NM Delnor Hospital
Intra-Peritoneal Antibiotic Guideline
August 2022

Background[1]

Patients on peritoneal dialysis commonly develop peritonitis. When this occurs, data show potentially better outcomes if the infection is treated intra-peritoneally instead of systemically unless the patient is septic.

Antibiotic Administration[1]

A. Initial empiric antibiotics should cover both gram-positive and gram-negative organisms. Initial regimens appropriate at NM Delnor Hospital include:
   - Cefazolin plus gentamicin
   - Vancomycin plus gentamicin
   - Ceftriaxone, cefepime, or aztreonam may be used as an alternative to gentamicin for gram-negative coverage if the patient cannot receive aminoglycosides due to allergy (cefepime or aztreonam if *Pseudomonal* coverage desired)
   - Other regimens may be appropriate depending on the patient's culture history

B. Antibiotics instilled intra-peritoneally should be allowed to dwell at least 6 hours
C. Daily intermittent dosing of the antibiotics is preferred, particularly for vancomycin and gentamicin
D. Recent studies suggest that dose adjustment of the antibiotic in patients who have substantial residual renal function is not necessary
E. Antibiotics to be administered intra-peritoneally will be added to the dialysate bag(s) in the cleanroom within the pharmacy prior to initiation of the peritoneal dialysis.
   a. It is necessary to verify stability of the antibiotic combination to be sure they can all be added to the same dialysate bag together.
   b. In general, it is considered safe to combine vancomycin and gentamicin or cephalosporins in the same bag (but not necessarily in a concentrated syringe).

Antibiotic Dosing[1]

The following table is from the most recent Peritonitis Guideline from 2022. It outlines recommended dosing for both intermittent and continuous dosing of many antibiotics. Information that will be needed prior to determining the dose to be added to the dialysate bags includes:

- Patient weight (use recommended dosing weight per selected antibiotic)
- The size of the dialysate bags to be used (easier if they plan to use one size for all exchanges if doing continuous)
- Exchange rate and duration
- Presence of residual renal function (if still present, consider increasing dose for renally cleared drugs[3])

<u>Intermittent Antibiotic Dosing</u>
Intermittent dosing is preferred for vancomycin and aminoglycosides. For simplicity and standardization, we will recommend intermittent dosing for all antibiotics when possible.

- Verify with the ordering physician that intermittent dosing is ok (if continuous ordered)
- Antibiotic will be added to the last bag of the dialysis session and will dwell for the specified time per the physician. ("Last Bag Fill")

- As noted previously, a minimum dwell time of 6 hours will be necessary for adequate antibiotic exchange

- Will need to verify bag size and type of dialysate
  - Usual bag size for 'last bag fill' is 2L
- Calculate dose of each antibiotic based on the "Intermittent" column in the table below

Continuous Antibiotic Dosing

Some physicians prefer continuous antibiotic dosing. This requires more antibiotic compounding, but less overall manipulation of the access site. Continuous dosing is a recommended option for cephalosporin administration (although intermittent is also recommended). The recommended concentration below will be added to each of the dialysate bags prior to initiation of dialysis and will be run overnight during the entire exchange. Six liter dialysate bags are usually used for the overnight exchanges. If a loading dose is required, it would be placed in the first exchange bag(s), followed by the maintenance dose in all subsequent bags (separate entries in Epic).

Table 5. IP antibiotic dosing recommendations for treatment of peritonitis.

Antibiotic	Intermittent (1 exchange daily for at least 6 h)	Continuous (all exchanges)
Aminoglycosides		
Amikacin	2 mg/kg daily[173]	Not advised
Gentamicin	0.6 mg/kg daily[174,175]	Not advised
Netilmicin	0.6 mg/kg daily[165]	Not advised
Tobramycin	0.6 mg/kg daily	Not advised
Cephalosporins		
Cefazolin	15 mg/kg daily (for long dwell)[176,177] 20 mg/kg daily (for short dwell)[178,176]	LD 500 mg/L, MD 125 mg/L[d 168,179]
Cefepime	1000 mg daily	LD 500 mg/L, MD 125 mg/L[d 168]
Cefoperazone	No data	LD 500 mg/L, MD 62.5–125 mg/L[180]
Cefotaxime	500–1000 mg daily[181]	no data
Ceftazidime	1000–1500 mg daily (for long dwell) 20 mg/kg daily (for short dwell)[178]	LD 500 mg/L, MD 125 mg/L[d 168,182]
Ceftriaxone	1000 mg daily[183]	No data
Penicillins		
Penicillin G	No data	LD 50,000 unit/L, MD 25,000 unit/L[13]
Amoxicillin	No data	MD 150 mg/L[184]
Ampicillin[a]	4 gm daily[185]	MD 125 mg/L[186]
Ampicillin/ sulbactam		LD 1000 mg/500 mg, MD 133.3 mg/66.7 mg[187,188]
Piperacillin/ tazobactam	No data	LD 4 gm/0.5 gm, MD 1 gm/0.125 gm[189]
Ticarcillin/clavulanic acid	No data	LD 3 gm/0.2 gm, MD 300 mg/20 mg/L[190]
Others		
Aztreonam	2 gm daily[191]	LD 500 mg/L[192], MD 250 mg/L[192,193]
Ciprofloxacin	No data	MD 50 mg/L[194]
Clindamycin	No data	MD 600 mg/bag[195]
Daptomycin	300 mg daily[196]	LD 100 mg/L[197,198,199], MD 20 mg/L[197,200]
Fosfomycin	4 g daily[201,202]	No data
Imipenem/cilastatin	500 mg in alternate exchange[203]	LD 250 mg/L, MD 50 mg/L[182]
Ofloxacin	No data	LD 200 mg, MD 25 mg/L[204]
Polymyxin B	No data	MD 300,000 unit (30 mg)/bag[188]
Quinupristin/ dalfopristin	25 mg/L in alternate exchanges[b205]	No data
Meropenem	500 mg daily (for long dwell in APD)[207] 1000 mg daily (for short dwell in CAPD)[208,209]	MD 125 mg/L[206]
Teicoplanin	15 mg/kg every 5 days[210]	LD 400 mg/bag, MD 20 mg/L[211,140]
Vancomycin	15–30 mg/kg every 5–7 days[c141,212] for CAPD 15 mg/kg every 4 days[213] for APD	LD 20–25 mg/kg, MD 25 mg/L[214]
Antifungal		
Fluconazole	IP 150–200 mg every 24 to 48 h[215,216] (oral route is preferred: see Table 6)	No data
Voriconazole	IP 2.5 mg/kg daily[217] (oral route is preferred: see Table 6)	No data

