Detroit receiving Hospital and University Health Center vancomycin dosing nomogram table

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<th>80</th>
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Figure 1. Detroit Receiving Hospital and University Health Center vancomycin dosing nomogram. (Updated 5/99)

Useful information: 1 kg = 2.2 lbs

1. An overweight male, 43 years of age, 6’2” in height and 300 lbs in weight acquired S. pneumonia. His serum creatinine is 1.20 mg/dL. What is the initial dosage of vancomycin recommendation based on the nomogram above? Using this dosing regimen, compute the expected steady-state $C_{\text{max}}$ and $C_{\text{min}}$ values for IV bolus. Is the therapeutic goal attained?

300 lbs = 136 kg

Use the following equation to compute the volume of distribution:

\[ V_d (in \ L) = 0.178(\text{age in years}) + 0.22(\text{TBW in kg}) + 15 \]

\[ V_d = 52.6 \ L \]

\[ IBW = 50 + 2.3 * (height \text{ in inches} - 60) = 50 + 2.3 * (74 - 60) = 82.2 \text{ kg} \]

\[ ABW = IBW + 0.4 * (TBW - IBW) = 82.2 + 0.4 * (136 - 82.2) = 103.7 \text{ kg} \]

We will use the ABW since TBW is more than 120% of IBW.
**Vancomycin CL ~ CL\text{Cr}**

Based on the nomogram, you will use 1000 q8h dosage regimen.

\[
CL_{CR} = \frac{(140 - 43)(103.7)}{72(1.2)} = 116 \text{ mL/min}
\]

\[
116 \text{ mL/min} \times \frac{1 \text{ L}}{1000 \text{ mL}} \times \frac{60 \text{ min}}{1 \text{ hr}} = 6.96 \text{ L/hr}
\]

\[
K_e = \frac{CL}{V_d} = \frac{6.96 \text{ L/hr}}{52.6 \text{ L}} = 0.132 \text{ hr}^{-1}
\]

**For IV bolus,**

\[
C_{\text{max,ss}} = \frac{S \cdot F \cdot \text{dose}}{V_d} \frac{1}{1 - \exp(-k\tau)} = \frac{1(1)(1000 \text{ mg})}{52.6 \text{ L}} \frac{1}{1 - \exp(-0.132 \text{ hr}^{-1} \cdot 8 \text{ hr})} = 29.2 \text{ mg/L}
\]

\[
C_{\text{min,ss}} = C_{\text{max,ss}} \exp(-k\tau) = 29.2 \exp(-0.132 \text{ hr}^{-1} \cdot 8 \text{ hr}) = 10.2 \text{ mg/L}
\]

**For IV infusion,**

\[
C_{\text{max,ss}} = \frac{S \cdot F \cdot \text{dose}}{CL \cdot T} \frac{1 - \exp(-k\tau)}{1 - \exp(-k\tau)} = \frac{1(1)(1000 \text{ mg})}{6.96 \text{ L/hr} \cdot 1 \text{ hr}} \frac{1 - \exp(-0.132 \text{ hr}^{-1} \cdot 8 \text{ hr})}{1 - \exp(-0.132 \text{ hr}^{-1} \cdot 8 \text{ hr})} = 27.2 \text{ mg/L}
\]

\[
C_{\text{min,ss}} = C_{\text{max,ss}} \exp(-k\tau) = 27.2 \text{ mg/L} \cdot \exp(-0.132 \text{ hr}^{-1} \cdot 7 \text{ hr}) = 10.8 \text{ mg/L}
\]

*The estimated trough concentration is about 10 mg/L, so either an increase dose or decrease the dosing interval is needed. The goal is to maintain steady-state trough concentrations in the range between 15 and 20 mg/L.*

2. Due to an unknown cause, a female patient, 38 years of age, 5’6” in height and 170 lbs in weight, suffered a loss of volume of distribution and a corresponding increase in serum creatinine level by 10% and 70%, respectively. Adjust her treatment, assuming that the previous serum creatinine = 2.6 mg/dL. MIC of vancomycin against her infection is maintained at 4 µg/mL. Compute both $C_{ss, \text{max}}$ and $C_{ss, \text{min}}$ based on IV bolus administration and separately for IV infusion.

