PHA 5128 Dose Optimization II, Spring 2013, Case Study IV

If you have any questions regarding this case study, do not hesitate to contact Benjamin Weber (benjaminweber@ufl.edu). Please remember that attendance is mandatory.

Problem 1 (Carbamazepine)

A 49 year old male patient, 83.3 kg in weight, is to receive immediate release carbamazepine regimen.

1. Compute the daily dose required to achieve a steady state plasma concentration of 7.5 mg/L, assuming monotherapy.
2. If the patient receives phenobarbital medication of 2.0 mg/kg Q12h for the past 3 months and the doctor decides to include a concomitant therapy of carbamazepine in order to better control his seizure, compute the daily maintenance dose required to attain a target steady state concentration of 7 mg/L carbamazepine, using an immediate release formulation. Later on, over the course of treatment, blood samples were evaluated for carbamazepine and were reported to be 12.5 mg/L. How should his daily dose be adjusted to get to the desired concentration?

Problem 2 (Phenytoin)

M.T., a 49-year-old, 55kg female, had been taking 250mg/day of sodium phenytoin; however, her dose had been increased to 300mg/day because her seizures were poorly controlled and because her phenytoin plasma concentration was only 3mg/L. Now she complains about minor CNS side effects and her measured plasma phenytoin concentration is 26mg/L. This level was decided to be too high for this patient, so the maintenance dose was discontinued. How long would it take for the phenytoin concentration to drop to 15 mg/L after discontinuation of dose?

The following equation may be helpful to solve this problem:

$$T = \left(K_M * \ln\left(\frac{C_0}{C}\right) + (C_0 - C)\right) * \frac{V_d}{V_{max}}$$

Problem 3 (Digoxin)

A.P., a 75-year-old, 65-kg man (non-obese), was admitted with complaints of increased shortness of breath and yellow sputum production. He has a medical history of congestive heart failure. During his hospital stay, he developed atrial fibrillation and was given digoxin to slow his ventricular rate. He received 3 doses 0.25-mg digoxin IV every 3 hours (starting at 9pm on day 1) and was given a maintenance dose of 0.25-mg tablets each morning (starting at 9am on day 2). His serum creatinine is stable at 1.3 mg/dL.

Calculate his expected digoxin plasma concentration at 9am on day 4. (Hint: A graph of the expected concentration time profile might be helpful to answer this problem)

A digoxin level obtained at 9am on the morning of day 4 was 1.5μg/L. Do you observe any discrepancy between expected and observed digoxin plasma concentration level? If yes, explain the discrepancy between expected and observed dose.

Problem 4 (Methotrexate)

V.A., a 53-year-old, 65-kg woman (non-obese, SCr = 1.2 mg/dL) is to receive a course of methotrexate (MTX) therapy for acute lymphoblastic leukemia. Her regimen will consist of 400-mg MTX loading dose to be administered over 15 minutes followed by an IV infusion of 50 mg/h for the next 36 hours. Calculate her anticipated MTX plasma levels (in μM) for the following scheduled sampling times: 24h, 48h, and 60h, after the beginning of the 50 mg/h infusion. You may assume that steady state has been achieved after 24h. A sketch of the expected plasma-concentration-time profile may be helpful to answer this problem.