2432. Durability Against Antibiotics After Response to Fecal Microbiota Transplantation in Recurrent Clostridioides difficile Infection

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Background. Fecal microbiota transplantation (FMT) cures ~90% of patients with recurrent *Clostridioides difficile* infection (rCDI). Ongoing or repeated exposure to risk factors, especially antibiotics (a modifiable risk factor but often necessary), may lead to future CDI. However, it is not known if FMT provides durable protection against future CDI despite subsequent antibiotic exposure. We studied the long-term durability of FMT against antibiotic exposure post-FMT.

Methods. A retrospective cohort study of patients undergoing FMT via colonoscopy for rCDI from Sep 2012 - Jun 2018 was performed. Patients were followed up for 1 year after FMT; data regarding future CDI episodes (watery diarrhea with positive stool test after interim symptom resolution), healthcare exposure, systemic non-CDI antibiotics and acid blocker therapy were collected. Primary outcome was 'durability' of response to FMT (defined as no CDI within 1 year post-FMT). Descriptive statistics, Chi square test, Wilcoxon test and multivariate logistic regression were used as appropriate.

Results. The study included 460 patients; median age 57 years (range 18–94 years), 65.2% (300) female. Overall 31.6% (144) received antibiotics; median number of courses of antibiotics, 2 (range 1–7). Of those who received antibiotics, the incidence of future CDI was 24.3% (n = 34), compared with 9% (n = 28) of those who did not receive antibiotics (P < .001). Median time to first CDI episode post-FMT was 103 (range 5–338) days. Incremental antibiotic courses did not lead to increased risk of future CDI (comparing 1, 2 or ≥3 courses, p = .68). In patients with antibiotic exposure, age and risk factors were similar in patients with and without future CDI (Table 1). Amongst those without antibiotic exposure, inflammatory bowel disease (IBD) predicted future CDI (p = .02). After controlling for risk factors and comorbidities, antibiotic use (p = .004) and IBD (p = .02) independently increased risk of future CDI.

Conclusion. The majority of patients with rCDI have a durable response to FMT despite ongoing risk factors. These data suggest that three-fourth of patients who receive antibiotics after FMT do not develop future CDI. IBD and antibiotic exposure independently increase the risk of future CDI.

Table 1: Comparison of patients with and without future CDI in those receiving antibiotics post-FMT (n=144)

	Without future CDI % (n)	With future CDI % (n)	P value
Age	59 (23-94)	58.5 (22-90)	0.29
Sex female	66.0 (70)	58.8 (20)	0.44
Number of antibiotic courses	2 (1-7)	2 (1-7)	0.64
Acid blocker therapy	42.5 (45)	38.2 (13)	0.66
Healthcare exposure	100 (105)	100 (33)	-
Liver disease	17.9 (19)	32.4 (11)	0.07
Cancer	17.9 (19)	11.8 (4)	0.39
Dialysis	6.6 (7)	11.8 (4)	0.33

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2433. Oral Vancomycin Plus Intravenous Metronidazole for Severe Clostridioides difficile Infection in Critically Ill Patients

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Background. Molecular strain 027/NAP1/BI (NAP1) is a common cause of *Clostridioides difficile* infections (CDI). Despite high morbidity and mortality, optimal therapy remains elusive. There is also a paucity of data regarding optimal treatment of critically ill patients with severe CDI. We aimed to determine the impact of combination therapy (intravenous metronidazole [IV MTZ] plus oral vancomycin [PO VAN]) on clinical outcomes in critically ill patients with severe CDI, including those with NAP1 CDI.

Methods. Retrospective cohort of adult patients admitted to an intensive care unit (ICU) from April 2016 to October 2018 with a positive *C. difficile* PCR and an order for PO VAN. Patients with an order for IV MTZ for at least 72 hours formed the combination therapy group. A subset of patients had stool samples collected for NAP1 identification via GeneXpert *C. difficile* Epi molecular assay. The primary outcome was 30-day in-hospital mortality. A subgroup was matched using Acute Physiology and Chronic Health Evaluation (APACHE) II Scores. Cox regression was conducted to identify variables associated with time to mortality.