Do you need to adjust the dosing frequency based on the computation that you have obtained? If so, estimate the next dose based on a desired steady-state trough concentration of 20 mg/L.
Estimate AUC/MIC ratio for the patient’s original condition and in her new condition, assuming that vancomycin is administered as an IV bolus and follows a one-compartment model (*Hint: use the equation* \( AUC = \frac{C_0}{K_e} \). *What is your recommendation?*

170 lbs = 77 kg

\[
V_d (\text{in } L) = 0.17(\text{age in years}) + 0.22(\text{TBW in kg}) + 15 \\
V_d = 38.4 L
\]

\[
\text{New } V_d = 38.4 L \times 0.9 = 34.6 L
\]

\[
\text{IBW} = 45 + 2.3 \times (66 - 60) = 58.8 kg \\
\text{ABW} = 58.8 + 0.4 \times (77 - 58.8) = 66.1 kg
\]

*Her TBW is 130% of her IBW, therefore we use the ABW for the calculation of CL.*

\[
\text{CL}_{Cr,\text{for female}} (\text{mL/min}) = \frac{(140 - \text{Age})(\text{ABW in kg})}{(85)(\text{SCR}_s, \text{in mg/dL})}
\]

\[
\text{CL}_{Cr} = \frac{(140 - 38 \text{ yr})(66.1 \text{ kg})}{85(2.6)} = 30.5 \text{ mL/min}
\]

\[
\text{New } \text{CL}_{Cr} = \frac{(140 - 38 \text{ yr})(66.1 \text{ kg})}{85(2.6 \times 1.7)} = 17.9 \text{ mL/min}
\]

*Vancomycin CL ~ CL_{Cr}*

Based on the nomogram, you will use 1000 q24h dosage regimen. There is no need to adjust her dosing regimen.

\[
17.9 \text{ mL/min} \times \frac{1 L}{1000 \text{ mL}} \times \frac{60 \text{ min}}{1 \text{ hr}} = 1.07 L/hr
\]

\[
K_e = \frac{\text{CL}}{V_d} = \frac{1.07 L/hr}{34.6 L} = 0.031 hr^{-1}
\]

\[
\frac{1}{t_{\frac{1}{2}}} = \frac{\ln 2}{0.031} = 22 \text{ hr}
\]

*For IV bolus,*

\[
C_{max,ss} = \frac{S \cdot F \cdot \text{dose}}{V_d} \cdot \frac{1}{1 - \exp(-k\tau)} = \frac{1(1)(1000 \text{ mg})}{34.6 L} \cdot \frac{1}{1 - \exp(-0.031 \text{ hr}^{-1} \cdot 24 \text{ hr})} = 55.1 \text{ mg/L}
\]

\[
C_{min,ss} = C_{max,ss} \exp(-k\tau) = 55.1 \text{ mg/L} \times \exp(-0.031 \text{ hr}^{-1} \cdot 24 \text{ hr}) = 26.2 \text{ mg/L}
\]
For IV infusion,

\[ C_{\text{max,sv}} = \frac{S \cdot F \cdot \text{dose}}{CL \cdot T} \cdot \frac{1 - \exp(-kT)}{1 - \exp(-k\tau)} = \frac{1(1000 \, \text{mg})}{1.07 \, L/hr} \cdot \frac{1 - \exp(-0.031 \, hr^{-1} \cdot 1 \, hr)}{1 - \exp(-0.031 \, hr^{-1} \cdot 24 \, hr)} = 54.4 \, mg/L \]

\[ C_{\text{min,sv}} = C_{\text{max,sv}} \exp(-k\tau) = 54.4 \, mg/L \exp(-0.031 \, hr^{-1} \cdot 23 \, hr) = 26.7 \, mg/L \]

