Socioeconomic Status Factors Associated with Increased Incidence of Community-Associated Clostridium difficile Infection

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Background. Recurrent Clostridium difficile infection (rCDI) poses major challenges to healthcare providers and patients. Fecal Microbiota Transplantation (FMT) is an effective therapy for rCDI, but the exact mechanism of its efficacy is unknown. Current metagenomics literature indicates that abundance of Bacteroidetes and Firmicutes may protect against CD proliferation and recurrence. However, this is too broad to be useful for developing refined and targeted microbial-specific therapy for rCDI, because the long-term safety of FMT remains unknown. We examined the phylogeny of bacteria pre- and post-FMT to determine the key organisms associated with successful FMT to the genera level.

Methods. A subset of patient stool samples (n = 35) from a phase 2 study comparing fresh vs. frozen FMT for rCDI was sequenced at four time points: pre-FMT; at day 10; at week 5; and at week 13, following the last FMT. The matching donor stool was sequenced simultaneously with the corresponding patients’ pre- and post-FMT samples.

Results. Using the binary outcome to a single FMT as the response, we developed an in-house machine learning algorithm, $\Phi$-LASSO, to isolate key genera using the bacterial phylogenetic structure. Engraftment was defined as: newly detected operational taxonomic unit (OTUs) in the patient post-FMT, which were present in the donor but undetected in the patient pre-FMT. Augmentation was defined as: non-donor OTUs whose levels substantially increased post-FMT. Figure 1 (below) displays the distribution of engrafted and augmented OTUs at varying thresholds. We observed increases over time points within each threshold level.

Figure 1: Observed (a) engraftment of distinct donor OTUs on patients and (b) augmentation of distinct OTUs in patients for day 10 (D10), week 5 (W5), and week 13 (W13) post-treatment.

Conclusion. In this preliminary study, using $\Phi$-LASSO, we have shown that specific microbes to the genera level are uniformly present in successful FMT. This information may lead to developing refined and targeted microbial-therapy for rCDI.

Disclosures. All authors: No reported disclosures.

1247. Lyophilized Fecal Microbiota Transplantation Capsules for Recurrent Clostridium difficile Infection
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Background. Fecal microbiota (FM) transplantation (FMT) is a highly effective treatment of recurrent C. difficile infection (rCDI). We have published data showing efficacy of fresh, frozen and lyophilized donor microbiota administered by colonoscopy. Most groups are moving toward use of frozen product given by enema and in evaluating encapsulated product for oral delivery.

Methods. This was a prospective, randomized study of subjects with rCDI (≥ 3 episodes) treated with encapsulated lyophilized FM 100 g given once or 100 g given on two successive days (total 200 g) vs. frozen FM product 100 g given by single enema by 100 g of frozen product (P = 0.239). In the second phase of the study cure rate for oral capsules 200 g FM was 17/19 (91%) vs. 20/21 (94%) for the subjects treated by enema by 100 g of frozen product (P = 0.782). No side effects were felt to be related to the procedure or the FMT products were recorded during 6 months follow-up. Two subjects died during follow-up between 3 and 6 months after study due to underlying medical conditions felt to be unrelated to FMT. Microbiota analysis were performed on 40 subjects of which 19/40 (48%) had received capsules. Figure 1 showed that restoration of the intestinal microbiome diversity and Taxa began apparent by 2 days after FMT in both groups and resembled the donor product by 2 weeks with stabilization of the microbiota diversity and Taxa persisting for the 90 days of observation.

Conclusion. Administration of encapsulated, lyophilized FM resulted in durable restoration of intestinal microbiome diversity comparable to results seen with frozen product given by enema.

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