

DOSING DRUGS IN PATIENTS WITH RENAL INSUFFICIENCY

John Foxworth, PharmD

Clinical Pharmacology Section

Department of Medicine Noon Conference

February 26, 1997

"An exact science is dominated by the idea of approximation."

Bertrand Russell

VII. References

Pocket references

Drug Prescribing in Renal Failure. Bennett WM, Aronoff GR, et al. (eds). American College of Physicians, Philadelphia, PA, third ed. Available from American College of Physicians, Customer Service Center, 800-523-1546, etc. 2600. Recommended.

Handbook of Drug Use in Patients with Renal Disease. Brater DC. Improved Therapeutics, 3601 Ames Rd, Lancaster TX, 75134. 1st ed. 1982.

Other references

Creatinine Clearance

1. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron*. 1976;16:31-41.
2. Docktor WJ. Creatinine clearance. in *Applied Clinical Pharmacokinetics*. Mungall D (ed). Raven Press, New York NY. 1983.
3. Luke DR, Halstenson CE, et al. Validity of creatinine clearance estimates in the assessment of renal function. *Clin Pharmacol Ther*. 1990;48:503-8.
4. Greenblatt DJ, Ransil BJ, et al. Variability of 24-hour urinary creatinine excretion by normal subjects. *J Clin Pharmacol*. July, 1976. pp. 321-8.
5. Chrymko MM, Schentag JJ. Creatinine clearance predictions in acutely ill patients. *Amer J Hosp Pharm*. 1981;38:837-40.
6. Levey AS, Perrone RD, et al. Serum creatinine and renal function. *Ann Rev Med*. 1988;39:465-90.
7. Bjornsson TD. Use of serum creatinine concentrations to determine renal function. *Clin Pharmacokinetics*. 1979;4:200-22.
8. Clearance and renal excretion, in *Clinical Pharmacokinetics - Concepts and Applications*. Rowland M and Tozer TN (eds). Lea and Febiger, 1980 Philadelphia.
9. Platt DR, Gannon R. Creatinine clearance: Corrected versus uncorrected. *DICP, Ann Pharmacotherapy*. 1988;22:32-3.
10. Robert S, Zarowitz BJ. Is there a reliable index of glomerular filtration rate in critically ill patients? *DICP, Ann Pharmacotherapy*. 1991;25:169-78.
11. Sheiner LB, Beal SL. Some suggestions for measuring predictive performance. *J Pharmacokinetics and Biopharmaceutics*. 1981;9:503-12.

Dose Reduction Methods and Guidelines

1. See first reference under "pocket references" above.

Other references

1. Touchette MA, Slaughter RL. The effect of renal failure on hepatic drug clearance. *DICP, Ann Pharmacother*. 1991;25:1214-23.

2. Gibson T. Influence of renal disease on pharmacokinetics. In Evans WE, Schentag JJ, Jusko WJ (eds). Applied Pharmacokinetics: principles of therapeutic drug monitoring. Applied Therapeutics, Spokane, WA, 1986, 2nd ed.
3. Matzke GR, Keane WF. Drug dosing in patients with impaired renal function. In DiPiro JT, Talbert RL, et al (eds). Pharmacotherapy: A Pathophysiologic Approach. Elsevier, New York, NY. 1989, 1st ed.
4. Bakris GL, Talbert R. Drug dosing in patients with renal insufficiency. Postgrad Med. 1993;94:153-64.
5. Talbert RL. Drug dosing in renal insufficiency. J Clin Pharmacol. 1994;34:99-110.
6. Swan SK, Bennett WM. Drug dosing guidelines in patients with renal failure. West J Med. 1992;156:633-8.
7. Ducharme MP, Smythe M, et al. Drug-induced alterations in serum creatinine concentrations. Ann Pharmacother. 1993;27:622-33.

Full handout available on request from jfoxworth@pop.umkc.edu

CASES

1. A male patient presents with a temperature of 101.5 , and other physical signs and symptoms of a complicated urinary tract infection. The patient was recently hospitalized, and as part of his evaluation, a twenty-four hour urine collection for creatinine clearance was obtained. Presently, as the supervising resident, you recommend gentamicin and ampicillin as initial treatment for this patient's infection. Evaluation of the recent discharge summary (which you are able to locate) reveal these data pertaining to renal function: Twenty-four hour urine collection, total urine creatinine 1365 mg, and concurrent serum creatinine 1.2 mg/dL. The patient weighs 77 kg, is six feet in height, and is 40 years of age. A repeat serum creatinine in the ER is also 1.2 mg/dL.
 - A. Is the twenty-four hour urine collection adequate?
 - B. Calculate the creatinine clearance from the collection data provided.
 - C. "Estimate" the creatinine clearance from the serum creatinine.
 - D. Correct the estimate for 1.73 m² (72 kg).
 - E. If the collection clearance and the "estimate" are different, which would you accept as valid and why?

