Vancomycin AUC Dosing Fundamentals

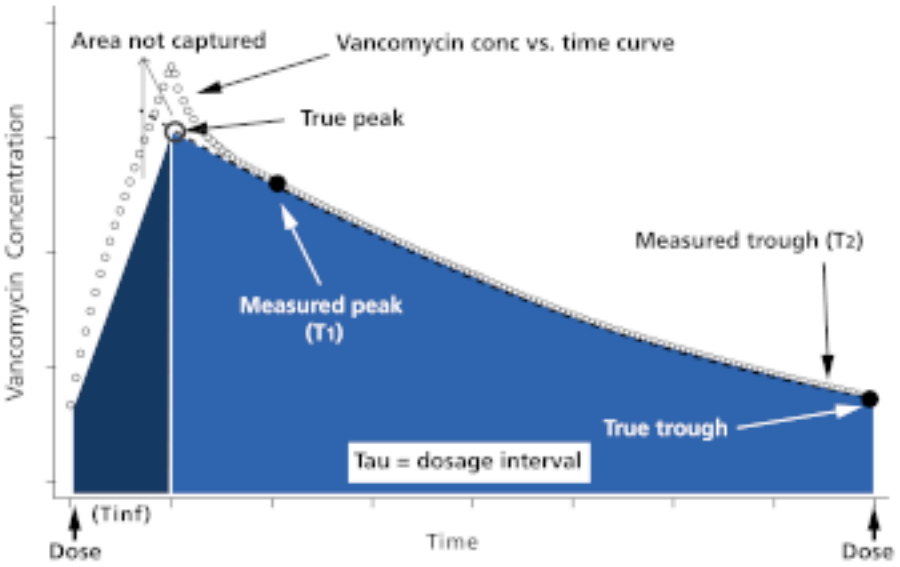
Source: https://www.sanfordguide.com/vanco_auc/

Introduction

Sanford Guide Editor Douglas Black, Pharm.D. developed this quick reference guide to assist providers in implementing the latest guidelines for vancomycin therapy in patients with staphylococcal bacteremia, endocarditis, and invasive infection.

Summary: How is AUC_{24} Used?

- Area under the serum concentration vs. time curve for 0-24 hours (AUC_{24}) has emerged as the preferred method for monitoring vancomycin therapy in patients with staphylococcal bacteremia, endocarditis, and invasive infection.
- See Am J Health Sys Pharm 2020, 77:835. The **target AUC_{24} is 400-600 µg/mL x hr regardless of MIC**.
    - Note: traditional pediatric dosing of 45-60 mg/kg/day frequently does not achieve target AUC in term infants and older children with normal renal function. Use of AUC_{24} closer to 400 µg/mL is adequate for most non-CNS infections. Clin Infect Dis Jul 13 2020
    - Comprehensive "pro" and "con" discussion: Clin Infect Dis 2021; 72:1497 & 1502



Adapted from Adv Drug Deliv Rev 2014;77:50, Fig. 5.

- Subsequent dose adjustments are determined using the calculated AUC_{24} because the AUC_{24} is proportional to total daily dose.
- Reference: Adv Drug Deliv Rev 2014;77:50.

How To Calculate AUC_{24} for Vancomycin

- AUC24 is calculated using either Bayesian modeling, which falls outside the scope of this document, or a more transparent "trapezoidal" model, which calculates AUC through the measurement of two trapezoids which fill most of the area under the curve.
- Two postdistributional concentrations obtained at steady state are used to determine AUC_{24} with log-linear equations. The AUC for one dosage interval is separated into two trapezoids, AUC under the infusion curve (AUC_{inf}) and AUC under the elimination curve (AUC_{elim}). The sum of AUC_{inf} and AUC_{elim} provides AUC for one dosage interval, and AUC_{24} is subsequently calculated.
- The measured peak and trough concentrations are back-extrapolated and forward-extrapolated to the true peak and true trough, respectively, to capture as much of the AUC for one dosage interval as possible.
- Calculating AUC_{24} in this manner inevitably slightly underestimates the true AUC_{24} because of a small area not captured by the two trapezoids.

Vancomycin AUC Calculator

- These calculations can be done with a calculator, paper and pencil, using an Excel spreadsheet, or via an online calculator such as the Sanford Guide Vancomycin AUC_{24} Calculator. While all methods will result in the same outputs, advantages of using an online calculator include easy access from any device, the ability to quickly copy or export results and append them to a patient record, and the ability to cite a specific source and methodology for determining AUC_{24}.
- Answers to some common questions about therapeutic vancomycin monitoring can be found at our FAQ page. Sanford Guide also hosted a 30 minute webinar on vancomycin dosing, which can be viewed at our YouTube channel.

