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Session: 148. C. difficile: From the Bench to Bedside
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Background. Fecal microbiota transplantation (FMT) has shown to be effective for recurrent Clostridium difficile infection (rCDI). However, significant costs for donor screening and a lack of suitable donors and laboratory facility have restricted the availability of the treatment. In order to expand access to FMT, we have investigated the efficacy of lyophilized FMT, comparing it to the published historical efficacy of frozen FMT in preventing further episodes of CDI in patients with rCDI. This study was designed to be open-labeled to expedite and minimize costs associated with conducting a two-armed randomized controlled trial, given that the efficacy of frozen FMT is known to be 85%. Additionally, using lyophilized FMT offers two major advantages: 1) its prolonged shelf life reduces cost because fewer donors need to be screened, and 2) it can be transported without freezing.

Methods. This is an open-labeled, prospective study involving 50 patients with a history of 2 or more rCDI who have failed at least 1 course of tapered vancomycin therapy. Eligible patients received lyophilized FMT via retention enema within 8 days of each treatment and were followed for 13 weeks post last FMT to determine efficacy and safety of FMT.

Results. The efficacy of lyophilized FMTs in preventing further episodes of CDI in patients with rCDI was 80%. The adverse events associated with lyophilized FMT were similar to frozen FMT.

Conclusion. Lyophilized FMT in treating rCDI showed similar efficacy and safety to frozen FMT. Lyophilized FMT appears to be promising in preventing further episode of CDI and increasing accessibility for patients with rCDI.

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1255. Probiotics to Reduce Clostridium difficile Infection: Clinical Experience in a Tertiary Care Center
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Background. There is conflicting clinical data regarding the efficacy of probiotics to prevent Clostridium difficile infection (CDI). The goal of this study is to compare rates of hospital acquired Clostridium difficile infection (HA-CDI) among patients receiving antibiotics with or without concomitant administration of probiotics.

Methods. This is a retrospective chart review of hospitalized patients who received antibiotics alone vs. antibiotics plus a multi-strain probiotic preparation of lactobacillus over a six month time period. Probiotics were given at the discretion of the physician. The primary outcome was incidence in HA-CDI (defined as onset after hospital day three) between groups.

Results. A total of 1,576 patients met selection criteria, with 927 patients receiving antibiotics alone and 649 patients receiving antibiotics plus probiotics. HA-CDI rates were 0.9% and 1.8% (P = 0.16), respectively. In a subgroup analysis of patients in the antibiotic only group, 33 patients who received similar antibiotic exposure as the probiotics group (n = 284) had no difference in rates of HA-CDI (1.8% vs. 1.8%, P = 1.0). 

Conclusion. Probiotic administration did not decrease rates of HA-CDI in our institution. We recommend prioritizing resources to other CDI reduction measures such as decreasing antibiotic exposure and preventing transmission.

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1256. Efficacy of Oral Vancomycin, Oral Metronidazole, or IV Metronidazole Prophylaxis at Reducing the Risk of Clostridium difficile Recurrence
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Background. Secondary prophylaxis (SP) for Clostridium difficile infection (CDI) with oral vancomycin or oral/IV metronidazole when initiating antibiotics is common, though few studies are available to support this practice. The purpose of this study was to assess the efficacy of prophylaxis within a year of index CDI.

Methods. This retrospective chart review looks at subsequent courses of antibiotics and CDI in patients with initial positive CDI testing in 2013–16. A positive CDI test within 90 days of antibiotics was a recurrence. The use of antibiotics for SP was noted, along with other factors associated with CDI relapse. Non-parametric exact tests were used for univariate analysis. These variables were included in a multivariate proportional hazards model.

Results. We found 597 antibiotic episodes in 230 patients. 130 episodes (21.8%) received antibiotics alone and 649 patients receiving antibiotics plus probiotics. HA-CDI rates were 0.9% and 1.8% (P = 0.16), respectively. In a subgroup analysis of patients in the antibiotic only group, 33 patients who received similar antibiotic exposure as the probiotics group (n = 284) had no difference in rates of HA-CDI (1.8% vs. 1.8%, P = 1.0). 

Conclusion. Probiotic administration did not decrease rates of HA-CDI in our institution. We recommend prioritizing resources to other CDI reduction measures such as decreasing antibiotic exposure and preventing transmission.

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1257. Tetracyclines are Associated with a Reduced Risk of Clostridium difficile Infection: A Systematic Review and Meta-analysis
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Background. Efforts towards antibiotic stewardship help reduce risk of Clostridium difficile infection (CDI) but there is a need to delineate antibiotic choices to reduce CDI risk. Tetracyclines may be associated with a low risk for CDI but the evidence is conflicting. We conducted a systematic review and meta-analysis to determine the relationship between tetracyclines use and CDI.

