Utilizing AUC to Optimize Vancomycin Dosing Regimens

Summary and Review

Optimal Pharmacodynamic Target for Vancomycin:

Studies (in vivo and in vitro) have demonstrated that the pharmacodynamic parameter that best predicts efficacy of vancomycin is the ratio of the area under the curve (AUC) to the MIC (AUC/MIC). Studies have demonstrated that an AUC/MIC $\geq$ 400, compared with an AUC/MIC < 400, was associated with improved clinical response and microbiologic eradication. Current dosing guidelines acknowledge that the AUC/MIC is likely the most useful PD parameter for predicting vancomycin efficacy, however because of the difficulty in gathering the available information in the clinical setting to calculate AUC/MIC, the trough serum concentration can be used as a surrogate marker of AUC (see below).

Please note that the above mentioned AUC targets are only applicable for treatment of staph aureus and not other gram positive bacteria.

Implications for Trough Only Monitoring:

The current vancomycin dosing guidelines recommend maintaining a minimum trough concentration between 15 and 20 mg/L as a surrogate marker for an AUC/MIC ratio $\geq$ 400. However, achieving a trough in the acceptable range may not always translate to achieving a target AUC/MIC. This correlation depends entirely on the PK parameters of the patient and the MIC of the infecting organism.

How to Utilize the AUC/MIC estimation?

Since monitoring only troughs may not always predict clinical success, also estimating the predicted AUC of a given regimen gives us an additional layer of data to better evaluate potential dosing regimens. Regimens that may achieve an estimated "therapeutic trough" may not yield an adequate AUC/MIC ratio (see examples below).

How do I interpret the AUC & AUC/MIC estimation?

The predicted estimates of AUC & AUC/MIC do not replace ongoing trough monitoring of vancomycin dosing regimens and troughs should still be monitored in order to better determine the patient's actual vancomycin clearance and the need for any subsequent dosing adjustment(s). We should ALWAYS still target troughs greater than 10 for ALL indications and 15-20 for more serious infections (sepsis, bacteremia, pneumonia, osteomyelitis, meningitis, etc.). However, since the AUC/MIC ratio is the most accurate predictor of efficacy for Vancomycin we also need to assess this data as well to give us as much information as possible to critically evaluate initial dosing regimens. We should utilize initial regimens that not only achieve troughs within the desired therapeutic range but that also have an AUC/MIC ratio as close to 400 as possible when AUC/MIC > 400 may not be possible.

The vancomycin dosing calculator defaults to an MIC of 1.5 but can be adjusted once the culture is finalized and the MIC value for Vancomycin is available. Our microbiology lab has determined that the majority of our MIC values of 2 are typically ½ dilution lower (MIC=1.5) when tested via E-test (gold standard for determining MIC).

What if I can't achieve an estimated AUC/MIC $\geq$ 400 based on the estimated value provided in the dosing calculator?

Per the most recent MRSA treatment guidelines:

"For isolates with a vancomycin MIC $\leq$ 2 (susceptible), the patient's clinical response should determine the continued use of vancomycin, independent of the MIC."

Regardless of the actual MIC value and subsequent AUC/MIC ratio IF the patient has had an adequate clinical response then no change in therapy is necessary. The AUC/MIC data provided in the calculator is simply additional information to assist you in formulating vancomycin dosing regimens. Troughs should still be maintained within the desired therapeutic ranges.

Vancomycin Level Prediction From Maintenance Dose

Age	56	yrs
Gender	m	
Height	72	inches
Actual Weight	150	kg TBW
SCr	2.9	
Maint. Dose	1500	mg
Dosing Interval	24	hours

% Ideal:	193.3	%
IBW:	77.6	kg
Adj.BW:	106.6	kg
Maint. Dose:	14.1	mg/kg Adj.BW
Load/Vd:	106.6	kg Adj.BW
(uses Adj.BW unless pt weighs < IBW)		
CrCl:	77.6	kg IBW
(uses IBW unless pt weighs < IBW)		

Infusion Length	1.5	hour(s)
CrCl	31.22	ml/min
Vd	74.6	L
Ke	0.0303	
1/2 life	22.86	hours

Vd factor: (uses 0.7 if left blank)

MIC: 1.5 (uses 1.5 if left blank)

