Neonatal vancomycin: exploring levels at NHS Tayside, Scotland

CP-118

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BACKGROUND

- Vancomycin is used to treat secondary Gram-positive infections
- Dosing recommendations at NHS Tayside are as per the British National Formulary for Children (BNFc) (see table below)
- BNFc target vancomycin trough level is 10-15mg/L[1]
- Low vancomycin levels are associated with treatment failure and high levels are associated with an increased risk of adverse effects

Corrected Gestational Age (CGA) (weeks)	Dosage (mg/kg)	Frequency
< 29	15	**24 hourly**
29 - 35	15	**12 hourly**
> 35	15	**8 hourly**

OBJECTIVES

- Review neonatal vancomycin dosing and pharmacokinetic modelling literature
- Audit Tayside vancomycin target trough achievement (based on BNFc dosing)
- Predict vancomycin levels for a Tayside sample using published pharmacokinetic models and compare predicted levels to actual levels
- Formulate recommendations for neonatal vancomycin dosing

METHOD

Sampling

- Retrospective data collection from medical notes
- Inclusion criteria:

- All babies within the neonatal unit that had at least one vancomycin level analysed

- Exclusion criteria:

- None, vancomycin dosing protocol is used for all neonates within the unit

Data collection

- Patient identifiers were obtained of all neonates that had a vancomycin level analysed from 1 January 2009 to 30 June 2012
- Identifiers were used to link blood levels to medical notes and medical notes were obtained and reviewed

Data analysis

- Data was analysed using Excel (2010) and STATA (version 12.0)

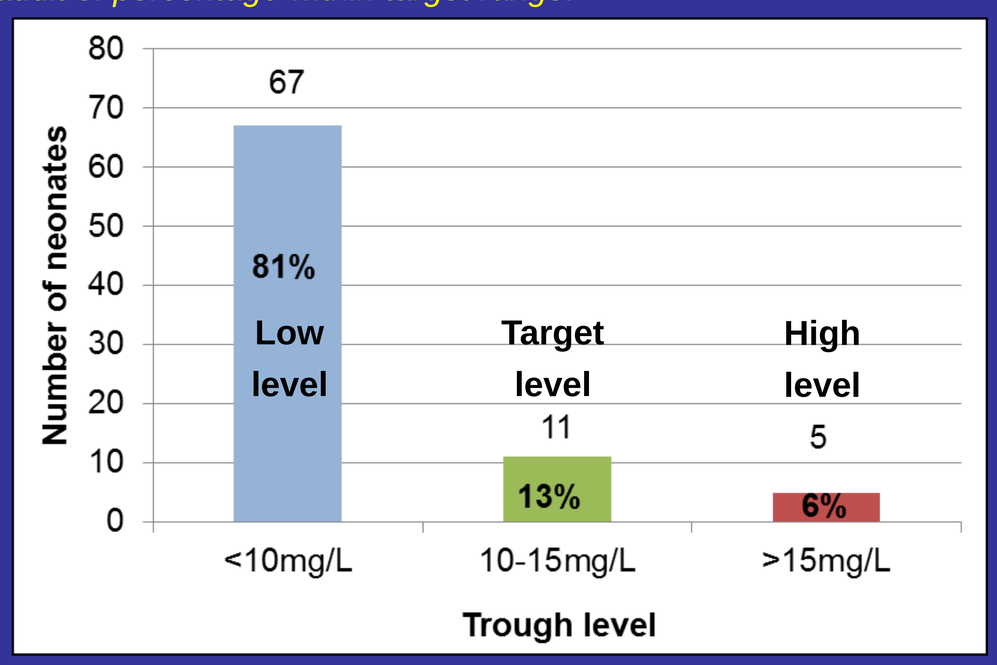
- Patient characteristics e.g. gestational age, CGA, dosing weight, serum creatinine
- Clinical audit of percentage of initial levels within target range
- Comparison of neonatal population pharmacokinetic models using signed and unsigned mean percentage prediction error
- Multiple linear regression of percentage prediction error from pharmacokinetic models against patient characteristics

