Abstract: PROSPECT Pilot Results

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Background: Probiotics are live microorganisms that may confer health benefits when ingested. Randomized trials in critically ill patients suggest that probiotics decrease the incidence of ventilator-associated pneumonia (VAP) by 25% and the overall incidence of infection by 18%. However, these trials were small, mostly single-center, and at risk of bias. The aim of the PROSPECT Pilot Trial was to determine the feasibility of conducting a larger trial of probiotics to prevent VAP in mechanically ventilated patients in the intensive care unit (ICU).

Methods: We randomized patients who were expected to be mechanically ventilated for ≥72 hours to receive either $1x10^{10}$ colony forming units (CFU) of *L. rhamnosus* GG (Culturelle, Locin Industries Ltd) or an identical placebo, twice daily via gastric or duodenal tube. Patients were excluded if they were at increased risk of *L. rhamnosus* GG infection or had strict contraindications to enteral medication. Patients, families, and clinical and research staff were blinded. Feasibility objectives were: 1) Recruitment of at least 150 patients over 1 year; 2) Successful protocol adherence (administration of ≥ 90% of prescribed doses); 3) Minimal contamination (<5% of patients receive an open-label probiotic); and 4) An overall VAP rate of ≥10%. Clinical outcomes, which will be the focus of the main trial, were all respiratory and other infections, diarrhea (total, antibiotic-associated and *Clostridium difficile*), ICU and hospital length of stay and mortality.

Results: We randomized 150 patients from 14 centers in Canada and the US (informed consent rate of 83.3%). All feasibility goals were met: 1) Recruitment was achieved in 1 year; 2) protocol adherence was 97.4%; 3) No patients received open label probiotics; 4) The VAP rates ranged from 10-40% depending on the definition.

Conclusions: The PROSPECT Pilot Trial supports the feasibility of a larger trial to investigate the effect of enteral *L. rhamnosus* GG on VAP and other nosocomial infections in mechanically ventilated critically ill patients.

Trial Registration: The Pilot Trial is registered at www.clinicaltrials.gov. Trial registration number: NCT01782755

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