Are we babying our vancomycin doses? A local review of intermittent vancomycin dosing in neonates

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Background:

Vancomycin is frequently used within the Neonatal Intensive Care Unit (NICU) for empiric and directed treatment of systemic gram-positive infections[1,2]. Attaining therapeutic levels is crucial to improve treatment efficacy and reduce drug toxicity, however, poses as a major challenge in critically unwell infants due to pharmacokinetic and physiological differences[1]. There is currently no consensus guideline for empiric intermittent vancomycin dosing in this cohort; this is reflected in an Australian context as dosing practices vary between institutions.

Aim:

To assess compliance and evaluate appropriateness of local neonatal intermittent vancomycin dosing guidelines at Mercy Hospital for Women, Heidelberg, Victoria (a level 6 NICU and tertiary referral centre).

Method:

A retrospective audit was conducted at Mercy Hospital for Women between 13th May 2020 to 13th May 2023. A list of patients identified to have received intravenous vancomycin was extrapolated from Merlin® dispensing software and Pyxis® MedStation (automated medication dispensing system). Clinical notes and pathology data were reviewed against audit criteria via scanned medical records.

Table 1. Audit inclusion criteria

Inclusion Criteria	Exclusion Criteria
✓ Inpatients identified to have been prescribed and administered intermittent vancomycin	× Subsequent infective episodes requiring further vancomycin treatment
	× Inpatients on continuous vancomycin therapy
✓Therapeutic drug monitoring undertaken and recorded on pathology portal	× External hospital transfers
	× Once only doses
	× Incomplete medical records
	× Incorrect trough sampling

Results:

Sixty-five out of ninety-nine patients (prescribed vancomycin) met inclusion criteria. All patients were commenced on intermittent vancomycin for treatment of late onset sepsis. Forty-seven patients (72.3%) had a positive blood culture growth of either Coagulase-negative Staphylococci or Methicillin-resistant Staphyloccocus Aureus. Starting doses for all patients were prescribed and administered as per protocol.

The target trough level is 10 – 15 mg/L for general infections or 15 – 20 mg/L for severe infections in neonates[1]. Trough levels are to be taken within an hour prior to the fourth vancomycin dose.

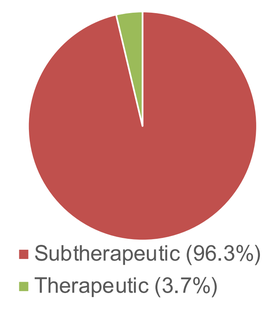
The audit identified:

- 87.7% correct sampling time (within an hour prior to fourth dose)
- 12.3% incorrect sampling time
  - 4.6% trough levels taken too early (2 - 3 hours)
  - 7.7% trough levels taken prior to third dose, with documented justification of concerns for subtherapeutic levels

Figure 1. Audit findings of different corrected gestational age (CGA) groups and their respective trough levels

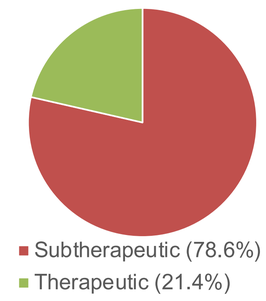
24 – 28+6 weeks CGA (n = 27)

- **50%** of patients never obtained a therapeutic level
- Time to first therapeutic level: **6.8 days**



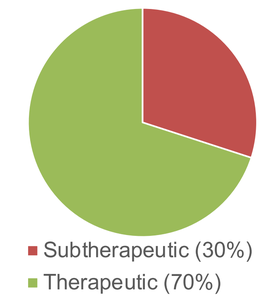
29 – 34+6 weeks CGA (n = 28)

- **15.8%** of patients never obtained a therapeutic level
- Time to first therapeutic level: **3.6 days**



≥ 35 weeks CGA (n = 10)

- All patients eventually obtained a therapeutic level
- Time to first therapeutic level: **1.9 days**



Discussion:

A revised regimen was implemented to guide intermittent vancomycin starting doses at Mercy Hospital for Women. The modest dose increases take into consideration the subset of patients attaining therapeutic levels with previous dosing guidelines and mitigating risk of these infants reaching supratherapeutic levels. The regimen was benchmarked against other neonatal services within Australia. An earlier time to first therapeutic level is expected for patients < 35 weeks CGA.

Table 2. Summary of updated intermittent vancomycin regimen

CGA	Previous dosing regimen (IV)	New dosing regimen (IV)	Changes
< 29 weeks	15 mg/kg/dose daily	10 mg/kg/dose 12 hourly	Increased total daily dose, in two divided doses
29 – 34+6 weeks	15 mg/kg/dose 12 hourly	10 mg/kg/dose 8 hourly	Same total daily dose, in three divided doses
≥ 35 weeks	15 mg/kg/dose 8 hourly	15 mg/kg/dose 8 hourly	No change

Limitations:

Data within each CGA group was limited, especially in patients greater than 35 weeks CGA. Inflammatory markers such as C-reactive protein and white cell count were not included in the initial audit. Serum creatinine levels were not routinely tested as a marker of renal function.

Conclusion:

Audit findings show that premature infants were likely to return subtherapeutic vancomycin levels using previous empiric dosing guidelines. There is plan for future audits to evaluate the impacts of dosing practice changes on clinical patient outcomes.

References:
1) Sosnin N, Curtis N, Cranswick N, et al. Vancomycin is commonly under-dosed in critically ill children and neonates. British Journal of Clinical Pharmacology. 2019; 85(11): 2591-2598.
2) Harvey E, Ashiru-Oredope D, Hill L, et al. Need for standardised vancomycin dosing for coagulase-negative staphylococci in hospitalised infants. Clinical Microbiology and Infection, European Society of Clinical Microbiology and Infectious Diseases. 2023; 29(1): 10-12.