LD: loading dose in mg; MD: maintenance dose in mg; IP: intraperitoneal; APD: automated peritoneal dialysis.
[a]IP ampicillin is not recommended for treatment of enterococcal peritonitis.[218]
[b]Given in conjunction with 500 mg intravenous twice daily.
[c]Supplemental doses may be needed for APD patients and dwell time of at least 6 h is preferred.
[d]Increase in doses by 25% may be needed for patients with significant residual kidney function.[168]

Monitoring of Vancomycin and Gentamicin[1,2]

Vancomycin[1]

About 90% of intra-peritoneal vancomycin is absorbed in the presence of peritonitis. It is unclear whether monitoring levels for vancomycin is useful from an efficacy perspective, however, due to the potential toxicities of excessive vancomycin, monitoring from a safety perspective will be necessary. The amount of vancomycin that is anticipated to be cleared by peritoneal dialysis varies. Of note, treatment failure may be more likely in patients with residual renal function due to increased vancomycin clearance. It therefore may be necessary to be more aggressive in the dosing for these patients.[3]

Here are some general recommendations to follow for vancomycin monitoring:

Intermittent Dosing

- For intermittent exchanges, it is expected that re-dosing every 4 to 5 days will be needed
- Check a random level (preferably at least 4 hours after the last exchange is complete)
    - About every 4-5 days post-dose for intermittent (depending on prior levels and patient-specific factors)
    - Consider redosing when vancomycin level is ≤15mcg/mL

Continuous Dosing

- For continuous exchanges, an initial load of 15-20mg/kg of vancomycin should be given in the first bag
    - Follow by a maintenance dose of 15mg/L of fluid added to each remaining dialysate bag to maintain the systemic level at 15mcg/mL
- Check random level about every 3-4 days for continuous dosing depending on patient (less frequent once stable levels achieved)

Gentamicin[2]

With the recommended dosing regimen, about 50% of patients may still be exposed to excessive systemic gentamicin levels. Little evidence exists to support monitoring of levels to mitigate toxicity or improve efficacy, however. Due to the risk of ototoxicity and further renal damage, it is recommended that therapy be changed to target the organisms present as soon as identification and susceptibilities are known. Of note, treatment failure may be more likely in patients with residual renal function due to increased gentamicin clearance. It therefore may be necessary to be more aggressive in the dosing for these patients (doses up to 0.9 mg/kg have been used).[3]

Here are some general recommendations to follow for gentamicin monitoring in case of prolonged administration while awaiting culture data:

- Check a random gentamicin level (preferably at least 4 hours after last exchange complete) after 2nd day/round of treatment
- Redose gentamicin when 'trough' level is ≤0.5mcg/mL
- Recheck random levels daily and redose as above while therapy is continued
- Not recommended to continue longer than 5 days without ID consult

References

1. Li PKT, Szeto CC, Piraino B, et al. ISPD peritonitis recommendations: 2016 update on treatment and prevention. *Perit Dial Int* 2016; 36(5):481-508.
2. Tang W, Cho Y, Hawley C, et al. The role of monitoring gentamicin levels in patients with gram-negative peritoneal dialysis-associated peritonitis. *Perit Dial Int* 2014; 34(2):219-26.
3. Piraino B. Effective treatment of PD peritonitis. *Clin J Am Soc Nephrol* 2017; 12:1919-21.
4. Li PKT, Chow KM, Cho Y, et al. ISPD peritonitis guideline recommendations: 2022 update on prevention and treatment. *Perit Dial Int* 2022; 42(2):110-53. doi: 10.1177/08968608221080586.