

Dose adjustment in renal disease

1. What are the main factors that influence drug dosing in renal disease?
2. Name and contrast the two methods for adjusting drug dose in renal disease.
3. What are the pharmacokinetic considerations in designing a dosing regimen? Why is dosing once a day for aminoglycosides recommended by many clinicians?
4. Protein binding of drugs is often affected by renal and hepatic disease. How are those changes accounted for in dose adjustment?
5. Drug clearance is often decreased 20–50% in many patients with congestive heart failure (CHF). Explain how it may affect drug disposition.

Learning Questions

1. The normal dosing schedule for a patient on tetracycline is 250 mg PO (peroral) every 6 hours. Suggest a dosage regimen for this patient when laboratory analysis shows his renal function to have deteriorated from a Cl_{Cr} of 90 to 20 mL/min.
2. A patient receiving antibiotic treatment is on dialysis. The flow rate of serum into the kidney machine is 50 mL/min. Assays shows that the concentration of drug entering the machine is 5 g/mL and the concentration of drug in the serum leaving the machine is 2.4 g/mL. The drug clearance for this patient is 10 mL/min. To what extent should the dose be increased if the average concentration of the antibiotic is to be maintained?
3. Glomerular filtration rate may be measured by either insulin clearance or creatinine clearance.
 - a. Why is creatinine or insulin clearance used to measure GFR?
 - b. Which clearance method, insulin or creatinine, gives a more accurate estimate of GFR? Why?
4. A uremic patient has a urine output of 1.8 L/24 hours and an average creatinine concentration of 2.2 mg/dL. What is the creatinine clearance? How would you adjust the dose of a drug normally given at 20 mg/kg every 6 hours in this patient (assume the urine creatinine concentration is 0.1 mg/mL and creatinine clearance is 100 mL/min)?
5. A patient on lincomycin at 600 mg every 12 hours intramuscular was found to have a creatinine clearance of 5 mL/min. Should the dose be adjusted? If so, (a) adjust the dose by keeping the dosing interval constant; (b) adjust the dosing interval and give the same dose; and (c) adjust both dosing interval and dose. What are the significant differences in the adjustment methods?
6. Using the method of Cockcroft and Gault, calculate the creatinine clearance for a woman (38 years old, 62 kg) whose serum creatinine is 1.8 mg/dL.
7. Would you adjust the dose of cephmandole, an antibiotic which is 98% excreted unchanged in the urine, for the patient in Question 6? Why?
8. What assumptions are usually made when adjusting a dosage regimen according to the creatinine clearance in a patient with renal failure?

9. The usual dose of gentamicin in patients with normal renal function is 1.0 mg/kg every 8 hours by multiple IV bolus injections. Using the nomogram method (), what dose of gentamicin would you recommend for a 55-year-old male patient weighing 72 kg with a creatinine clearance of 20 mL/min?

10. A single intravenous bolus injection (1 g) of an antibiotic was given to a male anephric patient (age 68, 75 kg). During the next 48 hours, the elimination half-life of the antibiotic was 16 hours. The patient was then placed on hemodialysis for 8 hours and the elimination half-life was reduced to 4 hours.

- a.** How much drug was eliminated by the end of the dialysis period?
- b.** Assuming the apparent volume of distribution of this antibiotic is 0.5 L/kg, what was the plasma drug concentration just before and just after dialysis?

11. There are several pharmacokinetic methods for adjustment of a drug dosage regimen for patients with uremic disease based on the serum creatinine concentration in that patient. From your knowledge of clinical pharmacokinetics, discuss the following questions.

- a.** What is the basis of these methods for the calculation of drug dosage regimens in uremic patients?
- b.** What is the validity of the assumptions on which these calculations are made?

12. After assessment of the uremic condition of the patient, the drug dosage regimen may be adjusted by one of two methods: **(a)** by keeping the dose constant and prolonging the dosage interval, or **(b)** by decreasing the dose and maintaining the dosage interval constant. Discuss the advantages and disadvantages of adjusting the dosage regimen using either method.