The trough is a concern since it is above 25 mg/L. You will need to either decrease the dose or increase the dosing interval.

\[ \text{New} C_{\text{max,sv}} = C_{\text{min}} + \frac{\text{Dose}}{V_d} = 26 \, mg/L + \frac{1000 \, mg}{38.4 \, L} = 52 \, mg/L \]

\[ k = \frac{\ln\left(\frac{C_{\text{max}}}{C_{\text{min}}}\right)}{\tau} = \frac{\ln \frac{52}{26}}{24} = 0.029 \, hr^{-1} \]

\[ \text{New} CL = k \cdot V_d = 0.029 \, hr^{-1} \times 34.6 \, L = 1.0 \, L/hr \]

Based on the new clearance value, we will compute the dosing interval and the dose.

If we use the trough concentration at 20 mg/L, then you will get

\[ \tau = \frac{\ln(\frac{40}{20})}{0.029 \, hr^{-1}} = 24 \, hr \]

\[ \text{Dose} = V_d \times C_{\text{max}} \times (1 - e^{-k\tau}) = 34.6 \times 40 \times (1 - e^{-0.029 \, hr^{-1} \cdot 24 \, hr}) = 694 \, mg \approx 700 \, mg \]

700mg q24h is a more convenient dosing regimen.

To compute AUC/MIC,

\[ C(0 \, hr) = \frac{\text{Dose}}{V_d} = \frac{1000 \, mg}{34.6 \, L} = 28.9 \, mg/L \]

\[ \text{AUC} = 28.9 / 0.029 = 997 \, mg \cdot hr/L \]

\[ \text{AUC} / \text{MIC} = 997 / 4 = 249 \, mg \cdot hr/L \]

The AUC/MIC is below the recommended target of 400 mg*h/L. Consider switching to another antibiotic.

3. A patient has the following drug concentration-time profile for a specific oral antibiotic:

<table>
<thead>
<tr>
<th>Time (hr)</th>
<th>Concentration (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>1</td>
</tr>
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</table>
The MIC value for this drug against the infection being treated is 50 µg/mL. Use linear interpolation to compute the duration that the drug concentration is above MIC. (Hint: First, plot the time-concentration profile, then determine the MIC value where the concentration-time curve crosses this value on both the ascending and the descending phases of the profile. Determine the slope between the two concentration-time points where the MIC value crosses. Use the slope value to approximate the time corresponding to the MIC value. Then take the difference between the approximated “MIC” time of the descending phase and the “MIC” time of the ascending phase. This difference is the duration or time above MIC.)

\[ \text{Slope}_1 = \frac{\Delta C}{\Delta t} = \frac{70 - 20 \, \mu g / mL}{2 \, \text{hr}} = 50 \, \mu g / mL / \text{hr} \]

\[ 50 = \frac{70 - 50}{2 - t_i} \]

\[ t_i = 1.6 \, \text{hr} \]
\[
\text{Slope}_2 = \frac{\Delta C}{\Delta t} = \frac{40 - 70 \mu g/mL}{16 - 12 \text{ hr}} = -7.5 \mu g/mL/hr
\]

\[-7.5 = \frac{40 - 50}{16 - t_2}\]

\[t_2 = 17.3 \text{ hr}\]

\[
\text{Time above MIC} = t_2 - t_1 = 17.3 - 1.6 = 15.7 \text{ hr}
\]

4. TRUE (T) or FALSE (F)

In geriatric population, the oral bioavailability of low-extraction drugs is often changed from the young population.

T F

In the geriatric population, the oral bioavailability of high-extraction drugs is often different from the young population.

T F

Free unbound drug concentrations tend to be decreased for low extraction drugs in the elderly population due to a change in protein binding.

T F

An increase in fat tissue in the elderly tends to decrease the volume of distribution of lipophilic drugs.

T F

Glomerular filtration rate is increased in the elderly due to an increase in creatinine formation.

T F