Assumptions for Determining AUC_{24}

- Vancomycin peak and trough concentrations are obtained under steady-state conditions.

Determining Vancomycin AUC_{24} in Pediatric Patients

- None of the equations used are age-specific, and no age-specific assumptions are made during any calculation. Doses are entered (not selected), so they are not constrained by the size of doses typically used in adults. Therefore the calculation is based on kinetics from the measured levels and not PK parameters that change with age. For these reasons, this method of determining AUC may be used for both adults and children.

Data Required to Determine AUC_{24}

- Vancomycin dose (mg)
- Dosing interval (Tau, in hours)
- Duration of Vancomycin infusion (Tinf, in hours)
- Measured Vancomycin peak concentration (µg/mL)
- Time from start of Vancomycin infusion to measurement of peak concentration (T1, in hours)
- Measured Vancomycin trough concentration (µg/mL)
- Time from start of Vancomycin infusion to measurement of trough concentration (T2, in hours)

Clinical Example of Vancomycin Dosing Using AUC_{24}

- A patient with normal renal function is receiving vancomycin 1 gm IV q12h. A trough is drawn 30 minutes before the fourth dose, the fourth dose is infused over one hour, and the peak is drawn one hour after the infusion is complete. Because the patient is at steady state, the trough concentration measured 30 minutes before the fourth dose will be equivalent to a trough measured 30 minutes before the fifth dose (refer to above graphic). The peak is reported as 22 µg/mL, trough 8 µg/mL. These data are entered into the calculator, spreadsheet, or equations:
    - Dose (mg): 1000
    - Dosing interval (Tau, hours): 12
    - Duration of infusion (Tinf, hours): 1
    - Measured peak (µg/mL): 22
    - Time from start of infusion to peak (T1, hours): 2
    - Measured trough (µg/mL): 8
    - Time from start of infusion to trough (T2, hours): 11.5
- The calculation determines the AUC_{24} to be 349 µg/mL x hr (outside the target range).
- If using the Sanford Guide vancomycin calculator, the daily dose range that will achieve the target AUC_{24} of 400-600 µg/mL x hr is reported. The provider can then input a new combination of dose, duration of infusion, and dosing interval, and the calculator predicts the AUC_{24}, peak, and trough concentration that should result.

AUC_{24} Calculation

1. Calculate the elimination rate constant (k_e)

$$ke = \frac{ln(\frac{Measured\ Peak}{Measured\ Trough})}{T2 - T1}$$

2. Calculate true peak

$$True\ Peak = \frac{Measured\ Peak}{e^{(-ke)(T1-Tinf)}}$$

3. Calculate true trough

$$True\ Trough = (Measured\ Trough)(e^{(-ke)(Tau-T2)})$$

4. Calculate AUC_{inf}

$$AUC_{inf} = \frac{(True\ Trough + True\ Peak)}{2}\ (Tinf)$$

5. Calculate AUC_{elim}

$$AUC_{elim} = \frac{True\ Peak - True\ Trough}{ke}$$

6. Calculate AUC24

$$AUC_{24} = [(AUC_{inf}) + (AUC_{elim})]x(\frac{24}{Tau})$$

Dose Adjustment Using AUC24

- Subsequent dose adjustments can be determined using the **calculated AUC_{24} because the AUC_{24} is proportional to total daily dose**.
- If the calculated AUC_{24} falls outside the target range, dose or interval (or both) can be adjusted to achieve a value in the range. If the AUC_{24} is already within the range, dose can be adjusted to target the upper or lower end of the range as desired, e.g., to achieve an AUC_{24} close to 400 for pediatric dosing.

Equations to Determine Predicted Peak and Trough

1. Calculate volume of distribution (Vd)

$$V_D = \frac{(Dose)(1 - e^{-ke \cdot Tinf})}{Tinf \cdot ke(True\ Peak - [True\ Trough \cdot e^{-ke \cdot Tinf}])}$$

2. Calculate vancomycin clearance (CL)

$$CL = V_D \cdot ke$$

3. Predict new peak concentration

$$New\ Peak = \frac{New\ Dose}{CL \cdot New\ Tinf} \cdot \frac{1 - e^{-ke \cdot New\ Tinf}}{1 - e^{-ke \cdot New\ Tau}}$$

4. Predict new trough concentration

$$New\ Trough = New\ Peak \cdot e^{-ke(New\ Tau - New\ Tinf)}$$