Louth: Antimicrobial Guidelines - Louth Hospitals: Antimicrobial Guidelines: Paediatric Vancomycin Guideline

Children's Health Ireland Vancomycin Paediatric Dosing and Monitoring Guideline 2020

Background

Vancomycin is a glycopeptide antibiotic active against *Staphylococcus aureus* and other gram positive susceptible bacterial infections. It is indicated for use when there is resistance pattern such as methicillin-resistant *Staphylococcus aureus* (MRSA) or when the patient demonstrates intolerance to alternative antibiotics. It is not the first line treatment for methicillin-sensitive *Staphylococcus aureus* (MSSA) as it is less effective than beta-lactams.

- **Mechanism of action:** Vancomycin acts by inhibiting the production of the peptidoglycan polymers of the bacterial cell wall by preventing the transfer and addition of the muramylpentapeptide building blocks that make up the peptidoglycan molecule itself.
- **Time dependent killing:** For vancomycin, it has been shown that its efficacy is best predicted by the area under the concentration-time curve over 24 hours (AUC24) divided by the MIC (AUC/MIC). This method of therapeutic drug monitoring is not practical at a ward level, therefore trough levels taken an hour before the dose is due is recommended in this guideline to determine efficacy.
- When treating an infection caused by bacteria with a vancomycin MIC less than 1 mg/L, aim for a trough of 10-15mg/L
- If the vancomycin MIC is greater than 1 mg/L, a trough of 15-20mg/L may be required

Under dosing and sub-therapeutic levels may result in the emergence of drug resistance and subsequent treatment failure.

Adverse Effects

- Common: Decrease in blood pressure, flushing of the upper body ("red man syndrome"), exanthema and mucosal inflammation, pruritus, urticarial, renal insufficiency, increased serum creatinine and urea.
- Uncommon: Transient or permanent loss of hearing (ototoxicity associated with persistent high levels).
- Rare: Hypersensitivity reactions, anaphylactic reactions, vertigo, tinnitus, dizziness, nausea.
- Rapid infusions can result in "Red man syndrome". "Red man" is a red rash over the upper body that is mediated by a mass histamine release. It is **NOT** an allergy - please contact Micro/ID for advice. Note the rate and the concentration the rate reaction has occurred. Further infusions should be run at a slower rate and more dilute concentration. Document changes in the drug kardex and patient notes.

Vancomycin Dosing, Therapeutic Drug Monitoring and Dose Adjustments in Patients with Normal Renal Function

A. Vancomycin Dosing in Normal Renal Function

For child > 1 month with normal renal function:

- Vancomycin 15mg/kg 6 hourly IV (Maximum single dose 750mg, maximum daily dose 3g)
- Loading dose of **25mg/kg (max 2g)** can be given to achieve faster therapeutic levels. A loading dose would be indicated for patients with bacteraemia, endocarditis, osteomyelitis, meningitis, necrotising fasciitis and empyema for children 12 years and above or under if advised by Micro/ID.

B. Vancomycin Monitoring in Normal Renal Function

- Levels should be taken through venepuncture/capillary blood samples.
- **Do not withhold** the dose when waiting for a level to come back.
- Sub-therapeutic levels can result in treatment failure or the emergence of drug resistance.
- Toxic or high levels of vancomycin can result in nephrotoxic and/or ototoxicity. It is important to monitor renal function for the duration of treatment of vancomycin as it is renally cleared. Monitor creatinine and urea a minimum of twice weekly for the duration of vancomycin treatment.
- If a prolonged course of vancomycin is required a base line auditory test should be carried out.
- If the patient is on additional nephrotoxic medication (e.g. NSAIDs, aciclovir, aminoglycosides, diuretics, omeprazole), monitor renal function more frequently. For Acute Kidney Injury (AKI) monitoring and classification please see section on renal impairment below.
- NB: Check U&E/ creatinine each time you check a vancomycin level.

Important

Vancomycin levels are processed in the Biochemistry Laboratory in OLOL from **8am to 8pm Mon - Fri and from 9am to 5pm on Sat - Sun.**

Consultant request only outside of these hours.

