Case 1 - Prospective

A 65 Y.O. male with a Sr.Cr. of 1.4 mg/dl develops a cellulitis. The Gram stain shows a Gram + cocci. The physician suspects *Staph. aureus* and wants to start vancomycin. The patient is 5' 4" and weights 86 Kg. What would be the appropriate dose to use?

Estimate LBW:

$$LBW = 50\ Kg + 2.3 * (Htin. - 60) \qquad = 59.2\ Kg \qquad \text{Eq. 1}$$

Estimate CrCl-Wt:

BMI = 86 Kg / (65 in * 0.0254 m/in)^2 = 32.5

so CrCl-Wt = 59.2 Kg + 0.4 * (86 Kg – 59.2 Kg) = 69.9 *Kg* Eq. 2

Estimate CrCl:

$$CrCl = \frac{(140 - Age) \cdot CrCl \cdot Wt}{SrCr \cdot 72} \qquad = 52.0\,\text{ml/min} \qquad \text{Eq. 3}$$

Population PK data for vancomycin estimates the elimination rate constant and half-life:

$$k_e = \frac{44 + (8.3 \cdot CrCl)}{10000} \qquad = 0.0476\ Hr.^{-1} \qquad \text{Eq. 4}$$

$$t_{½} = \frac{\ln 2}{k_e} \qquad = 14.6\,Hr \qquad \text{Eq. 5}$$

Estimate the volume of distribution:

$$V_{ss} = V_d\,factor \cdot ActWT \qquad V_{ss} = 0.7 L/Kg \cdot 86\ Kg = 60.2\ L \qquad \text{Eq. 6}$$

Estimate Tau (the 5th equation in the Sawchuk-Zaske list):

$$\tau = \frac{\ln(C_{\text{max/desired}}/C_{\text{min/desired}})}{k_e} + t_{\text{inf}} \qquad = \frac{\ln(36/15)}{0.0476\,Hr^{-1}} + 1.5\,Hr = 19.9\,Hr \qquad \text{Eq. 7}$$

Select a practical Tau (e.g. Q4H, Q6H, Q8H, Q12H or Q24H) based on this estimate. Here Q24H.

Using the practical interval, estimate the new dose (the 6th equation in the Sawchuk-Zaske list):

$$R_0 = C_{\text{max,desired}} \cdot V_{ss} \cdot k_e \left[\frac{1 - e^{-k_e \tau}}{1 - e^{-k_e t_{\text{inf}}}}\right] \qquad \text{Eq. 8}$$

$$= 36 mg/L \cdot 60.2\,L \cdot 0.0476\,Hr^{-1} \left[\frac{1 - e^{-0.0476\,Hr^{-1}\,24Hr}}{1 - e^{-0.0476\,Hr^{-1}\,1.5Hr}}\right] = 1019.4\ mg/Hr$$

$$Dose = R_0 \cdot t_{\text{inf}} \qquad = 1019.4\ mg/Hr \cdot 1.5\ Hr = 1529\,mg \qquad \text{Eq. 9}$$

Make a practical recommendation (Vancomycin is usually dose in 250 mg increments):

1500 mg Q24H

Verify that this will give you desirable steady state peak and trough concentrations:

$$C_{ss,pk} = \frac{R_0}{V_{ss} \cdot k_e} \bullet \frac{(1 - e^{-k_e t_{\text{inf}}})}{(1 - e^{-k_e \tau})} \qquad \text{Eq. 10}$$

$$C_{ss,pk} = \frac{1500\,mg / 2\,Hr.}{60.2\,L \cdot 0.0476\,Hr^{-1}} \bullet \frac{\left(1-e^{-0.0476 \cdot 2}\right)}{\left(1-e^{-0.0476 \cdot 24}\right)} = 34.9\,mg/L$$

$$C_{ss,tr} = C_{ss,pk} \cdot e^{-k_e(\tau - t_{\inf})} = 34.9\,mg/L \cdot e^{-0.0476\,(24-2)} = 12.25\,mg/L \qquad \text{Eq. 11}$$

Case 2 – Trough Only

The above patient was given 1000 mg Q24H and the trough right before the fifth dose was 11.4 mg/dL. What new dose would you recommend?

Vancomycin routine monitoring should be a single trough level at steady state. The patient should be at steady just before the fifth dose. So for a single level dosage adjustments are proportional. Use the following equation and let's target 15 in this case:

$$\left({Dose}/{Tau}\right)_{new} = \left({Dose}/{Tau}\right)_{current} * {C_{desired}}/{C_{measured}} \qquad \text{Eq. 12}$$

= (1000 mg/24 hr) * 15 mg/dL / 11.4 mg/dL = 54.8 mg/hr

Generally, if the ratio of $C_{desired}$ / $C_{measured}$ is 1.5 or more then decrease the dosing interval (Tau) from 12 hours to 8 hours (or 24 hours to 12 hours). If the ratio is less than 0.67 then increase the dosing interval from 12 hours to 24 hours or 24 hours to 36 hours. If the ratio is between 0.67 and 1.5, then do not change the dosing interval, only alter the dose.

