PD-related infection and is associated with increased healthcare utilization, treatment costs, and adverse outcomes. The treatment of such infections is important in reducing patient morbidity and mortality.

Empiric Antibiotic Therapy

- **Initial Treatment**: Start broad-spectrum antibiotics to cover both gram positive and gram-negative organisms (common pathogens: *Staphylococcus aureus*, coagulase-negative staphylococci, and gram-negative bacteria)
    - Preferred empiric regimen at Sharp Healthcare: vancomycin + aminoglycoside (tobramycin preferred if high suspicion for *Pseudomonas aeruginosa* infection)
    - Monotherapy with cefepime has been shown to be as effective as combination cefazolin and ceftazidime therapy[1-2]
    - Other regimens may be appropriate depending on the patient's culture history

Antibiotic Administration

- Current guidelines recommend that intraperitoneal (IP) antibiotics be the preferred route of administration, due to higher drug exposure at the site of infection, unless there are signs and symptoms of systemic sepsis or a foreseeable delay in IP administration. If there are signs of sepsis or an anticipated delay in IP administration, IV is the preferred route.[3]
    - For patients with both IV and IP antibiotic orders, the pharmacist should clarify with the prescribing physician on the appropriate route for the patient's clinical scenario to avoid duplication, supra-therapeutic levels, and increased risk for toxicity.
- Intraperitoneal antibiotics should be allowed to dwell for at least 6 hours.
- Daily intermittent dosing of antibiotics is generally preferred, especially for Vancomycin and aminoglycosides, due to the risk of accumulation and toxicity. Ceftazidime given intermittently may result in a higher production of pyridine byproduct than with continuous dosing, although clinical impact unclear (may be used at physician's discretion). [4-5]
- Antibiotics administered via IP route will be added to the dialysate bag(s) in the pharmacy cleanroom prior to the initiation of peritoneal dialysis.

- Pharmacists should check for compatibility of the antibiotic combinations to be sure they can all be added to the same dialysate bag together (see Table 1 for commonly administered antibiotic combinations)
- After antibiotics are added, do not use dialysate bags beyond 24 hours to ensure adequate concentration levels throughout the dosing interval

Antibiotic Dosing

- Please refer to Table 2 below for antibiotic dosing recommendations for both intermittent and continuous modalities
- To verify the dose that is added to the dialysate bag, pharmacists should check the following:
  - Patient weight
  - Size and type of the dialysate bag
  - Exchange rate and duration
  - If patient will require a dwell with last exchange (for intermittent dosing)
  - Presence of residual renal function/urine output
    - For patients with residual renal function (i.e. CrCl >10 ml/min), may consider increasing beta-lactam dose by 25% (pharmacist to discuss dosing recommendation with provider)

Monitoring and Adjustment

- Monitor clinical response and peritoneal fluid culture results.
- Modify antibiotics based on culture results and sensitivity patterns.

Table 1. Compatibility of common antibiotic combinations given intraperitoneally (assumes 2L dialysate volume)[6]

Antibiotic combination	Dianeal	Extraneal
Cefazolin + Gentamicin/Tobramycin	Y	Y
Cefazolin + Ceftazidime	Y	Y
Vancomycin + Gentamicin/Tobramycin	Y	Y
Vancomycin + Ceftazidime	Y	Y

Table 2. Intraperitoneal Antibiotic Dosing Recommendations for Treatment of Peritonitis[a]

Drug	Intermittent[b] (dosed per exchange, give once daily unless specified)	Continuous[c] (dosed per mg/mL, give in all exchanges)
Cefazolin	15 mg/kg	LD 500 mg/L, MD 125 mg/L
Cefepime	1 g	LD 500 mg/L, MD 125 mg/L
Ceftazidime[d]	1 to 1.5 g	LD 500 mg/L, MD 125 mg/L
Gentamicin	0.6 mg/kg	Not advised
Meropenem	500 mg	MD 125 mg/L
Tobramycin[e]	0.6 mg/kg	Not advised
Vancomycin[e,f]	15-30 mg/kg q5-7 days for CAPD	LD 20–25 mg/kg, MD 25 mg/L

	15 mg/kg q4 days for APD	

[a] For patients with residual renal function, defined as CrCl >10 ml/min, consider increasing beta-lactam dose by 25%

[b] Intermittent dosing: Intraperitoneal antibiotics given once daily. Antibiotic-containing peritoneal dialysate should be allowed to **dwell for at least 6 hours** to allow adequate absorption

[c] Continuous dosing: Intraperitoneal antibiotics given in each exchange. Dosed by mg per L of dialysate (unless otherwise specified)

[d] Ceftazidime given intermittently may result in a higher production of pyridine byproduct than with continuous dosing, although clinical impact unclear (may be used at physician's discretion).

[e] Monitor serum levels to ensure drug is not accumulating and contributing to toxicity

[f] AUTOMATED PERITONEAL DIALYSIS patients may require supplemental doses

References:

1. Kitrungphaiboon T, et al. Intraperitoneal Cefepime Monotherapy Versus Combination Therapy of Cefazolin Plus Ceftazidime for Empirical Treatment of CAPD-Associated Peritonitis: A Multicenter, Open-Label, Noninferiority, Randomized, Controlled Trial. Am J Kidney Dis. 2019 Nov;74(5):601-609
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3. Li PK-T, Chow KM, Cho Y, et al. ISPD peritonitis guideline recommendations: 2022 update on prevention and treatment. *Peritoneal Dialysis International*. 2022;42(2):110-153
4. Kaur H, Harmanjeet H, Wanandy T, Castelino RL, Sud K, Jose MD, Peterson GM, Patel RP. High Pyridine Generation in Ceftazidime-Icodextrin Admixtures Used to Treat Peritoneal Dialysis-associated Peritonitis. Clin Ther. 2019 Nov;41(11):2446-2451
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