1. Introduction

• Persons with spinal cord injury (SCI) and neurogenic bladder have approximately 2-3 urinary tract infections (UTIs) per year on average.¹
• Current commonly used methods of non-antibiotic UTI prevention in SCI do not work.²
• SCI population has high numbers of multi-resistant organisms (MROs) colonisation and/or infections.³
• Non-antibiotic prophylaxis is preferable in preventing UTIs to avoid antimicrobial resistance burden.⁴
• Probiotics are preparation of micro-organisms in sufficient numbers that alter the microflora in a compartment of the host in order to exert beneficial health effects.⁵
• Falagas et al concluded Lactobacillus rhamnosus GR-1 and Lactobacillus fermentum RC-14 delivered intravaginally or orally, were efficacious in preventing UTIs in women.⁶
• Manley et al demonstrated clearance of vancomycin resistant enterococci in stool after treatment with Lactobacillus rhamnosus GG.⁷

2. Methods

• ProSCIUTTU was a multi-site, randomised, double-blind, double-dummy, placebo controlled factorial design trial
• Participants were recruited from SCI community in the state of New South Wales, Australia.
• Commenced in April 2011 and concluded in February 2014.
• Registered with Australian New Zealand Clinical Trials Registry (ACTRN 1261000512022).

Aims:
1. To test effectiveness of Lactobacillus rhamnosus GR1 + Lactobacillus reuteri RC14 (RC14GR1) AND/OR Lactobacillus rhamnosus GG + Bifidobacterium BB12 (LGBBB2) versus placebo in preventing UTI in persons with SCI
2. To examine whether probiotics change colonisation with MROs

Participants:
• Inclusion criteria – over 18, known neurogenic bladder, stable SCI and bladder management, agreed not to take other probiotics
• Exclusion criteria – immunosuppression, long-standing infection on antibiotics, multi-resistant organisms (MROs) colonisation and/or infections.

Intervention:
• Each participants had to take two tablets daily and was enrolled for 24 weeks
• Participants were randomised into one of four groups:
  - Group A (RC14GR1 + LGBBB2)
  - Group B (RC14GR1 + placebo)
  - Group C (LGBBB2 + placebo)
  - Group D (double placebo)
• Participants had to provide microbiological swabs of rectum, nose, groin and urine cultures at 0,3,6 months. Urine cultures were also performed at study endpoint.
• Participants had to complete Short Form Health survey (SF-36) at 0, 6 months and study endpoint.
• Simple stratified (computer generated) randomisation protocol was used. Randomisation was stratified by bladder management types and inpatient/outpatient status.

Primary Outcome:
• Time from randomisation to occurrence of “symptomatic” UTI which was based on symptoms and microbiological diagnosis.

Analysis was by intention to treat and primary outcome was analysed using survival analysis with SAS 9.3.

3. Results

Patient demographics:
• Predominantly male (79%)
• Community dwelling (81%)
• Bladder management was mainly by indwelling or suprapubic catheters (60%)
• 47% of participants were tetraplegics
• 51% of participants had complete injuries.
• Mean time since injury was 12.3 years (95% CI: 10.5-14.1)
• Mean age 49.1 years (95% CI: 47.0-51.2)

Univariate analysis:
• RC14GR1 revealed treatment direction positive, with unadjusted hazard ratio 0.71 (95% CI: 0.41-1.23). However, log rank test statistic was not significant (p=0.22)
• LGBBB2 revealed treatment direction negative, with unadjusted hazard ratio 1.27 (95% CI: 0.74-2.18). However, log rank test statistic was not significant (p=0.39)

Multivariate analysis using Cox proportional hazards regression, adjusting for gender, inpatient status, bladder management, completeness of injury, time since injury and UTI 6 months prior to trial showed no significant effect of:
• RC14GR1 compared to placebo (adjusted HR 0.68, 95% CI: 0.39-1.19; p=0.17)
• LGBBB2 compared to placebo (adjusted HR 1.30, 95% CI: 0.74-2.26; p=0.36)

Post hoc multivariate analysis of RC14GR1 against three other treatment groups showed treatment direction positive, with adjusted HR of 0.46 (95% CI: 0.21-0.99, likelihood ratio chi square statistic significant p=0.03).

Adverse events:
• Majority of adverse events that led to participants discontinuing trial were bowel complaints like accidents and increased bowel motility. Other adverse events were symptoms of UTI and abdominal cramps. Two deaths were unrelated.

4. Discussion

• From this trial, there is no effect found of RC14GR1 or LGBBB2 for preventing UTI in this patient population using factorial design.
• Limitation of study – did not reach target recruitment of 370 participants.
• There remains the possibility that RC14GR1 may be a beneficial probiotic for preventing UTI when used alone, but this trial was not designed to test this hypothesis.

References