AUC:MIC	442.22	
EST Peak	38.03	mcg/ml
EST Trough	19.23	mcg/ml

NOTE: Optimal AUC:MIC ratio 400 or greate

Load Options (Load/Vd Wt):

2000 mg =	18.8	mg/kg
1750 mg =	16.4	mg/kg
1500 mg =	14.1	mg/kg
1250 mg =	11.7	mg/kg
1000 mg =	9.4	mg/kg

NOTE: Consider loading dose only for indications requiring a trough of 15-20. (bacteremia, osteomyelitis, pneumonia, endocarditis, meningitis).
** Max recommended load = 2 gm **

In the above example this dosing regimen achieves BOTH a trough within the desired therapeutic range AND and an AUC/MIC ratio > 400.

This would be an acceptable initial regimen

Vancomycin Level Prediction From Maintenance Dose

Age	56	yrs
Gender	m	
Height	72	inches
Actual Weight	150	kg TBW
SCr	2.9	
Maint. Dose	500	mg
Dosing Interval	12	hours

% Ideal:	193.3	%
IBW:	77.6	kg
Adj.BW:	106.6	kg
Maint. Dose:	4.7	mg/kg Adj.BW
Load/Vd:	106.6	kg Adj.BW
(uses Adj.BW unless pt weighs < IBW)		
CrCl:	77.6	kg IBW
(uses IBW unless pt weighs < IBW)		

Infusion Length	1	hour(s)
CrCl	31.22	ml/min
Vd	74.6	L
Ke	0.0303	
1/2 life	22.86	hours

Vd factor: (uses 0.7 if left blank)

MIC: 1.5 (uses 1.5 if left blank)

AUC:MIC	294.84	
EST Peak	21.65	mcg/ml
EST Trough	15.51	mcg/ml

NOTE: Optimal AUC:MIC ratio 400 or greate

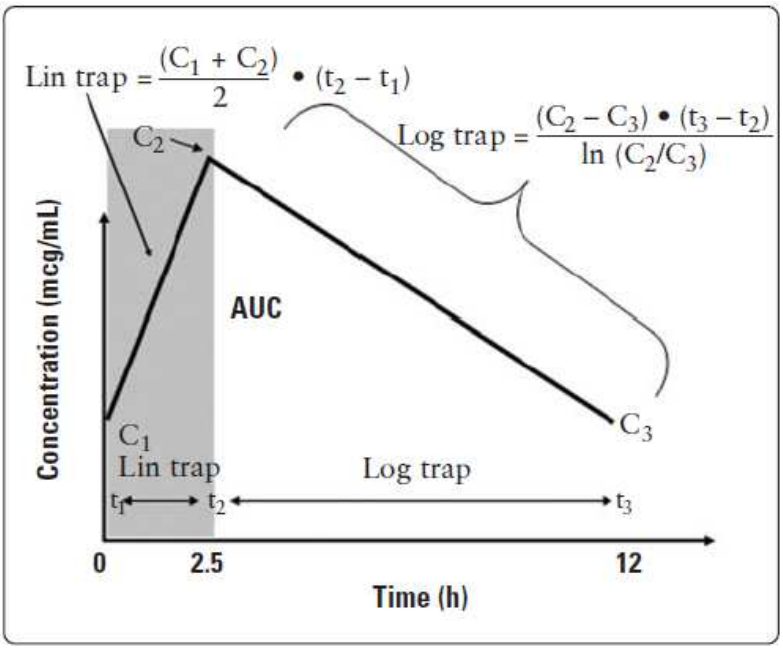
Load Options (Load/Vd Wt):

2000 mg =	18.8	mg/kg
1750 mg =	16.4	mg/kg
1500 mg =	14.1	mg/kg
1250 mg =	11.7	mg/kg
1000 mg =	9.4	mg/kg

NOTE: Consider loading dose only for indications requiring a trough of 15-20. (bacteremia, osteomyelitis, pneumonia, endocarditis, meningitis).
** Max recommended load = 2 gm **

In the above example this dosing regimen achieves a trough within the desired therapeutic range but it DOES NOT achieve an adequate AUC/MIC ratio.

This would NOT be an optimal initial regimen



The above graph is a display of the calculation that is utilized by the vancomycin dosing calculator to estimate AUC. The above equations calculate both the AUC while the dose is being infused (lin trap) as well as being eliminated (log trap).