2. A patient with a long history of seizure disorder (grand mal), hypertension, and end stage renal disease (recent measured creatinine clearance was 10 ml/min), has a phenytoin concentration drawn in clinic. The result is 6.3 µg/ml (therapeutic range = 10 - 20 µg/ml). The patient has had no recent seizures, and has been stable on the current phenytoin dose for some time. What should be done?

3. A 60 year old male patient with a history of hypertension, ethanol-induced pancreatitis, and chronic renal failure presents to the ER with new onset atrial fibrillation and signs and symptoms of pancreatitis. The liver function is normal and the patient is taking no meds. A recent serum creatinine was 3.5 mg/dL, and the weight is 60 kg (equal to ideal weight). The ER physician elects to administer IV digoxin in order to slow the ventricular response (currently 120 beats per minute).
 - A. What loading dose of digoxin would you suggest?
 - B. Twenty-four hours later, the ventricular rate is 80 bpm. What oral maintenance dose of digoxin would you suggest?
 - C. The patient is admitted because of acute and painful pancreatitis, so that he may be made NPO and supported. Meperidine is ordered at a dose of 75 mg IM every 6 prn. Discuss this therapy.

CASES WITH ANSWERS

1. A male patient presents with a temperature of 101.5 , and other physical signs and symptoms of a complicated urinary tract infection. The patient was recently hospitalized, and as part of his evaluation, a twenty-four hour urine collection for creatinine clearance was obtained. Presently, as the supervising resident, you recommend gentamicin and ampicillin as initial treatment for this patient's infection. Evaluation of the recent discharge summary (which you are able to locate) reveal these data pertaining to renal function: Twenty-four hour urine collection, total urine creatinine 1365 mg, and concurrent serum creatinine 1.2 mg/dL. The patient weighs 77 kg, is six feet in height, and is 40 years of age. A repeat serum creatinine in the ER is also 1.2 mg/dL.

A. Is the twenty-four hour urine collection adequate? *Can't tell with certainty because of substantial variability in 24 hour creatinine urinary excretion. See reference Greenblatt DJ, Ransil BJ, et al. Variability of 24-hour urinary creatinine excretion by normal subjects. J Clin Pharmacol. July, 1976. pp. 321-8.*

B. Calculate the creatinine clearance from the collection data provided.

$$CrCl = UV/P$$

$$= \frac{Cr_u}{1440} \times 100$$

$$\frac{1365}{1440} \times 100 = 79 \text{ ml/min}$$

C. "Estimate" the creatinine clearance from the serum creatinine.

$$\frac{(140-40) 77}{1.2} = 89 \text{ ml/min}$$

D. Correct the estimate for 1.73 m² (72 kg).

$$\frac{(140-40)}{1.2} = 83 \text{ ml/min}$$

E. If the collection clearance and the "estimate" are different, which would you accept as valid and why? *estimate*

2. A patient with a long history of seizure disorder (grand mal), hypertension, and

end stage renal disease (recent measured creatinine clearance was 10 ml/min), has a phenytoin concentration drawn in clinic. The result is 6.3 µg/ml (therapeutic range = 10 - 20 µg/ml). The patient has had no recent seizures, and has been stable on the current phenytoin dose for some time. What should be done? *nothing - pt should remain on same dose - therapeutic range is probably lower in this type of pt + no clinical need to change*

3. A 60 year old male patient with a history of hypertension, ethanol-induced pancreatitis, and chronic renal failure presents to the ER with new onset atrial fibrillation and signs and symptoms of pancreatitis. The liver function is normal and the patient is taking no meds. A recent serum creatinine was 3.5 mg/dL, and the weight is 60 kg (equal to ideal weight). The ER physician elects to administer IV digoxin in order to slow the ventricular response (currently 120 beats per minute).

A. What loading dose of digoxin would you suggest?

May need to decrease by 50% because volume of distribution is lower, tailor to ventricular response

B. Twenty-four hours later, the ventricular rate is 80 bpm. What oral maintenance dose of digoxin would you suggest?

B.
$$MD = LD \times \frac{14\% + CrCl}{5}$$

= 0.5 mg X 0.18 = ~ 0.1 mg (0.125 mg/day)

OR

usual dose by 50%

C. The patient is admitted because of acute and painful pancreatitis, so that he may be made NPO and supported. Meperidine is ordered at a dose of 75 mg IM every 6 prn. Discuss this therapy.

C. *meperidine is metabolized to normeperidine (psychosis, dysphoria, seizures) which is excreted renally*

dose by 50% or use another drug