Methods. A systematic search of Medline, Embase, and Web of Science was performed from January 1978 up to December 2016 including studies assessing the association between tetracycline and CDI; compared with other antibiotics; to assess the risk of CDI after exposure to tetracyclines vs. other antibiotics. Study quality was assessed using the Newcastle-Ottawa scale. Weighted summary estimates were calculated using generalized inverse variance with random-effects model using Review Manager version 5.3 (Cochrane Inc).

Results. Six studies; 4 case control and 2 cohort studies reported the association of CDI with tetracyclines or other antibiotics prior to CDI including patients from 1993 to 2012. Meta-analysis of all studies using the random-effects model demonstrated that tetracyclines were associated with decreased risk of CDI compared with other antibiotics (OR, 0.62; 95% CI, 0.47–0.81; P = 0.005). There was significant heterogeneity among the studies, with an I² of 53% (Figure 1). No publication bias was seen.

Subgroup analysis of studies evaluating the risk of CDI with doxycycline only demonstrated a decreased risk of CDI with doxycycline compared with other antibiotics (OR, 0.55; 95% CI, 0.40–0.75; P = 0.0002). A subgroup analysis based on CDI diagnosis definitions revealed a decreased risk of CDI with tetracyclines (OR, 0.59; 95% CI, 0.44–0.80; P = 0.0006) in studies that used clinical definitions (presence of diarrhea with a positive stool test), but not among the studies that used ICD-9 codes for CDI diagnosis (OR, 0.95; 95% CI, 0.45–2.01; P = 0.90).

Conclusion. Tetracyclines are associated with a lower risk of developing CDI compared with other antibiotics. It is reasonable to use these over other antibiotics when appropriate (community acquired pneumonia, bronchitis, chlamydia, rickettsial or spirochetal infections) to reduce CDI.

Forest plot demonstrating decreased odds of CDI with tetracyclines use by a random-effects model

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1258. Durability and Long-Term Clinical Outcomes of Fecal Microbiota Transplantation (FMT) Treatment in Patients with Recurrent C. difficile Infection
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Background. Fecal microbiota transplant (FMT) has been shown to be safe and effective for treatment of recurrent C. difficile infection (RCDI). The aim of this study is to determine factors impacting the durability of FMT and assess patient long-term clinical outcomes with the satisfaction.

Methods. Eligible patients who received FMT for RCDI at Emory Hospital between July 1, 2012 and December 31, 2016 were contacted via telephone for a follow up survey. Of 232 patients who received FMT, 27 were deceased and 15 were unable to be contacted, leaving 190 patients for analysis.

Results. Of the 190 patients, 142/190 (74.7%) patients had completed at least one year follow up survey. Of those, 130/142 (91.3%) patients were satisfied with the treatment. Of those who were not satisfied, 9/142 (6.3%) patients cited the need for a second FMT as the reason for dissatisfaction, 8/142 (5.6%) patients did not like the experience of FMT, and 8/142 (5.6%) patients cited other reasons.

Conclusion. The majority of patients are satisfied with FMT. However, additional research is needed to identify factors that impact durability and satisfaction with FMT.

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to be reached with listed phone number. Of the remaining 190 eligible patients, 137 patients completed the survey.

Results. The median time-period between FMT and follow up was 22 months. Median number of failed antibiotic courses for RCDI post FMT was 4. Overall, 82% (113/137) of patients experienced resolution of RCDI post FMT (non-RCDI group) while 18% (24/137) of patients had recurrence of CDI post-FMT (RCDI group). In the RCDI and non-RCDI groups, antibiotic use post-FMT for non-CDI-related infections was 75% and 38% (P = 0.0004), respectively. PPI use post-FMT was 38% and 31% (P = 0.28), and probiotic use post-FMT was 63% and 41% (P = 0.026) in the RCDI and non-RCDI groups, respectively. There were 18 hospitalizations in the RCDI group and 9 were related to C. difficile complications; of the 36 hospitalizations in the non-RCDI group, only 1 was related to chronic complication of a previous C. difficile infection. Overall, 11% of patients reported improvement or resolution of medical conditions not related to CDI post-FMT while 33% reported diagnosis of a new medical condition or development of new symptoms; none of the new medical conditions or symptoms were attributable to the procedure. In all, 95% of patients indicated willingness to undergo FMT in the future if they experience another bout of C. difficile infection.

Conclusion. The findings show that FMT is a highly effective treatment option for RCDI with a cure rate, defined as resolution of RCDI post-FMT or recurrence attributable to antibiotic use post-FMT, of 96% (131/137) in the study group. Furthermore, clinical outcomes and patient satisfaction post-FMT indicate the safety of the procedure.

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1259. Clinical and Economic Evaluation of commercialized Fecal Microbiota Transplant (cFMT) for Patients with Recurrent Clostridium difficile Infection (CDI) in a Large Community Hospital
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Background. Recurrent CDI is common despite antibiotic therapy; FMT is effective to reduce recurrent infections. We report our experience with Commercialized FMT (cFMT) products by providing ready-to-use capsules, for oral administration, or solution, for administration via colonoscopy.

