



RACP Foundation Research Awards

FINAL REPORT

Project / Program Title	A comparison of continuous or intermittent infusions of vancomycin in neonates	
Name	Dr Amanda Gwee	
Award Received	2015 Basser Research Entry Scholarship	
Report Date	27 July 2018	
Chief Investigator / Supervisor	Amanda Gwee/Prof Nigel Curtis	
Administering Institution	The Royal Children's Hospital	
Funding Period	Start Date:	1 August 2015
	Finish Date:	1 August 2017

PROJECT SUMMARY

One of the common treatments for babies with serious infections is an antibiotic called vancomycin. My study is the first to compare two different ways of dosing vancomycin in babies to determine which is the most effective and safe way to give vancomycin to babies. I am also studying what levels of vancomycin we need in the blood to treat the bugs that cause infections in babies. I am developing an online tool so that the dose of vancomycin can be customised to individual babies so that each baby gets the best possible treatment for their infection.

PROJECT AIMS / OBJECTIVES

Part 1: Multicentre randomised controlled trial comparing intermittent infusions (IIV) to continuous infusions of vancomycin (CIV) in young infants

Primary aim

1. Therapeutic drug levels: To determine the proportion of young infants achieving target therapeutic vancomycin levels in blood at their first steady state level.

Secondary aims

To determine in relation to vancomycin in young infants the:

1. Adverse effects: Rate of drug adverse-effects including infusion-related side effects (red man syndrome) and renal toxicity.

2. Pharmacokinetics: Time taken to achieve target therapeutic vancomycin levels using non-linear mixed effects modelling (NONMEM).

Part 2: In vitro pharmacodynamic study of vancomycin for *Staphylococcus epidermidis*

Primary aim

To investigate the pharmacodynamic properties of vancomycin in vitro for *Staphylococcus epidermidis*, one of the most common coagulase-negative staphylococci causing sepsis in young infants.

SIGNIFICANCE AND OUTCOMES

Part 1: Randomised controlled trial comparing IIV to CIV in young infants

Of 111 infants randomized, 104 were included in the intention-to-treat analysis. Our study showed that CIV is associated with earlier and improved attainment of target concentrations compared with IIV. Lower total daily doses are required to achieve target levels with CIV. There is no difference in the rate of drug adverse effects. These findings are significant as they show a clear advantage of CIV over IIV and can be directly incorporated into clinical guidelines.

We intend to build the population pharmacokinetic model into a web application to trial the use of a model-based dosing regimen in the neonatal unit. The treating clinician will enter the post-menstrual age, creatinine level and weight of the patient into the web application and this will then generate a personalised vancomycin dose tailored to the baby.

Part 2: In vitro pharmacodynamic study

Our study found that vancomycin exhibits time-dependent killing of *S. epidermidis* isolates and no tolerance or resistance when these isolates were exposed to vancomycin concentrations less than 10 mg/L. This suggests that free drug levels just above the bacterial MIC are adequate to kill CONS isolates and therefore, for the treatment of CONS infections in neonates, lower target levels for vancomycin dosing may be sufficient.

We intend to further study this by doing an in vivo pharmacodynamic modelling study in young infants.

PUBLICATIONS / PRESENTATIONS

Part 1: Randomised controlled trial comparing IIV to CIV in young infants

There will be 3 publication from this trial.

The protocol has been submitted and is under final review in an open access journal.

The results of this trial has been submitted for publication and is currently under review.

The manuscript outlining the development of the pharmacokinetic model and model simulations is drafted and is currently under review by co-authors.

Part 2: In vitro pharmacodynamic study

The manuscript has been submitted for publication and is currently under review.