



INFECTIOUS DISEASES

Etiology

- Infectious diseases are responsible for 15% of the mortality in hemodialysis patients
- Hemodialysis patients are more susceptible to infections due to the effect of uremic toxins, malnutrition and dialysis to:
 - impair phagocytosis and chemotaxis by polymorphonuclear leukocytes
 - depress natural killer cell activity
 - defect β and T lymphocyte function
 - impair the function of $FC\gamma$ receptors (found on macrophages, neutrophils, beta cells, killer cells and when these cells are triggered, they trigger phagocytosis. In uremia these receptors are impaired causing impaired phagocytosis.)
 - induce absolute lymphopenia
 - present an iron overload
- Additionally, all dialysis patients are at risk of infection due to the frequent vascular & peritoneal accesses.
- Dialysis patients early infections may go unnoticed as they often have lower basal temperatures resulting in “afebrile” readings and the other signs of infection may mimic uremic symptoms. Tuberculosis in renal patients is usually extrapulmonary and mimics symptoms of inadequate dialysis.
- Often dialysis patients are diabetic which independently presents greater risk of infection through reduced peripheral blood flow and peripheral neuropathy.
- Renal failure patients are at higher risk for antimicrobial adverse drug reactions due to accumulation (e.g. seizures with β Lactams) and antimicrobial resistance due to frequent exposure.

Hemodialysis concerns

- Hemodialysis access site infections are most commonly due to gram-positive skin organisms and treatment should be started as early as possible. The standard empiric therapy is Cefazolin intravenously during dialysis.
- Other IV and oral agents may be used when culture & sensitivity deem appropriate.

Peritoneal Dialysis Concerns – Peritonitis

- Peritoneal dialysis (PD) has been used since the 1940’s. Peritonitis, while still the major complication of PD, has been greatly reduced due collapsible disposable bags, and improved catheter design & material. Sterile technique accounts for the disparate infection rate between patients which has been reported as 1 case per 15 months on PD or a 60-70% risk in the first year. Recurrent peritonitis is a common reason for discontinuing PD.
- Most peritonitis is caused by skin pathogens contaminating the catheter. Nasal carriers of staph. aureus encounter peritonitis more frequently. Enteric pathogens may be involved due to:
 - transmural migration through the intact intestinal wall due to hypertonic dialysate
 - catheter perforation of the intestine leading to polymicrobial infections
 - blood born pathogens entering the peritoneum
 - migration of organisms from the female genital tract

- Gram positive organisms (Staph. epi, Staph aureus & Strept) account for 60-80% of pathogens. Gram negatives including E. coli, Klebsiella & Psuedomonas account for 15-30% of pathogens. Prognosis is favourable if treated. Treatment is with intraperitoneal antibiotics as the intravenous route offers no therapeutic advantage.
- Signs and symptoms of peritonitis include a cloudy dialysate, abdominal pain & tenderness (in 60-80% of cases), nausea & vomiting (30%), fever (10-20%) & diarrhea (10%).
- Prognosis is favourable if treated. Treatment is with intraperitoneal antibiotics as the intravenous route offers no therapeutic advantage. Often, an initial dose is given as a load. Then smaller “top-up” doses are given to maintain concentrations above the mean inhibitory concentration (MIC) for most of the dosing interval. Removal of the catheter may be necessary.
- **http://www.ispd.org** lists the most recent antimicrobial recommendations.