Here the ratio is 15 mg/dL / 11.4 mg/dL = 1.30 so change only the dose:

54.8 mg/hr * 24 hr = 1315 mg (Round to the nearest 250 mg increment)

1250 mg Q24H

Case 3 – Trough Only

A 52 year old black female patient, 5'7" and 79 Kg and with a SrCr = 1.3 mg/dL was given 1000 mg Q12H and the trough right before the fifth dose was 17.3 mg/dL. What new dose would you recommend?

$$\left({Dose}/{Tau}\right)_{new} = \left({Dose}/{Tau}\right)_{current} * {C_{desired}}/{C_{measured}} \qquad \text{Eq. 13}$$

= (1000 mg/12 hr) * 15 mg/dL / 17.3 mg/dL = 72.3 mg/hr

Here the ratio is 15 mg/dL / 17.3 mg/dL = 0.87 so change only the dose:

72.3 mg/hr * 12 hr = 867 mg (Round to the nearest 250 mg increment)

750 mg Q12H

Case 4 – Trough Only

A 5' 5" 88 Kg. 72 Y.O. Hispanic female patient has been on vancomycin 750 mg Q12H for 3 days. A single trough level came back at 6.6 mg/dl. What new dose would you recommend?

$$\left({}^{Dose}/_{Tau}\right)_{new} = \left({}^{Dose}/_{Tau}\right)_{current} * {}^{C_{desired}}/_{C_{measured}} \qquad \text{Eq. 14}$$

= (750 mg/12 hr) * 15 mg/dL / 6.6 mg/dL = 142 mg/hr

Here the ratio is 2.3 so let's change the Tau to every 8 hours and adjust the dose.

142 mg/hr * 8 hr = 1136 mg (Round to the nearest 250 mg)

1250 mg Q8H

Case 5 - Retrospective

A 5' 6" 68 Kg. 19 Y.O. female burn victim has been on vancomycin 1 Gm Q12H for 5 days. Levels are done and come back with a Pk/Tr = 17/4.1 mg/dl. The skin grafts still show signs of cellulitis and the physician wants to increase the dose. What would you recommend? (The Pk was 60 minutes after a 90 minute infusion.)

Calculate the elimination rate constant:

$$k_e = \frac{\ln\left({}^{C_{pk}}/_{C_{tr}}\right)}{t_{tr} - t_{pk}} \qquad = \frac{\ln\left({}^{17}/_{4.1}\right)}{12 - 2.5} = \frac{\ln\left({}^{17}/_{4.1}\right)}{9.5\ Hr.} = 0.15\ Hr^{-1} \qquad \text{Eq. 15}$$

(In terms of the dosing interval the infusion was started at t = 0, it stopped at 1.5 hr, and the pk was measured at 2.5 hr and the trough (extrapolated) was at 12 hours, therefore $t_2 - t_1$ is 12 -2.5 = 9.5. This is where most errors in calculations are made.)

$$t_{1/2} = \frac{\ln 2}{k_e} = 4.6\ Hr$$

Calculate the maximum concentration:

$$C_0 = \frac{C_{pk}}{e^{-k_e\left(t_{pk} - t_{\inf}\right)}} \qquad = \frac{17 mg/L}{e^{-0.15 Hr^{-1}\left(2.5\ Hr - 1.5\ Hr\right)}} = 19.75\ mg/L \qquad \text{Eq. 16}$$

Calculate the volume of distribution:

$$V_{ss} = \frac{R_0}{k_e} \cdot \frac{1 - e^{-k_e t_{\inf}}}{(C_0 - C_{tr} \cdot e^{-k_e t_{\inf}})} \quad \text{Eq. 16}$$

$$= \frac{1000mg / 1.5\,Hr}{0.15\,Hr^{-1}} \cdot \frac{1 - e^{-0.15 Hr^{-1} \cdot 1.5 Hr}}{(19.75\,mg/L - 4.1\,mg/L \cdot e^{-0.15\,Hr^{-1} \cdot 1.5 Hr})} = 54.4\,L$$

Using C_o, k_e and V_{ss} estimate a dosing interval, a dose and predict the steady state peak and trough using a practical regimen using Eq 7, Eq. 8, Eq 9, Eq. 10 and Eq. 11.

$$\tau = \frac{\ln(36/15)}{0.15\,Hr^{-1}} + 1.5\,Hr = 7.34\,Hr \approx 8Hr \quad \text{Eq. 17}$$

$$R_0 = 36\,mg/L \cdot 54.4\,L \cdot 0.15\,Hr^{-1} \left[\frac{1 - e^{-0.15 Hr^{-1} 8 Hr}}{1 - e^{-0.15 Hr^{-1} 1.5 Hr}}\right] = 1018.8\,mg/Hr \quad \text{Eq. 18}$$

$$Dose = 1018.8 mg/Hr \cdot 1.5\,Hr = 1528\ mg \approx 1500mg \quad \text{Eq. 19}$$

Make a practical recommendation and then verify:

1500 mg Q8H

$$C_{ss,pk} = \frac{1500mg / 2\,Hr.}{54.4\,L \cdot 0.15\,Hr^{-1}} \bullet \frac{\left(1 - e^{-0.15 \cdot 2}\right)}{\left(1 - e^{-0.15 \cdot 8}\right)} = 34.1\,mg/L \quad \text{Eq. 20}$$

$$C_{ss,tr} = 35.3\,mg/L \cdot e^{-0.15(8-2)} = 13.9\,mg/L \quad \text{Eq. 21}$$

(Note: for that dose adjust the infusion to 2 Hr)