Neonatal vancomycin: exploring levels at NHS Tayside, Scotland

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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
- Low vancomycin levels are associated with treatment failure and high levels are associated with an increased risk of adverse effects

### 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 |

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

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

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

### Clinical audit of percentage within target range:

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

DISCUSSION

- No published literature evaluating trough level achievement using BNFc dosing
- 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

### REFERENCES