Te Niwha

Research Project Impact Case Study

Patient reported preferences for intravenous or oral antibiotics in the treatment of *Staphylococcus aureus* bacteraemia: an exploratory descriptive qualitative study

Short Research Title

Patient reported preferences for IV or oral antibiotics in the treatment of *S. aureus* bloodstream infection

Key researchers

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Introduction

We are part of the international *Staphylococcus aureus* Network Adaptive Platform (SNAP) trial, aiming to find better treatments for *S. aureus* bacteraemia (SAB), a serious bloodstream infection that has high rates in New Zealand and a mortality of 15-20%. SAB is traditionally treated with very long courses of intravenous (IV) antibiotics. Compared with IV antibiotics, oral antibiotics may have less risk, cost, and inconvenience. There is increasing evidence that partial *oral* antibiotic treatment for SAB and other serious infectious diseases is safe and effective. Work by New Zealand researchers in healthy volunteers shows that 'boosting' oral antibiotics with probenecid, a traditional gout treatment which works by blocking the excretion of oral beta-lactam antibiotics by the kidney, achieves very high serum levels of antibiotic.

PR-O-SNAP is a SNAP sub-study measuring serum antibiotic levels from patients on IV antibiotics and oral antibiotics either with or without probenecid boosting (probenecid combination therapy, PCT). We hypothesise that probenecid will significantly raise the serum levels of oral antibiotics, up to the levels obtained by IV administration. We also undertook a qualitative study to understand patient preferences around IV and oral antibiotics.

Results

We have recruited 122 patients treated for SAB with IV and oral antibiotics. Patients were recruited from Middlemore, Wellington, Hutt and Tauranga hospitals. 70% were male; 13% are Maaori, and 20% are Pacific.

We have samples for 83 patients on IV cefazolin, 33 patients on oral cefalexin and 49 patients on oral cefalexin boosted with probenecid. Preliminary analysis shows that >95% of patients on oral cefalexin with and without probenecid spent >50% of the dosing interval above the MIC of the organism (recommended targets for treatment of SAB). Preliminary results do not permit accurate estimation of the proportion of patients spending 100% of the dosing interval above the MIC, however with cefalexin alone this number is likely to be under 50%, whereas with probenecid boosting, this number appears to be closer to 80%. Formal pharmacological modelling is now in process. We aim to publish the results for the IV cefazolin, oral cefalexin alone, and oral cefalexin + probenecid groups once this is complete.

We also have samples for flucloxacillin (not many, as flucloxacillin has fallen out of favour for treatment of SAB due to results from the main SNAP trial) and benzylpenicillin (17 patients), oral amoxicillin (4 patients) and oral amoxicillin boosted with probenecid (18 patients). Preliminary analysis also suggests more than adequate drug levels achieved with oral amoxicillin and suggest a boosting effect with probenecid in this group.

When the main SNAP trial publishes outcome results, we will also incorporate clinical outcome data into PR-O-SNAP.

For the results of the qualitative patient preference study, we interviewed 17 outpatients and one inpatient:

	Participants, n=18 (%)
Age in years (mean, range)	55.7, 22-86
Female	11 (61.1)
Ethnicity	
Māori	2 (11.1)
Pacific	5 (27.8)
NZ European	9 (50.0)
Indian/Fijian Indian	2 (11.1)
Place of residence	
South/East Auckland	11 (61.1)
Wellington and greater Wellington region	6 (33.3)
Tauranga	1 (5.6)

Table 1. Characteristics of PROSNAP patients participating in qualitative study

Impact

Despite growing evidence suggesting that oral antibiotic treatment is safe and effective in selected patients with severe infection, clinicians have been slow to adopt this paradigm. Hesitancy may be based around concerns about the quality of evidence so far, beliefs about the relative efficacy of IV and oral antibiotics, a reluctance to go against generations of traditional (but non-evidence-based) teaching, and clinician perspectives of patients' expectations. The PR-O-SNAP study will further reassure clinicians of the efficacy and safety of oral antibiotic treatment in SAB and other serious infections, by demonstrating that oral antibiotics (particularly when boosted by probenecid) achieve serum antibiotic levels well above recommended targets for SAB treatment (and in fact, very similar levels to those achieved with IV antibiotics). Oral treatment is cheaper, more convenient, safer, confers shorter hospital stays, is associated with less plastic waste, and is preferred by patients. It is easier to deliver at home and improves access to whanau support for those living remotely.

The qualitative work on patient preferences has elicited findings which will inform shared decision-making between clinicians and patients and has allowed patients to have a voice in research in New Zealand.

This project has allowed us to mentor an emerging Māori researcher (Ms Loughlin McGrath, Tapuiki, Te Arawa) and an emerging pharmacist researcher (Ms Natasha Pool, Counties Manukau Health). Valuable collaborations with Prof. Jason Roberts in Australia, Assoc. Prof. Mei Zhang, and Dr Paul Chin in Christchurch, the wider global SNAP team, and University of Auckland researchers (Dr Gigi Lim) have arisen from PR-O-SNAP activity. In this way, PR-O-SNAP has succeeded in its aim to *'Deliver integrated research programme in partnership with researchers, clinicians, Maori and Pacific people'* and *'Contribute to international research through collaborations in infectious disease research'.*