Vancomycin Continuous Infusion Guidelines for use in the Intensive Therapy Unit

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Vancomycin is a glycopeptide antibiotic routinely used in critical care to treat Gram-positive bacteraemia, in particular resistant Gram-positive organisms. Vancomycin requires serum concentration monitoring and potential side effects include nephrotoxicity and ototoxicity. Additionally, rapid infusion can cause 'red man' syndrome. During therapy with intermittent infusion administration, serum monitoring involves measuring trough concentrations, aiming for a level of 5-15 mg/L. Optimal therapy with vancomycin depends on maintaining trough concentrations above the minimum inhibitory concentration (MIC), as vancomycin activity is not enhanced as peak concentrations are increased.[1,2] Effectiveness increases as the duration of time with serum concentrations above the MIC for the target pathogen increases. Exceeding MIC by more than 4-5fold does not result in further activity.[1,2,3] Traditional intermittent infusion administration results in high peak concentrations and low trough concentrations. It has therefore been suggested that continuous intravenous infusion may be a suitable method of administration, as this would allow maintenance of serum concentrations at a desired level.[3] It has also been shown that continuous infusion provides more predictable and constant serum concentrations, with the target serum concentration acquired faster.[3] A target range of 15-25 mg/L has been suggested for severe infections.[2-5]

In view of the evidence, and following discussion with the ITU pharmacist in Glasgow Western Infirmary, where they implemented a successful guideline[5] a few years ago, staff at Ninewells ITU concluded that continuous vancomycin infusion would be an appropriate therapy for the unit. The additional advantages include a lower risk of misinterpretation of vancomycin levels and a lower risk of side effects from high peak concentrations.

Guidelines have been developed based on the Western Infirmary guidelines and in discussion with pharmacy and microbiology. The NHS Tayside Antimicrobial Management Group (AMG) approved the guidelines in April 2008. It should be noted that trials of continuous infusion have demonstrated microbiological and clinical equivalence, not superiority. At present the AMG would not currently recommend this method of infusion for endocarditis treatment without prior discussion with an Infection Specialist.

References:

1. Klepser ME, Kalpana BP, Nicolau DP, *et al.* Comparison of bactericidal activities of intermittent and continuous infusion dosing of vancomycin against methicillin-resistant *Staphylococcus aureus* and *Enterococcus faecalis.* Pharmacotherapy. 1998; **18**(5): 1069-1074

2. Matthews Z. Vancomycin continuous infusion: a cohort of 23 intensive care unit patients. Aus J Hos Pharm. 2001;**31**:108-110

3. Wysocki M, Delatour F, Faurisson F, *et al.* Continuous versus intermittent infusion of vancomycin in severe staphylococcal infections: prospective multicenter randomized study. Antimicrob Agents Chemother. 2001; **45**(9): 2460-2467

4. James JK, Palmer SM, Levine DP and Rybak MJ. Comparison of conventional dosing versus continuous-infusion vancomycin therapy for patients with suspected or documented Gram-positive infections. Antimicrob Agents Chemother. 1996;**40**(3): 696-700

5. Carmichael SJ, Thomson AH. Guidelines for the use of vancomycin by continuous infusion. North Glasgow NHS Trust, Western Infirmary (2003)

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LOADING DOSE

All patients should receive a weight-related loading dose, preferably via a central line

< 40kg	500mg IV in 100 mls 0.9% sodium chloride or 5% glucose over 1 hour
< 70 kg	1 g IV in 250 mls 0.9% sodium chloride or 5% glucose over 2 hours
≥ 70 kg	1.5 g IV in 250 mls 0.9% sodium chloride or 5% glucose over 2.5 hours

Central administration: the final concentration should not exceed 10mg/ml

Peripheral administration: the final concentration should not exceed 5 mg/ml

MAINTENANCE INFUSION

Start the maintenance IV infusion immediately after the loading dose. The dose depends on the patient's renal function. Infusions should be administered in 250 ml 0.9% sodium chloride or 5% glucose over 12 hours. The total daily dose should be split into two and the infusion rate set at 20.8 ml/hr.

Creatinine Clearance* (ml/min)	Daily maintenance dose	Dose in each 250 ml infusion bag for administration over 12 hours
<20 or CVVH/CVVHDF	500 mg	250 mg
20-34	750 mg	375 mg
35-59	1000 mg	500 mg
60-79	1500 mg	750 mg
80-99	2000 mg	1000 mg
>100	2500 mg	1250 mg

DOSE ADJUSTMENT

Request a serum level at 0700 hrs each day (with the morning routine bloods), or as advised by the pharmacist. For dosage adjustments use the following guidelines after 24 hours of treatment has been administered, and/or discuss with the pharmacist.

Vancomycin Concentration	Suggested dosage change
< 15 mg/L	Increase the daily dose by 500mg
15 – 25 mg/L	**No change**
> 25 mg/L	Decrease the dose by 500 mg**
> 30 mg/L	Stop the infusion and recheck serum level next morning. Restart at a lower dose

**if the patient is only receiving 500mg/day, reduce the dose to 250mg/day

***Estimated Creatinine Clearance (ml/min)** – if Creatinine < 60 µmol/L use 60 in calculation

$$\frac{(140 - \text{age (years)}) \times \text{weight (kg)}}{\text{Creatinine (µmol/L)}} \times \begin{cases} 1.23 \text{ (males)} \\ 1.04 \text{ (females)} \end{cases}$$

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