Antimicrobial Renal Dosage Adjustment Guidelines

Principles of Antibiotic Dosing in Renal Failure

1. **Fill the tank first.** Consider a loading dose to attain therapeutic concentrations rapidly (i.e. vancomycin 25-30 mg/kg, piperacillin/tazobactam 4.5g over 30 min for first dose before starting extended infusion).

2. **Balance risk of “too much” vs “too little” antibiotic.** Most antibiotics have a wide therapeutic index. Risk of underdosing (resistance and failure to treat the infection) may not be apparent for several days.

3. **The more severe the infection, the more concerned one should be about underdosing antibiotics.** Critically ill patients have an increased volume of distribution, enhanced GFR due to sepsis and vasoactive drugs, and antimicrobial loss via bleeding or drains.

4. **Drug elimination is often less impaired in acute kidney injury.** Higher doses may be necessary.

5. **Renal function should be estimated by the Cockcroft-Gault equation for purposes of drug dosing.** Other equations may be more accurate for staging CKD but have not been evaluated for drug dosing.

   \[
   \text{CrCl} = \frac{(140 - \text{age}) \times \text{weight}}{(72 \times \text{Serum creatinine})} \times 0.85 \text{ if female}
   \]

6. **After the load, decrease the dose proportionally based on the degree of renal dysfunction, but think about where you started.** Example: cefepime 2g q8h for meningitis versus 1g q8h for other indications

7. **Most equations to estimate CrCl are inaccurate with changing renal function and the more rapid the change, the more “off” your estimate will be.** This should be considered when adjusting doses (risk vs benefit!).

8. **Either the dose or interval can be adjusted.** Adjusting the interval is often more convenient but concentration dependent drugs require a therapeutic “peak” concentration for maximal killing (i.e. 10 x MIC for tobramycin).

9. **Estimation of removal of drug by extracorporeal methods (dialysis, SLEDD, or continuous modalities) is dependent on many factors.** In most patients, antimicrobials should be dosed based on residual renal function and then any additional removal by hemodialysis should be supplemented after the procedure. Some drugs, including aminoglycosides, cefazolin, cefepime and vancomycin have been studied and shown to be effective with only post-dialysis dosing in patients on a normal schedule. In hospitalized patients, however, this may not be practical if the dialysis schedule may change as antibiotics may not be given.

10. **The initial chosen dose should only be considered an estimate.** Be flexible!

References:

2. Drug Prescribing in Renal Failure. Dosing Guidelines for Adults. Fifth Ed. 2007
4. Micromedex
5. Lexicomp