RESULTS

Patient characteristics n=83:

Clinical Feature	Median	Range
Gestational Age (weeks+days)	28	23+1 – 41+3
Postnatal Age (days)	12	2 – 187
Corrected Gestational Age (gestational age + postnatal age) (weeks+days)	30+3	23+6 – 52+4
Dosing Weight (kg)	1.12	0.56 – 4.7
Serum Creatinine (µmol/L)	42	17 – 139

Clinical audit of percentage within target range:



RESULTS

Comparison of pharmacokinetic models:

- Of the published models considered, Grimsley and Thomson found serum creatinine impacts clearance whereas the other models found CGA[2-5]
- How well do the published population pharmacokinetic models predict observed trough levels for Tayside (using the individuals' actual dose received)?

Bias closest to zero And highest precision

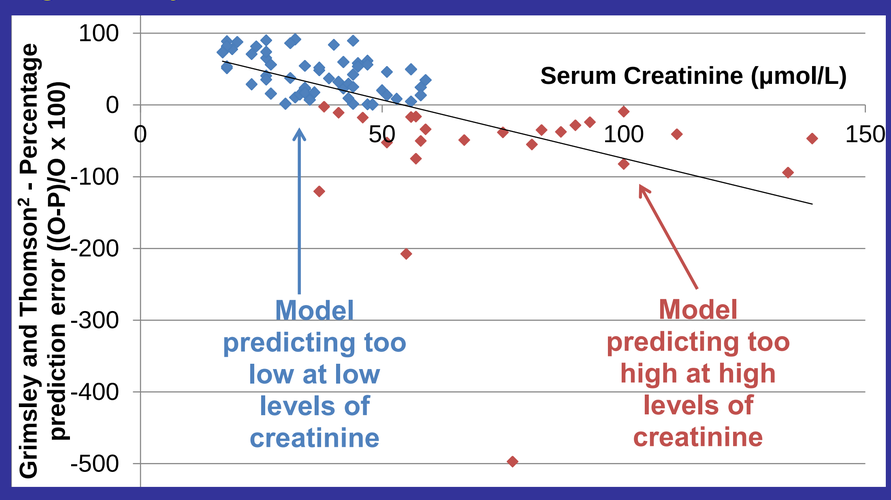
	Grimsley and Thomson[2]	de Hoog et al.[3]	Anderson et al.[4]	Seay et al.[5]
Mean percentage prediction error (100x(O-P)/O) (95% CI)	11.7 (-5.14 – 28.5)	-23.8 (-42.3 – 18.5)	-43.5 (-60.9 – -26.2)	-128 (-158 – -98.6)
Mean unsigned percentage prediction error	51.16	64.9	63.7	136

Bias – is it correct on average?

Precision – on average how close is it to the observed?

O is observed level
P is predicted level

- Grimsley and Thomson model is the best at predicting observed trough levels for the Tayside sample but it still contains significant prediction errors[2]
- The linear regressions showed that the percentage prediction errors within all models was significantly associated with serum creatinine



Dosing recommendations:

- The Grimsley and Thomson model was adjusted to account for the relationship between percentage prediction error and serum creatinine[2]
- Adjusted model was used to formulate a new dosing strategy with a 15mg/kg dose

Serum Creatinine (µmol/L)	Dosage (mg/kg)	Frequency
<40	15	8 hourly
40 - 80	15	12 hourly
> 80	15	Take a level 12hours post initial dose. Dose according to level with pharmacy advice if required.

DISCUSSION

- No published literature evaluating trough level achievement using BNFc dosing

Limitations:

- Actual dosing was not reviewed to ensure that neonates were dosed correctly
- The accuracy of the documentation and administration by staff could not be verified

CONCLUSION

- Current dosing based on BNFc is inadequate and is likely to be associated with treatment failure
- All evidence in this study suggests that serum creatinine is a better predictor of neonatal vancomycin clearance than CGA
- The new dosing strategy derived needs to be prospectively audited to measure potential improvements in target levels
- Significant uncertainty still exists around neonatal clearance and there is a need to better understand the causes of variation amongst neonates

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