

VANCOMYCIN : CONTINUOUS INFUSION PROTOCOL

INTRODUCTION

Vancomycin has traditionally been dosed as intermittent boluses. The monitoring of vancomycin to achieve efficacious levels and avoid toxicity is usually done as trough levels.

There have been a number of logistical and medical problems with the safe dosing and monitoring of vancomycin. This is particularly problematic in the Kimberley where we have endemic MRSA causing severe infections and a population of patients who are at risk from renal toxicity and cardiac complications of severe disease.

One strategy that can be used to simplify the dosing and monitoring of vancomycin is the use of a continuous infusion protocol. This is included in the most recent iteration of the Therapeutic Guidelines.

A continuous infusion should be considered in any patient who is at risk of nephrotoxicity or where achieving therapeutic levels rapidly is important eg. Bacteremia / sepsis.

Specific HIGH-RISK features for Vancomycin toxicity or difficulty with dosing includes:

1. Other nephrotoxic agents: ACE-I, diuretics, NSAIDs, Tazocin, aminoglycosides
2. Patients who are acutely unwell, on vasopressors or at risk of acute renal failure due to their underlying disease
3. Obese (BMI >30) – consider adjusted BW dosing (see Etg)
4. Pre-existing renal disease OR risk factors eg, diabetes, hypertension, CV disease
5. Previous Vancomycin nephrotoxicity, ototoxicity or “red man syndrome”
6. Patients with supra-normal renal clearance (I.e. high CrCl) eg. Paediatrics, sepsis, head injury

The most important consideration in preventing VANCOMYCIN toxicity is to avoid using it when it is not indicated. Generally, vancomycin should only be used in situations where the patient is suspected to have a severe invasive infection or after discussion with a specialist Infectious Disease or Microbiologist.

Continuous infusions of vancomycin are **NOT indicated** for patients with end-stage renal disease or dialysis. These patients will usually be treated with single dose vancomycin and review by pharmacy and the specialist team.

The basic principles of using a CONTINUOUS INFUSION of VANCOMYCIN are simple.

1. Give a loading dose based on the patient's weight (actual Body weight) - usually 25 mg/kg. In obese patients a dose based on adjusted body weight may be considered. (see box 1)
2. Give the loading dose over the specified time as per eTG (Box 2)
3. Calculate the daily dose for a continuous infusion based upon the patient's calculated creatinine clearance (**NOT the eGFR**) use the Cockcroft-Gault formula in adults
4. Commence the continuous infusion immediately after the loading dose is completed.
5. Run the infusion with as few interruptions as possible
6. Daily creatinine and vancomycin concentration are measured after achieving steady state (i.e 30 hours). This gives a "plateau level".
7. Use the plateau level to adjust the daily dose of vancomycin in the infusion based upon:
 - a. The actual level measured (box 3)
 - b. The creatinine clearance – recalculated each day
 - c. The clinical situation and microbiological data

Once the new vancomycin level and creatinine are available and the calculation has been made the dose in the infusion bag can be altered and the old bag discarded. DO NOT finish the existing bag if there is a need to adjust the dose. Change the bag and discard the previous bag immediately.

Running a continuous vancomycin infusion does have logistical requirements to make it manageable for the nursing staff and patients:

- Vancomycin needs to be run through a reliable IV cannula that allows the patient to move and not occlude the pump
- It will usually be necessary to have a second, separate IV in place to allow administration of other medicines without disrupting the vancomycin infusion.
- Consideration should be made for insertion of a PICC line in patients who will require IV vancomycin for more than a few days after the acute phase eg. Osteomyelitis.
- Extravasation of vancomycin needs to be detected quickly and the IV site changed to avoid complications and delays in vancomycin delivery.
- If patients are critically unwell eg. Hypotensive or oliguric it is reasonable to cease the infusion until the patient is more stable. This should be discussed with a senior doctor or HDU / ICU.