PERITONITIS GUIDELINES

- Initial empiric therapy: Cefazolin 500 mg/l dialysate loading dose, then 125 mg/l dialysate with each exchange intraperitoneally and
Gentamicin 0.6 mg/kg intraperitoneally (IP) once daily
- If a Gram positive organism is cultured,
 - Enterococci: stop Cefazolin, continue Gentamycin, add Ampicillin 125 mg/l dialysate IP with each exchange for 14 days
 - S. Aureus: stop Gentamycin, continue Cefazolin, add Rifampin 600 mg daily orally for 21 days
 - S. Epidermidis: stop Gentamycin but continue Cefazolin x 14 days
- If a Gram negative organism is cultured,
 - Single organism: Adjust antibiotics according to sensitivity (usually third generation cephalosporin)
 - Multiple organisms/anaerobes: Add Metronidazole 500 mg IV/PO Q8H - continue therapy x 21 days
 - Pseudomonas: Usually Tobramycin 0.6 mg/kg IP daily x 21-28 days with an antipseudomonal antibiotic (Ceftazidime, Piperacillin, Ciprofloxacin, Imipenem, etc) - usually requires hospitalization.
- Culture negative after 2-3 days
 - If clinical improvement, stop Gentamycin but continue Cefazolin x 14 days.
 - If no improvement, repeat gram stain and adjust therapy. Treat for 14 days.
- Note: In British Columbia, the antibiotics listed above are the most commonly used. Other agents may also be used. Please refer to the **http://www.ispd.org** for a complete list of antibiotics used to treat peritonitis.
- Patients may start their course of treatment in hospital and be discharged to complete their therapy at home.

Antimicrobial resistance

- Dialysis patients around the world were exposed frequently to Vancomycin in the recent past. This led to a disproportionate share in dialysis patients of Vancomycin resistant enterococci (VRE) as well as vancomycin & methicillin resistant Staphylococcus aureus. (VRMRSA).
- Recently new guidelines have limited the use of Vancomycin in dialysis patients empirically.
- Chronic carriers of MRSA are now identified and often prescribed Mupirocin intranasally BID x 5 days every four weeks or at the peritoneal dialysis exit site daily or Rifampin 300 mg BID x 5 days every 12 weeks.

Miscellaneous antimicrobials

Antifungal therapies

- Nystatin suspension or Clotrimazole lozenges are used for oral thrush; no dose adjustments are required.
- Fluconazole is used for severe candidiasis or fungal peritonitis; in hemodialysis patients, a loading dose followed by one recommended dose after each dialysis is given. In PD patients, a dose is usually administered every 1-2 days. May be administered intraperitoneally.

Acyclovir

- Acyclovir may be given for the usual indications but is important to remember that most antiviral agents are removed by hemodialysis and doses should be given after dialysis on dialysis days. On non-dialysis days, Acyclovir IV may be given every 24-48 hours. PD patients should be dosed at 2.5 mg/kg IV daily. Acyclovir po dosed BID-TID is acceptable for both dialysis populations.

Cotrimoxazole

- There are no established guidelines for dosing Co-trimoxazole in dialysis. Half dose supplementations after dialysis or adjusting the schedule to take the dose after dialysis are two methods used. Others simply prescribe a normal dose as it has a wide therapeutic window.
- For the treatment of urinary tract infections in dialysis patients, cotrimoxazole may be prescribed at full dose or half dose.

Antimicrobial dosing

- For patients with renal insufficiency, specific dosing recommendations are available in "Drug Prescribing in Renal Failure - Dosing Guides for Adults" from the American College of Physicians. This is a recommended reference for any pharmacy dispensing to renal patients.
- Many antimicrobials are eliminated by the kidneys and may require dosage reductions relative to the reduction in kidney function.
- Some antimicrobials require supplemental doses after each dialysis.
- Certain drugs should be avoided completely. Tetracyclines other than doxycycline have antianabolic effects and may cause an increase in blood urea nitrogen (BUN), potentiate

acidosis and increase phosphorous due to increased catabolism. Hence, tetracyclines other than doxycycline should be avoided.

Vaccinations

- All dialysis patients should have:
 - Pneumococcal vaccine every 5 years
 - H. influenzae vaccine annually (to be reviewed)
 - hepatitis B vaccine if titer is negative given as:
 - Engerix 40 mcg at 0,1,2 & 6 months
 - Recombivax 40 mcg at 0,1,6 months
- Renal patients tend to have a higher morbidity with these diseases. They may also become chronic carriers of hepatitis B and suffer a higher mortality rate.

Infectious Diseases: Useful References

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