Modeling Changes in Gastrointestinal and Respiratory Tract Bacterial Community Diversity Attributable to Common Antibiotic Exposures During Long-Term Acute Care

Erik L. Clarke1, Emily Reesey1, Ebbing Lautenbach1,2, Magda Wernovsky2, Brendan J. Kelly1,2

Divisions of Epidemiology1 and Infectious Diseases2, Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

Introduction

Background

Reduced gastrointestinal tract bacterial community diversity has been associated with increased risk for healthcare-associated infections. We sought to develop a model for concomitant change in bacterial community diversity at gastrointestinal and respiratory tract sites, drawing upon the first 30 of a recently completed cohort study of 92 mechanically-ventilated subjects recruited from a long-term acute care hospital (LTACH) for dense longitudinal oral, endotracheal aspirate (ET), and stool specimen collection.

Methods

We assessed bacterial composition via amplicon sequencing of the 16S rRNA gene, and resolved amplicon sequence variants (ASVs) using DADA2 (1.6.0) and the Silva database (v128). Diversity was calculated as the effective number of species, D, by exponentiating the Shannon diversity H:

\[ D = e^H = e^{\sum (p_i \log p_i)} \]

We fit a Bayesian multilevel, autoregressive model of D for each specimen j and subject i as a function of antibiotic k, administration duration q, and the previous value of D:

\[ D_{ij} = \text{LogNormal}(\alpha_i + \beta_i q_j + \beta_{ij} D_{i,j-1}, \sigma) \]

Subject intercepts \( \alpha_i \) and slopes \( \beta_i \) were partially pooled among subjects. Hamiltonian Monte Carlo via Stan (B.17) and R (3.5.0) was used to fit the model. Each chain fit without divergences and all parameters had an Rhat less than 1.1.

Changes in diversity due to antibiotic exposure

Oral swabs

- Loss of diversity from piperacillin/tazobactam
- Increase in diversity with IV vancomycin and cefepime
- Diversity increases more for patients starting with more GN bacteria

Endotracheal aspirate

- Loss of diversity after 4+ days of cefepime and pip-tazo administration, with some strong individual subject outliers
- High subject-level variability in response to vancomycin

Stool swabs

- Wide range of responses to amoxiclav and vancomycin between subjects
- 3+ days of vancomycin lowers diversity

Discussion

- Antibiotics have substantially different effects on diversity depending on body site and individual subject
- Longer courses of antibiotics do not always lower diversity
- Positive effects of antibiotics on diversity may be due to multiple factors:
  - Clearance of dominating bacterial infection
  - Patient recovery and associated diversity increase
- Subject-level variance from group response may indicate abnormal community structure or infection

Next steps:

- Expand model to the remainder of the cohort
- Explore causes of between-subject-level deviations
- Directly model bacterial abundances as function of antibiotic exposure

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