INITIAL DOSE of VANCOMYCIN

Box 1

- BMI < 30 kg/m² : load with 25 mg /kg **ACTUAL BODY WEIGHT**
- BMI > 30 kg/m² : load with 25 mg/kg on ADJUSTED BODY WEIGHT
 - Adjusted BW = IDEAL BW + 0.4 x (ACTUAL BW – IDEAL BW)
 - Eg. A 165 cm woman who weighs 88 kg has an IBW of 57 kg; therefore her adjusted BW is 57 + 0.4 x (88 – 57) = 69.4 kg

This dose is infused over the times recommended in eTG eg:

Box 2

Dose	Volume of 0.9% saline	Duration
750 mg	250 mL	90 minutes
1000 mg	250 ml	2 hours
1500 mg	500 ml	3 hours
2000 mg	500 ml	4 hours

- Refer to the injectable drug guidelines for more details

CONTINUOUS INFUSION of VANCOMYCIN is based on the CREATININE CLEARANCE

Note: this includes the weight as a variable so no further adjustment is required

Cockcroft-Gault formula for actual creatinine clearance: [Click for MdCalc link](#)

CrCl (mL/min) = $\frac{[140 - \text{age}] \times \text{weight} \times 1.23 \text{ (male) or } 1.04 \text{ (female)}}{\text{Serum creatinine}}$

Serum creatinine

EMPIRICAL VANCOMYCIN INFUSION for the first 24-hour bag:

CrCl	Daily (24-hr dose)	Volume / rate
< 20	No continuous infusion, discuss with renal team	
20 – 29	500 mg	500 ml @ 21ml/h
30 – 39	750 mg	500 ml @ 21 ml/h
40 – 54	1000 mg	500 ml @ 21 ml/h
55 – 74	1500 mg	500 ml @ 21 ml/h
75 – 89	2000 mg	1000 ml @ 42 ml/h
90 – 110	2500 mg	1000 ml @ 42 ml/h
> 110	3000 mg	1000 ml @ 42 ml/h

MONITORING

When using a continuous infusion there is no need to time blood samples to a trough.

Vancomycin levels should be taken after “steady-state” is achieved. This occurs at about 24 – 30 hours - approximately at the conclusion of the loading dose + the first 24 hour infusion bag is completed.

The level which is collected is a **PLATEAU CONCENTRATION**.

The target PLATEAU CONCENTRATION is 15 – 25 mg/L. The actual target depends on the severity of the infection and the MIC of the organism once known – though for most infections a level of 20 should be adequate.

In the initial phase of treatment daily creatinine and vancomycin levels should be collected and acted on in order to tailor the dose to the patient’s actual clearance.

Practically, blood should be collected at a time that allows the treating team to see the results and modify subsequent infusion bags in office hours where possible.

DOSE ADJUSTMENT

Ideally dose adjustments should be done in liaison with the ward Pharmacists and DMO

Prior to adjusting dose consider:

- The clinical state of the patient
- The current creatinine / renal function
- Any possible errors eg. Infusion disruptions or sampling errors
- If there is any doubt – re-sample to confirm spurious levels

RECOMMENDED DOSE ADJUSTMENT SCHEDULE

Vanc concentration	Adjustment recommendation
< 15 mg/L	Increase the total daily dose by 500 mg
15 – 25 mg /L	Maintain present dosage, consider 250 mg increase if clinically worse
26 – 30 mg/L	Decrease the daily dose by 500 mg
> 30 mg/L	Cease infusion, recheck level + Cr in 6 hours. Restart infusion at appropriate dose for the revised calc CrCl

DISRUPTED INFUSIONS

Whilst the timing of levels is not so crucial – it is important to note any disruptions to the infusions which may have resulted in lower than expected levels. Disruptions should be taken into account when modifying subsequent doses. For example, a level of 14mg/L taken when the 24 hour bag was actually infused over 28 hours would indicate that the dose was correct and the proper response would be to keep the dose the same and try to avoid further disruptions.