



RACP Foundation Research Awards

FINAL REPORT

Project / Program Title	Optimising vancomycin dosing in young infants using model-based dosing (through a web app) and earlier therapeutic drug monitoring	
Name	A/Prof Amanda Gwee	
Award Received	2020 RACP Research Establishment Fellowship	
Report Date	26/04/2021	
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	Finish Date:	01/01/2021

PROJECT SUMMARY

Bloodstream infections are one of the leading causes of death in babies worldwide. This project aimed to improve the treatment of serious infections in babies by optimising how one of the most commonly used antibiotics, vancomycin, is prescribed. Antibiotic dosing is challenging in babies due to changes in organ function with age, which ultimately affects the amount of antibiotic in babies' bodies. For this study, I developed a web application (app) for 'precision' dosing of vancomycin so that health workers could tailor the vancomycin dose to each individual child. The app was evaluated in four paediatric hospital and found to almost double the proportion of babies achieving effective antibiotic levels (41% to 75%). These results show that this innovative web app improves the treatment of children with serious infections by preventing over- and under-dosing.

PROJECT AIMS / OBJECTIVES

Due to the COVID-19 restrictions affecting clinical research studies in Victoria, I have completed study 1 which evaluated model-based dosing through an app (manuscript in preparation). Notably, we recruited 40 participants (instead of the 28 participants in the original proposal). In 2021, I will commence study 2, where I will evaluate the effectiveness of early drug monitoring and dose adjustment.

PRIMARY AIMS/OUTCOMES:

Aim: To determine the proportion of young infants achieving the target trough vancomycin concentrations (10 to 20 mg/L) at the first steady-state level using a model-based IIV dosing regimen through an app

Outcome: With model-based vancomycin dosing, 75% of young infants achieved target trough concentrations at their first steady state level (24 hours). This is a 34% increase in target attainment compared to that achieved with standard dosing using the British National Formulary for Children guideline.(41%).

SECONDARY AIMS/OUTCOMES:

Aim 1: The proportion of young infants with supra- (defined as >20 mg/L) or sub-therapeutic vancomycin concentrations at the first steady state level.

Outcome: 5/40 (12.5%) and 5/40 (12.5%) had supra- and sub-therapeutic levels, respectively.

Aim 2: The frequency of drug adverse effects (infusion-related and nephrotoxicity).

Outcome: No young infants experienced infusion-related drug reactions and 1/40 (2.5%) had reversible nephrotoxicity (rise in baseline creatinine level >1.5 x baseline).

SIGNIFICANCE AND OUTCOMES

This study showed that our app significantly improves the effectiveness of vancomycin dosing in babies. Our app supersedes existing dosing tools as it has now been validated in the world's first prospective, multicentre study of individualised vancomycin dosing using a web app in babies. Through improved dosing, it is anticipated that mortality and adverse outcomes related to serious staphylococcal bloodstream infections will be reduced and the emergence of drug-resistant bacteria prevented by ensuring early, effective antibiotic treatment.

In our study, we have collected health economic data (to be analysed in 2021) as we anticipate a reduction in treatment costs with the dosing app through reduced numbers of blood samples for vancomycin levels and reduced burden on clinical staff (in preparing new doses, as well as collecting and processing blood samples).

Importantly, the web app provides a platform to improve the dosing of other antibiotics through individualised dosing. We are already collecting data for these additional dosing calculators. Our study has demonstrated both feasibility and end-user acceptability of using a web app to improve antibiotic dosing in children. Further, we have built the app into our electronic medical record system to streamline the dosing process and ensure the long term sustainability and routine use of the app in clinical care.

PUBLICATIONS / PRESENTATIONS

Funding for this study has led to many advances in antibiotic dosing and monitoring in neonates:

1. New collaborations - the original proposal included 3 major neonatal units, however, due to significant interest in the study, we involved 4 study sites and recruited a greater number of participants (40 instead of 28) than originally planned.
2. Microsampling - through a new research collaboration with the University of Queensland we embedded a microsampling substudy within this study. Microsampling enables vancomycin levels to be measured using 20 times less blood (10 µl instead of 200 µl) of blood. This has incredible potential to transform our approach to vancomycin drug level monitoring and prevent adverse events related to blood sampling (e.g. anaemia) in babies.
3. Health economic analysis - to our knowledge, there are no studies that have evaluated the health economic impacts of individualised dosing using a web app. Ours will be the first study to report this.
4. Conference presentations - although our study findings have not been presented at this stage, the study methods have been presented at one conference (see below). Receipt of the Research Establishment Fellowship has led to significant advances in my research career, for which I am incredibly grateful to the RACP:
 1. Success in securing other research funding - NHMRC investigator grant (Emerging leadership 1). I was also a finalist for the Victorian Premier's Award for Health and Medical Research and the BUPA Emerging Health Researcher Award (awarded \$5000).
 2. Promotion to Associate Professor (level D, research and teaching) in the Department of Paediatrics, University of Melbourne just 2 years after graduating from my PhD.
 3. Promotion to team leader in the Murdoch Children's Research Institute where my team now comprises 2 research assistants and 4 PhD students.

ACKNOWLEDGEMENTS

Conference presentations:
2019 Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists - 'Dosing Antibiotics in Neonates' - invited oral.