Methods. The study was approved by IRB for adult patients with at least 3 episode of recurrent CDI despite antibiotic therapy, patients with severe infection were excluded. cFMT was administered in the hospital or at outpatient center. Each patient was evaluated 8 weeks post-transplant to assess for sustained clinical cure and side effects. The economic impact of FMT was evaluated using historical data from EHR including: CDI rate, CDI readmission rate, rate of CDI-associated death, cost of CDI admissions, and rate of use of each antimicrobial regimen.

Results. 33 patients enrolled (solution/colonoscopy 20 and capsule 13). Mean age was 74 vs. 67 y; female 56% vs. 64%, recurrent episode 4 vs. 3.1, CDI severity score 1.4 vs. 1.2. 95% (19/20) of patients who received cFMT via colonoscopy experienced sustained clinical cure vs. 85% (11/13) of patients who received capsule. One patient experienced an adverse event from capsule with nausea and vomiting, which resolved without sequelae. 2 of the 3 patients that experienced treatment failure received cFMT from the same donor Due to recurrent episodes. The cost of cFMT was $635 for capsules and $485 for solution which was far less than recurrent CDI associated costs.

Conclusion. cFMT is a viable alternative to traditional FMT and was both clinically and economically beneficial in patients with recurrent CDI in a community hospital. Further studies needed to confirm above findings.

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1261. Weight Changes in Fecal Microbiota Transplant for Cl. difficile
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Background. Fecal microbiota transplant (FMT) for relapsing Cl. difficile infections (CDI) allows for rapid repopulation of the colon microbiome and may prevent future relapses. FMT is considered safe, however subsequent impact on weight and metabolism is incompletely understood. Animal studies have shown that alterations in microbiota lead to changes in weight; this is also suggested in humans, based on limited anecdotal evidence. This study explores changes in weight associated with FMT.

Methods. We conducted a retrospective observational study of patients who underwent FMT at our 1100-bed community-based academic healthcare system. FMT protocol requires 2 documented CDI relapses and failed vancomycin taper. FMT methods include colonoscopy, EGD and oral capsules. Of note, donor stool (OpenBiome, Boston, Massachusetts) criteria include BMI ≤30. We conducted chart review for documented provider-measured weights pre- and post- FMT (≤ 1 year), and compared FMT weights to last recorded weight within 1-year period. We also evaluated weights in a subset of patients in the acute (2-6 week post FMT) timeframe.

Results. Between Apr 2014 - Oct 2016, 41 patients underwent FMT. Of these, 31 (75%) patients had adequate weight data available for review (Table). Overall patients gained an average 2.4%. During the acute phase, 20 patients (65%) had documented weights; of these 50 lost and 50 gained weight, with overall weight loss of 0.7%.

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1260. Fecal Microbiota Transplantation (FMT) for Recurrent/Refractory Clostridium difficile Infection (CDI) in Pediatric Immunocompromised Patients: A Single-center Experience
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Background. CDI is a common cause of bacterial diarrhea, especially in immunocompromised patients. Fecal Microbiota Transplant (FMT) has been shown to be an effective treatment for recurrent and refractory CDI. The outcomes of FMT treatment for recurrent CDI have been well described in adult populations; however, the data for immunocompromised (IC) patients especially among children are limited. We describe the experience of FMT for treatment of CDI in immunocompromised pediatric patients.

Methods. We collected clinical data for IC patients <21 years in our pediatric institution who had received FMT for recurrent, refractory, and/or severe CDI. IC patients included those with: solid organ transplantation (SOT) receiving immunosuppressive medications; neoplasm; hematopoietic stem cell transplantation (HSCT); inflammatory bowel disease (IBD) requiring immunosuppressive medication(s). We collected demographic and clinical data, as well as outcomes, including: resolution of diarrhea, CDI relapse, and adverse events within 3 months post-FMT.

Results. We performed 37 pediatric FMT for recurrent, refractory, and/or severe CDI between September 2012 and February 2017. Of these, 12 were immunocompromised children: 2 with SOT; 3 with neoplasm and/or HSCT; and 7 with IBD on immunosuppressive medication(s). Median age was 11.9 years old (range 3–16 years). 6 (50%) experienced resolution of diarrhea within 1 week post-FMT, and 9 (67%) were C. difficle-negative within 3 months of FMT (3 patients did not have follow-up testing). None had CDI relapse within 3 months post-FMT. 3 (25%) had adverse event(s) within 3 months post-FMT; 2 of whom had SAEs: 1 had graft rejection at 2 months post-FMT which ultimately required re-transplantation and 1 had aspiration pneumonitis immediately following FMT. 4 (50%) of the IBD patients had disease remission (clinical, biologic, and/or histologic) in the 3 months post-FMT.

Conclusion. FMT appears to be effective and reasonably safe for recurrent CDI in immunocompromised pediatric patients. However, the small numbers limit conclusions, especially about safety. Larger multi-center studies are needed to precisely determine safety and efficacy in this specialized population.

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