Type of Infection	Target trough concentration
Uncomplicated infections	10 to 20 mg/L
Complicated infections (e.g. bacteraemia, endocarditis, osteomyelitis, meningitis, necrotising fasciitis and empyema)	15 to 20 mg/L

Dosing Frequency	When to take trough level
Six hourly	Up to ONE HOUR **before 4th, 5th or 6th dose** When levels are therapeutic, repeat every 3 days

In patients with normal renal function, DO NOT withhold the next dose while awaiting the result of the trough level – this may result in the patient being under dosed

C. Vancomycin Recommended Dose Adjustment based on Trough Level Results

- After all dose adjustments repeat level as per recommendations above
- If there is a rise in creatinine, please calculate GFR and dose adjust as per recommendations in section on renal impairment below. Additionally assess patient for AKI as per the KDIGO definition in section on renal impairment below.

Trough level interpretation and maintenance dose adjustment for child >1 month (15mg/kg IV 6 HOURLY)		
Target trough level	**Trough level**	**Dose Adjustment**
10 – 20 mg/L If signs of AKI contact micro/ID and see section on renal impairment below	< 5mg/L	Increase dose by 20%
	5–9 mg/L	Increase dose by 10%
	10–20 mg/L	No change (unless target level is 15-20mg/L for complex infections* contact micro/ID)
	21–24 mg/L	Decrease dose by 10%, but do not omit a dose
	≥ 25 mg/L	Contact micro/ID for advice
*Complicated infections: Severe infection, reduced sensitivities, bacteraemia, endocarditis, osteomyelitis, meningitis, necrotising fasciitis and empyema		

Vancomycin Dosing, Therapeutic Drug Monitoring and Dose Adjustments in Patients with Renal Impairment

- Dosing is based on estimated GFR in patients with renal impairment. Please use the Schwartz formula below to calculate GFR
- Dosing and monitoring are expressed in the table below
- Please be aware that impaired renal function should be taken into account for both chronic kidney disease (CKD) and in acute kidney injury (AKI)
- If trough is high, consult nephrologist/Micro/ID for advice on subsequent dosing

GFR can be estimated by the Schwartz formula:

Child over 1 year:

GFR (mL/min/1.73 m ^{2}) = (40 × Height in cm) / Creatinine in micromol/L

Neonate:

GFR (mL/min/1.73 m ^{2}) = (30 × Height in cm) / Creatinine in micromol/L

To monitor for AKI please use the KDIGO model, if a patient is showing signs of AKI please review vancomycin and all nephrotoxic medication prescribed.

KDIGO classification of Acute Kidney Injury (AKI)

Stage 1 : Increase in creatinine of ≥50%

Or

Absolute increase in creatinine of 26.5micromol/L

Stage 2 : Increase in creatinine of ≥100%

Stage 3 : Increase in creatinine of ≥200%

Reference: Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney Int Suppl 2012;2:8.

Dose Adjustment and Monitoring for Renal Impairment in Infants and Children >1 month of age			
GFR (mL/min/1.73m ^{2})	**IV Dose**	**Frequency**	**When to take a trough level**
30-50	15mg/kg	12 hourly	Up to ONE HOUR **before the 3rd dose** . HOLD the next dose until level is back.
10-29	15mg/kg	24 hourly	Up to ONE HOUR **before the 2nd dose** . HOLD the next dose until level is back.
<10 / HD / PD	10 – 15mg/kg	STAT – subsequent dosing determined by serum levels.	Take level **12-18 HOURS after first dose** . HOLD the next dose until level is back.

Vancomycin Reconstitution and Administration

Dilution of reconstituted vials (500mg and 1g)	Dilute with sodium chloride 0.9% or glucose 5% to a concentration of up to 5mg/mL i.e. dilute each 500mg with at least 100mL
Rate of infusion	The rate must not exceed 10mg/minute, give over at least 60 minutes minimum using an infusion pump e.g. 750mg over at least 75 minutes, 1000mg over at least 100 minutes, etc
Infusion reactions	Rapid infusion may cause severe hypotension (including shock and cardiac arrest), wheezing, dyspnoea, urticaria, pruritus, flushing of the upper body ('red man' syndrome), pain and muscle spasm of back and chest. Stop the infusion if they occur. Effects may last between 20 minutes and up to several hours after stopping administration. Peripheral administration may cause injection site pain and thrombophlebitis - rotate injection sites.