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Pharmacokinetics and AUC Refresher

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Pharmacokinetics and AUC Refresher

There are a number of pharmacokinetics terms that are commonly used in the 2020 vancomycin guidelines when describing the dosing and monitoring of vancomycin. Understanding these terms is important as you transition to dosing via AUC.

Commonly Used Pharmacokinetics Terms

AUC: Area Under the Curve is defined as the "total exposure to the drug" within a certain window of time. It is a reflection of both the dose of the drug and the rate in which the drug is cleared from the body. Historically, AUC was calculated using multiple drug levels but now it can be estimated using fewer levels.

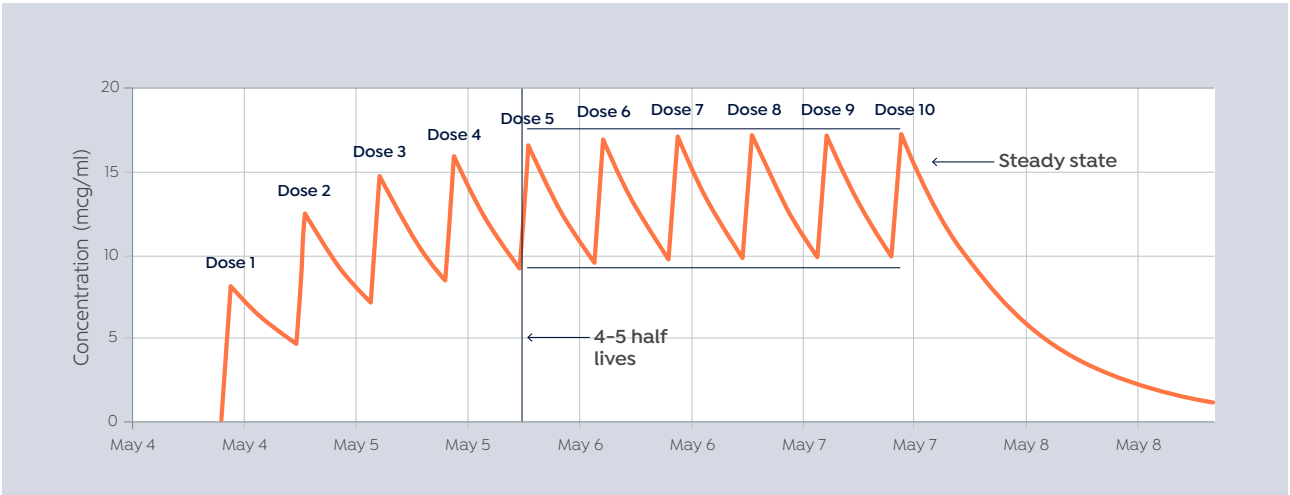
Cmax: The peak concentration of drug.

Cmin: The trough concentration of drug.

Half-life ($t_{1/2}$): The time needed for half of the amount of drug present in the body to be removed. The half-life will be different for each drug depending on how fast it's eliminated from the body.

Steady-state: When the rate of drug intake matches drug elimination, i.e. a consistent amount of the target drug in the bloodstream remains even though dosing continues. The amount of time it takes to reach steady state varies by drug and patient but occurs between 4 and 5 half lives. Visually this is represented when two or more consecutive peak and subsequent trough concentrations are equivalent.

Visual representation of steady state



MIC: The minimum inhibitory concentration (MIC) is the minimum amount of the antimicrobial drug needed to inhibit the visible growth of bacteria. There are different values for MIC depending on what type of antibacterial drug you use and how resistant a bacteria is to a specific antimicrobial drug. For example, a MIC=1 mg/L indicates that the visible growth of bacteria is inhibited by 1 mg/L of the drug. There are a number of ways that MIC can be measured, but the gold standard is using a technique called broth microdilution (BMD). Within the vancomycin guidelines (Rybak, et al. 2020) they mention that the target pharmacodynamic parameter to achieve is an AUC/MIC ratio (based on BMD) of 400-600. However, they go on to say that if the AUC is less than 1 mg/L per BMD that the dose does not need to be reduced.

Calculating AUC

All of these concepts permit the calculating of AUC by using non-Bayesian methods, usually by using a set of formulas. Unfortunately, as one might expect, this is a rather lengthy process. A publication by Meng et al.(2019) developed and implemented an abbreviated calculation version that still had 15 separate steps with multiple drug levels!

Problematically, however, most manual-calculation methods assume that the patient is already at steady-state. This has the consequence whereby if calculating dose adjustments manually, levels cannot be taken to permit this to be done until day 3 of therapy at the earliest. Even more problematically, the guidelines recommend that "targeted AUC exposures be achieved early within the course of therapy, preferably within the first 24 to 48 hours".

One of the major benefits of Bayesian dosing indicated by the revised guidelines is Bayesian dosing "doesn't require steady-state vancomycin concentrations to allow early assessment of AUC target attainment".

In other words, if you use Bayesian dosing, you can take a single level after the first dose is administered, and dose adjust immediately. While this method requires software, it is obviously much faster to calculate than the 15-step 'abbreviated' method, and quicker to adjust for the patient.

Bayesian dosing is also noted to be effective from a single level, although multiple levels (one shortly after the end of infusion, and one at the end of the dosing interval) is a preferred option if possible.

The Impact of AUC on Vancomycin Dosing

Moving away from a single lab-reported number in a range (trough) to using a calculated number (AUC) instead may appear somewhat challenging at first glance. That said, the guidelines do provide for flexibility – for example, noting that while two levels on a single dose are optimal, using Bayesian software permits the use of a single trough level.

Additionally, when utilizing Bayesian dosing for AUC calculations, it offers flexibility with the timing of the lab draw since it can utilize levels that are obtained at any time during the dosing interval.