Results. 138 patients were included; 60 (43.5%) received IV MTZ. Patients with IV MTZ had a higher median WBC count at diagnosis (20.9 vs 15.9, P = 0.0002) and were more likely to receive a higher dose of PO VAN (31.7% vs 12.9%, P = 0.008). 42 patients had NAP1 testing, 11 were positive (26.2%). There was no difference in probability of receiving IV MTZ based on APACHE II, however, NAP1+ were more likely to receive IV MTZ (50% vs 16.7%, P = 0.049). Clinical success was higher in the monotherapy group (46.8% vs 16.7%, P = 0.002). There was no difference in mortality (20% vs 14.1%, P = 0.368). In a subgroup of patients matched by APACHE II (n = 96), mortality remained non-significantly different (18.8% vs 14.6%, P = 0.785). Adjusted for IV MTZ, APACHE II (aHR = 1.06, 95% CI 1–1.12) and number of severity criteria (aHR = 2.08, 95% CI 1.40 – 2.97) were associated with mortality. There was no difference in mortality (9.1% vs 3.2% P = 0.459) or clinical success (18.2% vs 33.7%, P = 0.283) among NAP1+ vs. NAP- patients.

Conclusion. Our data questions the utility of IV MTZ with PO VAN for ICU patients with severe CDI, including NAP1 infections. There remains a possibility for confounding by indication in our analysis.

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2434. Proton Pump Inhibitor Use on Efficacy of Fecal Microbiota Transplant Administered by Trans-Oral Routes for Clostridioides Difficile Infection: A Systematic Review and Analysis

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Background. Current guidelines include fecal microbiota transplantation (FMT) in the management of recurrent Clostridioides difficile infections (CDI). However, FMT protocols are often facility dependent, and one variable is whether proton pump inhibitors (PPI) are given during preparation. Theoretically, PPIs reduce acidity and protects the transplanted microbiome for the most potent dose. On the other hand, PPIs have also been shown to negatively alter the microbiome and increase the risk of CDI. We conducted a systematic review of the literature to study PPI use on the efficacy of FMT delivered by the trans-oral route.

Methods. We searched PubMed/Medline, Cochrane Library, Embase, Scopus, and Web of Science through December 16th, 2018 using variations of keywords "fecal microbiota transplant" and "Clostridium difficile infection" with 4210 results. Two independent authors reviewed and excluded studies with unrelated topics, abstracts, case reports, or a low level of evidence. Studies with data on trans-oral FMT, PPI use, and the success rate were included. Final review yielded 11 studies including randomized controlled, case–control, cohort, retrospective and prospective trials. The primary outcome was the rate of FMT failure, defined as recurrence of symptoms with positive CDI testing at follow-up.

Results. Out of 233 included patients, 131 received a PPI per FMT protocol resulting in 27 cases of treatment failure. There were 23 cases of recurrence out of 102 patients who did not receive pre-FMT PPI. The primary outcome occurred in 20.6% in the group with PPI use vs. 22.6% in the group without (RR 0.91; CI 0.56 - 1.50). Limitations include the lack of studies directly comparing outcomes with respect to PPI use, and inability to control possible confounders such as chronic PPI use, amount of stool transplanted, and pre-FMT antibiotics.

Conclusion. We did not find a significant difference in efficacy between FMT protocols with regard to PPI use. It is possible that the theoretical benefit from increased survival of transplanted microbiota is offset by negative effects associated with PPIs. We suggest that routine use of PPIs in FMT be reconsidered in the absence of clear benefit. Further investigation is needed to optimize protocols for safety and efficacy.

PPI in upper route administration

Table 1: All included studies (Abstract)

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